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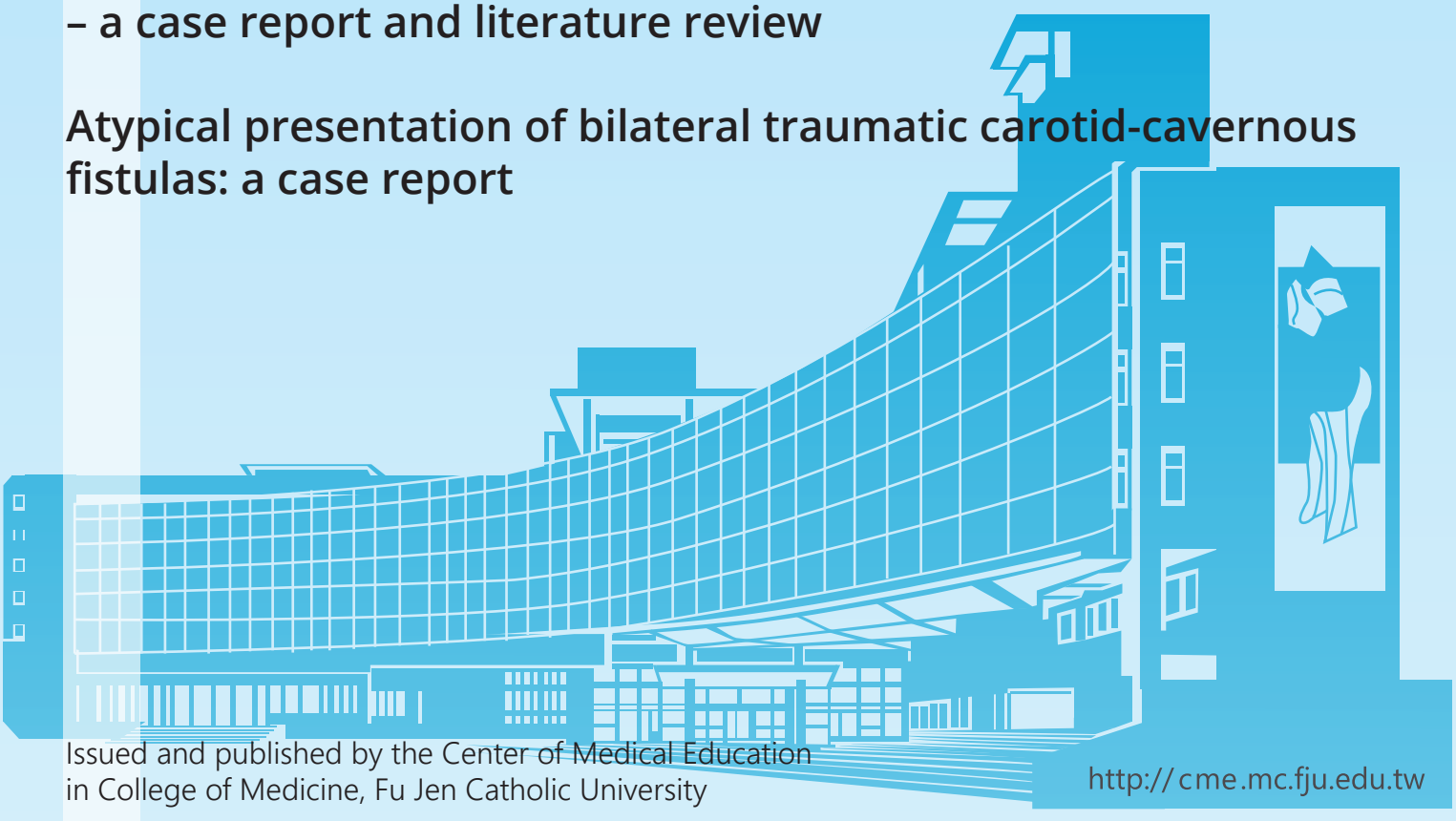

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Experiential analysis of withdrawal of life-sustaining care for terminal patients
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Original Research Article

Experiential analysis of withdrawal of life-sustaining care for terminal patients

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ABSTRACT

Objective: This study aimed to analyze the process and outcomes of withdrawing life-sustaining treatment (LST) in a regional hospital. ***Methods and Methods:*** This retrospective study collected data from patients who met the criteria for palliative shared care and underwent withdrawal of LST at a regional hospital in northern Taiwan between March 2016 and December 2023. The processes and outcomes were analyzed. ***Results:*** A total of 208 patients withdrew LST, including 95 males and 113 females, with a mean age of 83.2 ± 12.1 years. The most common underlying disease was renal failure (68 patients). In 187 cases, family members signed the consent form for withholding cardiopulmonary resuscitation and LST. The most frequently withdrawn intervention was endotracheal intubation (54 patients). The average time from LST withdrawal to death was 4.95 ± 7.8 days. The majority of patients (171, 82.2%) died after LST withdrawal, while 37 patients survived, with 13 (6.3%) discharged for home palliative care. The average time from LST withdrawal to death for those discharged was 6.7 ± 8.6 days. The hospital or this study does not have dedicated oncology or palliative care units, most LST withdrawals occurred in general wards, predominantly for non-cancer diagnoses (83.2%). While general nursing care was provided, the delivery of patient-centered spiritual and end-of-life care services in non-palliative settings with limited resources remains a challenge. The findings can inform in-service education and care for terminally ill patients in non-palliative wards.

Keywords: Terminally ill patients, withdrawal of life-sustaining treatment, palliative care regulations

INTRODUCTION

Along with the progress of medical technology, Taiwanese people hold a more conservative attitude towards the withdrawal of life-sustaining treatment due to the high value of life in the traditional culture[1]. But their thoughts have gradually changed in recent years. The right to a good death for terminally ill patients with cancer and motor neurone diseases has been guaranteed[2] since the Hospice Palliative Care Act was launched in Taiwan in 2000. In 2009, the National Health Insurance Agency also included eight categories of non-terminal cancer diseases in the palliative care benefit[3] to provide more patients a good quality of care in their end-of-life stage through palliative care. The amendment of the Hospice Palliative Care Act in 2013 made the implementation of withdrawing life-sustaining care for the terminally ill patients smoother as it lowered the threshold for removing life-sustaining care from the patients who were unconscious or unable to express their wishes clearly, which required originally the withdrawal of life-sustaining care being subject to unanimous agreement among health care proxies or the three closest family members, including spouse, adult children and grandchildren, along with an approval from the medical ethics committee of the medical institution and was changed into the withdrawal of life-sustaining care being possible with the written consent of the closest family member in this amendment, alleviating the pain of the terminally ill patients whose near-death processes were prolonged by the life-sustaining care[4]. The Patient Right to Autonomy Act announced in 2019 allows the patients to consider and make the choice with respect to LST, artificial nutrition or hydration for a specific clinical situation in the future in advance autonomously[5]. All of these events reflect the efforts of pursuing the right to a good death in Taiwan.

Some ethical issues also have been derived from the decision on whether to continue LST or withdraw these life-support measures, including the wishes of patients, the perceptions of family members and the allocation of medical resources. The healthcare teams should communicate with the patients and their families in detail frankly when deciding to withdraw the life-sustaining care[6]. And communications should be made fully to understand the patients' wishes and help their family members to be mentally prepared. Meanwhile the autonomy and dignity of the terminally ill patients should be ensured so that they have the right to choose a peaceful and good death[7].

Many studies have been made to discuss the issues related to LST withdrawal abroad while there are huge differences in medical, cultural and legal aspects among various countries[8]. In this study, the existing situation of LST withdrawal in a regional hospital was analyzed and the basic data of patients, terminal diagnosis, items regarding LST withdrawal, cognition of the patients and their families, the average time from LST withdrawal to death and spiritual needs of patients and their families were preliminarily discussed. The flowchart of cease or withdrawal of LST for the terminally ill patients in the hospital is as indicated in Figure 1.

MATERIALS AND METHODS

I. The hospital or this study, the patients who met the criteria for palliative shared care and underwent withdrawal of LST in a regional hospital of Taipei City were taken as the objects for data collection.

II. The object of this study was the patients who met the criteria for palliative shared care and underwent withdrawal of LST in the hospice ward or ICU.

III. The tools in this study included the Application Form for Receiving Patient in Palliative Shared Care and Visit Record of Nursing Staff for Palliative Shared Care issued by the National Health Insurance (NHI)[9].

IV. For data collection and analysis, in this study, we collected the data of total 208 patients who met the criteria for palliative shared care and underwent LST withdrawal during the period from March 2016 to December 2023 after being reviewed and approved by the Institutional Review Board of the hospital under research (TCHIRB-10912005-E).

V. After data collection, the statistical software IBM SPSS 25.0 was used for statistics and all continuous variables were expressed with mean ± standard deviation and class variables were expressed with numbers (percentages). The basic data of patients, terminal diagnosis, items regarding withdrawal of life-sustaining care, cognition of the patients and their families, the average time from LST withdrawal to death and spiritual needs of patients and their families were analyzed and preliminarily discussed.

RESULTS

During the study, LSTs of total 208 patients were withdrawn, including 95 males (45.7%) and 113 females (54.3%). The patients who were 81 years and above took the majority (141, 67.79%). The mean age of the patients was 83.2 ± 12.1 years. With regard to the main ter-

minal diagnosis, the most common underlying disease was renal failure (68 patients), followed by terminal cancer (35 patients, 16.8%) and other brain lesions (30 patients, 14.4%). With respect to religious belief, the most of the patients (168) held the general folk belief, accounting for 80.8%, followed by 21 patients with Buddhism belief, accounting for 10.1%. The majority of patients (171, 82.2%) died after LST withdrawal, while 37 patients survived after the withdrawal, most of whom (13, 6.3%) were discharged for home palliative care. The basic data of cases with LST withdrawal is listed in Table 1.

With regard to the signing status of Do Not Resuscitate (DNR), 1 patient (0.5%) didn't sign DNR and 207 (99.5%) patients signed DNR when the cases were collected and 208 patients (100%) singed DNR when the study was closed. Most of the families (205, 98.6%) were aware of the physical conditions and prognoses of the patients when the cases were collected and the majority of the families (206, 99.0%) were aware of these when the study was closed. (Refer to Table 2)

In this study, DNRs were signed by the family members of 186 patients (89.4%), the Prewritten Letter of Intention to Choose Palliative Care and Letter of Intent for LST Selection were signed by 21 patients (10.1%) themselves and 1 patient (0.5%) was an elderly man living alone without family members.

With respect to the items of LST withdrawal, endotracheal tube (Endo) was selected by most of the patients (54, 26.0%), followed by 51 patients (24.5%) whose intravenous (IV) and antibiotics were withdrawn and 44 patients (21.2%) whose hemodialysis (HD) was withdrawn. As for the location of LST withdrawal, it was ward for most of the patients (111, 53.4%) and Intensive Care Unit (ICU) for 97 patients (46.6%) (Table 3).

With regard to the days from LST withdrawal to death, most of the patients (18, 10.%) with Endo withdrawal died instantly after LST withdrawal, most of the patients (20, 11.7%) with IV and antibiotics withdrawal died in 1 - 2 days after LST withdrawal, most of the patients (13, 7.6%) with withdrawal of HD, IV and antibiotics died in 3 - 7 days after LST withdrawal and most of the patients (17, 9.9%) with HD withdrawal died in more than 7 days after LST withdrawal. (Table 4)

As for psychological, social and spiritual needs of patients and their families when facing LST withdrawal, it was unable to evaluate the aspects for most of the patients; but the psychological and social problems including disease cognition and adaptation difficulty were found among most of the family members (158, 76%) and the spiritual need for conquering the worry and fear of facing death was found among most of the family members (183, 88.0%) (Table 5).

Among 37 patients who survived after LST withdrawal, most (26, 70.3%) of them died finally no matter whether they were better with physical conditions improved, went home for general care or palliative care, discharged near death or stably. (Table 6).

DISCUSSION

According to Article 7 of the Hospice Palliative Care Act that was revised in 2013, the palliative care team may issue a medical order for a terminally ill patient who has no closest family members and has been informed by the palliative care team in view of his/her best benefits. Neither the consent form nor the medical order shall express any meaning contrary to the intention expressed by the terminally ill patient before he/she becomes unconscious or unable to express his or her will clearly[8, 11]. A case with medical order issued is described as follows: A 76-year-old male patient living alone was admitted to the hospital for chronic kidney disease. The patient had expressed his intention to the medical staff not to provide any first aid treatment to him but not yet signed the letter of intent when he was conscious. Later he was unconscious and transferred to ICU for hemodialysis due to acute renal failure and he was suffered from septic shock and multiple organ failure during the treatment. After related social workers were notified to search his family members and confirmed he had no family members, the palliative shared care team was consulted and two specialists of related diseases recognized the patient was a terminally ill patient. Therefore the medical staff issued a medical order in view of his best benefits for the terminally ill patient and stopped his hemodialysis. The patient passed away 1 week after hemodialysis was stopped and related social workers helped with his funeral arrangement.

In 2013, a study in Taiwan mentioned that about 20% of patients signed the "Do Not Resuscitate Letter of Intent" by themselves; but for the rest 80% of patients, the "Do Not Resuscitate" was signed by their family members, which was associated with our custom to avoid talking about death[8]. And it was commonly seen that for the patients who hadn't signed the DNR Letter of Intent in advance, the family members had to extend the treatments period as they couldn't evaluate whether the treatments might benefit the

patients or increase more pains to them calmly during emergencies and the extension indirectly caused more worries and fears of facing death of the family members[12].

Along with medical advances and the impact of aging society, the proportion of the population suffering from chronic diseases and cancer is increasing and the demand for palliative care is also increasing. Owing to the promotion of the Advance Care Planning specified in the Patient Right to Autonomy Act announced on January 6, 2016 in Taiwan, the people's awareness of death has been gradually increased. And the quality of end-of-life care for the elderly in the aging society will be improved further since the "terminal frail elderly" was included in the indication of palliative care benefit in June, 2022, which is in line with the development trend of international palliative care.

CONCLUSIONS

Taiwan has officially become an aging society since 2018 and it will become a super-aging society in 2025 Taiwamese elderly population will exceed 20%[13]. The average life span of people in Taiwan has been prolonged and the elderly care issue has become more and more important along with the progress of medical science and technology. Not aiming at disease cure, the palliative care is the medical treatment that focuses on symptom relief and life quality maintenance and doesn't accept the ineffective medical interventions including electroshock, chest compression, intubation etc. during terminally ill stage. However, for many non-cancer patients, due to the two characteristics of "prolonged terminal period of disease" and "difficulty in expecting the life span", the complexity of intervention of palliative care is increased. And the intervention timing of palliative care is very important. The palliative care after diagnosis allows the families or patients to know that the medical team will intervene in terms of symptom management and comfort care and also provide the care choices when acute or severe symptoms occur.

The following six practices of the medical teams of the hospital are summarized as reference for other hospitals: 1. Adequate Communication: The medical teams took the initiative to communicate with the families, explained the purpose and process of palliative care and responded to the concerns of the family so that the families understood that palliative care was adopted to protect dignity of the patients and alleviate their pains, rather than passively abandon treatments. 2. Intervention of Social Workers and Psychologists: They assisted the family members in cognitive adjustment and release of negative emotions with professional emotional support, the family members could better accept the decision on palliative care. 3. Religious Support: Religious figures enlightened the family members. For some family members, religious belief was an important pillar that helped them to reduce the spiritual pressure. 4. Support Group: The family members were encouraged to participate in a support group to share, support and understand with other family members, reducing their feelings of isolation and helpfulness. 5. Provision of Palliative Care Manuals: In addition to oral communications, written materials regarding concept, process and attentions of palliative care were provided to the family members to help them to acquire a better understanding without doubts. 6. Participation in joint decision making: The family members were allowed to participate in the decision making process to increase their sense of autonomy and peace of mind.

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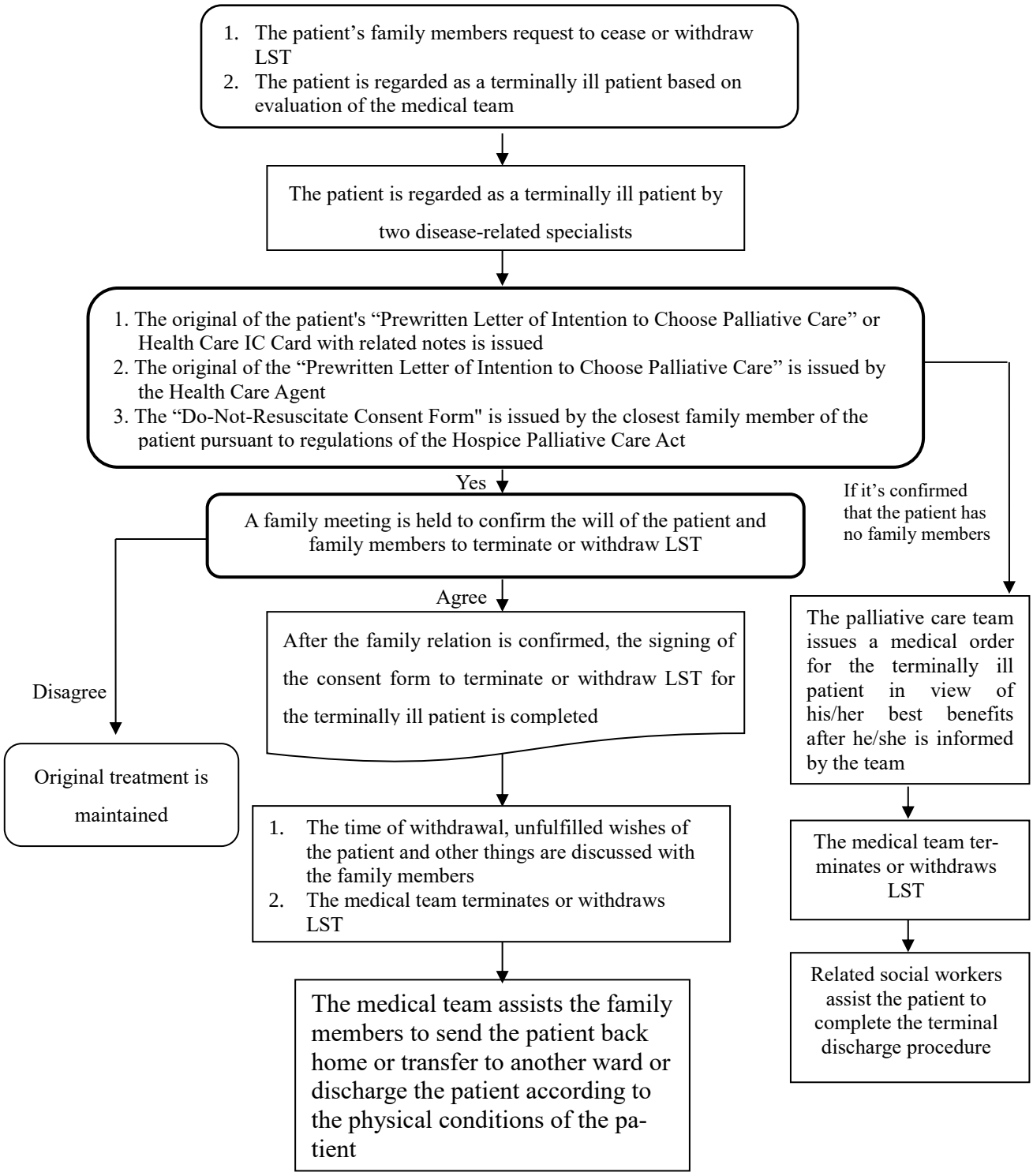

Figure 1. Flowchart of cease or withdrawal of LST for the terminally ill patients

TABLES

Table1. Basic Data of Cases with LST Withdrawal (N=208)

Item		Patient No. (%)
Gender	Female	113 (54.3)
	Male	95 (45.7)
Age	41 - 50	6 (2.9)
	51 - 60	6 (2.9)
	61 - 70	18 (8.6)
	71 - 80	37 (17.7)
	81 - 90	77 (36.8)
	Over 90	64 (30.6)
Education Degree	Illiteracy	9 (4.3)
	Elementary School	101 (48.6)
	Middle School	44 (21.2)
	High /Vocational School	35 (16.8)
	College	4 (1.9)
	University	14 (6.7)
	University or above	1 (0.5)
Religion Belief	Buddhism	21 (10.1)
	Taoism	8 (3.8)
	Christianity	5 (2.4)
	General Folk Belief	168 (80.8)
	Others	6 (2.9)
Marriage Status	Married	81 (38.9)
	Unmarried	10 (4.8)
	Widowed	99 (47.6)
	Divorced	18 (8.4)
Main Disease Diagnosed	Heart Failure	12 (5.8)
	Terminally frail older	14 (6.7)
	Gerontic/ Presenile Organic Psychosis	8 (3.8)
	Other brain deteriorations	30 (14.4)
	Other lung diseases	27 (13.0)
	Renal Failure	68 (32.7)
	Chronic Liver Disease and Cirrhosis	2 (1.0)
	Chronic Airway Obstruction	12 (5.8)
	Terminal Cancer	35 (16.8)
Case Close Reason	Death	171 (82.2)
	Improvement of Physical Condition	12 (5.8)
	Home Care	2 (1.0)
	Home Palliative Care	13 (6.3)
	Near-death Discharge	3 (1.4)
	Discharge with Stable Physical Conditions	7 (3.4)

Table2. Cognitions of Patients with LST Withdrawal and Their Families (N=208)

Item		Person No. at Case Collection (%)	Person No. at Study Closure (%)
Signing Status of DNR	Unsigned	1 (0.5)	0 (0.0)
	Signed	207 (99.5)	208 (100.0)
Patients' Cognitions on Diagnoses	Aware	20 (9.6)	21 (10.1)
	Unaware	1 (0.5)	1 (0.5)
	Suspicious or Partially Aware	4 (1.9)	0 (0.0)
	Unable to evaluate	183 (88.0)	186 (89.4)
Patients' Cognitions on Diseases and Prognoses	Aware	20 (9.6)	21 (10.1)
	Unaware	1 (0.5)	1 (0.5)
	Suspicious or Partially Aware	4 (1.9)	0 (0.0)
	Unable to evaluate	183 (88.0)	186 (89.4)
Families' Cognitions on Diseases and Prognoses	Aware	205 (98.6)	206 (99.0)
	Unaware	1 (0.5)	0 (0.0)
	Suspicious or Partially Aware	0 (0.0)	0 (0.0)
	Unable to evaluate	2 (1.0)	2 (1.0)

Table3. Summary of Items Selected for LST Withdrawal (N=208)

Item		Patient No. (%)
DNR	Consent Form	186 (89.4)
	Letter of Intent	21 (10.1)
	DNR issued based on medical order	1 (0.5)
Item of LST Withdrawal	ECMO	1 (0.5)
	Endo	54(26.0)
	HD	44(21.2)
	HFNC	1(0.5)
	IV & Antibiotics	51 (24.5)
	NG	5 (2.4)
	VPAP	25(12.0)
	Vasopressors	21 (10.1)
	Tracheostoma/ Respirator	6 (2.9)
Location of LST Withdrawal	ICU	97 (46.6)
	Ward	111 (53.4)

Table4. Number of Days from LST Withdrawal to Death (N=171)

Item	0 Day	1 - 2 days	3 - 7 days	> 7 Days
Number of Days from LST Withdra to Death (Range)				4.95 ± 7.8 (0 - 63)
ECMO	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
	18 (10.5)	10 (5.8)	9 (5.3)	9 (5.3)
HD	4 (2.3)	6 (3.5)	13 (7.6)	17 (9.9)
HFNC	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
IV & Antibiotics	4 (2.3)	20 (11.7)	13 (7.6)	6 (3.5)
NG	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
VPAP	5 (2.9)	2 (1.2)	8 (4.7)	5 (2.9)
Vasopressors	3 (1.8)	6 (3.5)	7 (4.1)	1 (0.6)
Tracheal Cannula/ Respirator	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)

Table 5. Psychological, Social and Spiritual Needs of Patients and Their Families with LST Withdrawal(N=208)

	Item	Patient No. (%)	Family Member No. (%)
Psychological & Social Problem	Emotional Disturbance	6 (2.9)	48 (23.1)
	Disease Cognition & Adaptation Difficulty	19 (9.1)	158 (76.0)
	Unfulfilled Wishes & Inadequate Preparation for Funeral	0 (0.0)	1 (0.5)
	Others	0 (0.0)	1 (0.5)
	Unable to evaluate	183 (88.0)	0 (0.0)
Spiritual & Religious Needs	Existential Loneliness & Isolation	6 (2.9)	15 (7.2)
	Worry & Fear of Facing Death	16 (7.7)	183 (88.0)
	Confusion about Meaning & Value of Life	1 (0.5)	6 (2.9)
	Being hard to let go	0 (0.0)	3 (1.4)
	Unable to evaluate	185 (88.9)	1 (0.5)

Table6. Survived Patients with LST Withdrawal (N=37)

Item	Relocated Patient No. (%)	Dead Patient No. (%)	Days No. from LST Withdrawal to Death (SD)
Improvement of Physical Condition	4 (10.8)	8 (21.6)	19.6 ± 23.5
Home Care	0 (0.0)	2 (5.4)	18.0 ± 12.7
Home Palliative Care	2 (5.4)	11 (29.7)	6.7 ± 8.6
Near-death Discharge	0 (0.0)	3 (8.1)	1.0 ± 0.9
Stable Discharge	5 (13.5)	2 (5.4)	5.0 ± 5.1

Experiential analysis of withdrawal of life-sustaining care for terminal patients

末期病人撤除維生醫療之經驗分析

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中文摘要

研究目的：本研究旨在分析某區域醫院撤除維生醫療之分析。**材料與方法：**本文為回溯性研究，收集北部某區域醫院 2016 年 3 月至 2023 年 12 月符合末期會診安寧共同照護（簡稱安寧共照），撤除維生醫療之病人為對象，分析其過程及結果。**結果：**共 208 位病人撤除維生醫療，男性 95 位，女性 113 位，平均年齡為 83.2±12.1 歲，病人疾病以腎衰竭最多達 68 位，本研究中由家屬簽署不施行心肺復甦術暨維生醫療同意書達 187 位，撤除項目以氣管內管最多有 54 位，撤除維生醫療後病人平均死亡時間為 4.95 ± 7.8 日，撤除後結案原因以死亡佔最多數 171 位(82.2%)；撤除後未死亡人數共計 37 位，其中以轉居家安寧 13 位(6.3%)最多最終收案後平均死亡時間為 6.7 ± 8.6 日，本院區未設置腫瘤及安寧病房，撤除維生醫療診斷以非癌居多佔 83.2%故撤除地點也已病房佔多數，非安寧病房之醫護人員除一般性照顧外，如何以病人為中心的提供靈性方面及臨終照顧等即時性服務，安寧療護如何在非特定場所及有限資源下，讓病人及家屬也能獲得身、心、靈的照護，結果可做為在職教育及非安寧病房病人照護之參考。

關鍵字：末期病人、撤除維生醫療、安寧緩和醫療條例

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Original Research Article

The Levels of Mastery Motivation in Preschoolers with Developmental Delay and Associations with Temperament

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ABSTRACT

Background and purpose: Mastery motivation makes important contributions to children's competence and school readiness. Children with developmental delay need to learn challenging tasks, so understanding the characteristics of their mastery motivation and the factors associated with it might increase their engagement. The aims of this study were to examine the characteristics of mastery motivation in preschoolers with developmental delay, and, by intergroup and intragroup comparison, examine the associations between temperament and mastery motivation for preschoolers with developmental delay. ***Methods:*** Eighty-five child-caregiver dyads participated, with forty dyads in the developmental delay group and forty-five in the typical development group (age from 1.5 to 4.58 years). The Dimensions of Mastery Questionnaire was rated by caregivers to assess all children's indicators of mastery motivation. cognitive/object, gross motor, social-interaction persistence with others, and expressive indicators of mastery of pleasure and negative emotions in reaction to challenges. The Early Children Behavior Questionnaire was completed by the caregivers to provide data on the children's temperament, and cognitive ability was collected in the developmental delay group. ***Results:*** Children with developmental delay had lower levels of mastery motivation on most of the instrumental domains and indicators of the expressive aspect than conference group. They showed their strength on domains of gross motor, social interaction with adults, and mastery pleasure and surgency/extraversion and effortful control of temperament had positive associations with their mastery motivation. ***Conclusion:*** Preschoolers with developmental delay showed vulnerable in mastery motivation and their temperament have important associations with their mastery motivation. To detect children's mastery motivation and temperament could be used to develop strategies to promote their engagement.

Keywords: developmental delay, mastery motivation, preschooler, temperament

INTRODUCTION

Mastery motivation is defined as a multifaceted psychological force that directs and maintains goal-directed behaviors[1]. Mastery motivation can be differentiated in specific domains, such as the cognitive/object persistence, gross motor persistence, and social interaction with others domains. The instrumental aspects (e.g. task-directed persistence), the expressive aspects (e.g. mastery pleasure, negative emotions) triggered when facing success and challenges in mastery situations are important indicators of mastery motivation[2].

Mastery motivation has a critical influence on competence[3] and school readiness[4] and has been emphasized for children who experience developmental delay or are at risk of disability[5]. Thorough examination of children's multiple domains and expressive indicators and investigation of the factors associated with mastery motivation in children with developmental delay should inform future interventions to improve their motivation.

Studies have shown that the development of mastery motivation can be impeded in children with disabilities or developmental delay[6,7,8]. A cerebral palsy group had lower levels of cognitive/object persistence, gross motor persistence, social persistence with adults, and social persistence with children than typically developing school-aged children [8,9]. However, a group difference in mastery motivation in adolescents with cerebral palsy only manifested in the cognitive/object and gross motor domains, and not in social persistence with adults and children[10]. A study considered the discrete negative emotion while facing challenges and found that school-aged children with cerebral palsy had lower levels of mastery pleasure, total negative reactions to challenge, and negative reaction–sadness/shame than did children with typical development, but no difference in negative reaction–anger/frustration[8].

Overall, previous evidence has indicated that children with cerebral palsy in their early childhood exhibit significantly higher levels in the cognitive/object, gross motor, and social domains and in mastery pleasure than do typically developing children[8,9]. However, such differences are not fully evident in adolescents with cerebral palsy[10]. This inconsistency may imply varying levels of motivation across developmental stages. Preschoolers aged 2–4 years with motor delay had lower levels in the cognitive/object, gross motor, and social motivation domains as compared with mental-age matched children with typical development, but they had no significant differences in expressive indicators of mastery pleasure or total negative reactions to failure[11]. Toddlers with language delay showed significantly lower social persistence with adults and with children, and lower gross motor persistence, than did children with typical development, but no differences in cognitive/object persistence, mastery pleasure, or total negative reactions to challenges[6].

Past studies have examined the levels of mastery motivation in children with developmental delay or disability from the intragroup difference by ranking mean motivation scores from highest to lowest. For children with cerebral palsy, the highest-scored instrumental domains of motivation were social persistence with adults and with children, but they exhibited lower gross motor and cognitive/object persistence[8,9,10]. For school-aged children or adolescents with cerebral palsy, the highest indicator of the expressive aspect was that of mastery pleasure, and their total negative reactions to failure were lower[9,10]. From the discrete emotion perspective, the highest indicator was that of total negative reactions to failure, followed by negative reaction–anger/frustration and negative reaction–sadness/shame[8]. Preschoolers with motor delay manifested higher levels of cognitive/object persistence, gross motor persistence, and social persistence with children, followed by social motivation with adults[11].

Toddlers with language delay had higher levels of gross motor persistence and cognitive/object persistence, followed by social persistence with adults and then social persistence with children[6]. Toddlers with developmental delay exhibited higher levels of mastery pleasure than total negative reactions to challenges, according to a within-group comparison; however, they had no significant differences compared to typically developing groups on mastery pleasure and total negative emotions while facing challenges[6,11].

In summary, differences in mastery motivation are observed in the instrumental domains of preschool-aged children with developmental delay. However, inter-group and intra-group comparisons have produced inconsistent findings. Preschool-aged children with developmental delays receive numerous intervention services. Cognitive delay, language delay, and autism spectrum disorder are common in neurodevelopmental disorders; however, current research on mastery motivation in

these three types of developmental delays among preschool-aged children remains limited. Therefore, examining the characteristics and contributors to children's mastery motivation can help parents and clinicians enhance the children's motivation.

Children's intra-personal factors make important contributions to their active engagement. For example, children's age and cognitive ability positively correlate with their mastery motivation[12,13]. Motivations have the basis of personality or temperament[14]. Temperament encompasses the relative strength or weakness of children's emotional responses, related behaviors, and self-regulation capacities, which are crucial for children's learning. Mastery motivation is closely linked to the fundamental emotional-motivational systems of children, and consequently to related with the variability of temperament[15].

Temperament is the individual differences manifested in emotion, activity in reactivity, and self-regulation, which is influenced by environment and experience. Surgency/extraversion, negative affectivity, and effortful control are three broad-band temperament factors in early childhood[16]. Surgency/extraversion refers to a positive affect and the tendency to approach new stimuli, and it might be associated with children's instrumental aspect of mastery motivation[17] and mastery pleasure. Negative affectivity refers to fear, sadness, and anger, which might be directly linked to children's persistence in pursuing goals and to negative emotion when facing failure[17]. Effortful control is a factor related to self-regulation; it provides the flexibility to regulate attention, inhibit the immediate influence of a dominant response, and activate behaviors when facing challenges, so it might have a positive association with children's mastery motivation; Effortful control might have a direct predicting effect on mastery motivation, especially for instrumental aspects of mastery motivation[17]. However, evidence suggests that effortful control observed in the laboratory has no predicting effect on preschoolers' motivation types, cognitive/object persistence, and social motivation[18,19].

Even though the contributions of children's temperament to mastery motivation are suggested, the findings are still inconsistent[20,21,22]. The first aim of this study was to examine the levels of mastery motivation in multiple domains and indicators of the expressive aspect in children with developmental delay by intergroup comparisons and within-group comparisons. The second aim was to investigate the associations of surgency/extraversion, negative affectivity, and effortful control with children's mastery motivation in the developmental delay group. We tested the following hypotheses: (1) The levels of most instrumental domains of mastery motivation and mastery pleasure will be significantly lower in children with developmental delay than in children with typical development. (2) The factors of temperament will make significant contributions to mastery motivation in children. Surgency/extraversion and effortful control might have more important positive associations with instrumental aspects.

MATERIALS AND METHODS

Participants

A total of eighty-five child-caregiver dyads, consisting of forty dyads in the developmental delay group (parents' education levels M = 14.6, SD = 2.38) and forty-five dyads in the typical development group (parents' education levels M = 16, SD = 1.31). The developmental delay group (33 males, 7 females) was aged 1.5 to 4.58 years (M = 2.92, SD = .76) and included sixteen children with speech delay, fourteen with autism spectrum disorder, and ten with cognitive delay, and none had physical handicaps, congenital defects, cerebral palsy, visual/hearing or genetic problems. The typically developing children (27 males, 18 females) ranged in age from 1.75 to 4.42 years (M = 2.95, SD = .67) and had no known perinatal or postnatal complications or developmental delay. There was no significant age difference between the two groups (t = -.30).

Measures

Mastery motivation

The Dimensions of Mastery Questionnaire[23] (DMQ 18) preschool version comprises 39 items across six subscales covering the instrumental and expressive aspects of mastery motivation. Parents rated how typical of their child a behavior was on a 5-point Likert-type scale from 1 (not typical at all) to 5 (very typical). The four instrumental domains are cognitive/object persistence, gross motor persistence, social persistence with adults, and social persistence with children. The two expressive subscales are mastery pleasure and total negative reactions to challenges. The Cronbach's alphas of subscales for children with developmental delay and their peers with typical development were .67–.87. Total negative reac-

tions to challenges were divided into anger/frustration and sadness/shame. The Cronbach's alpha of sadness/shame was .59. The item-total scale correlations were examined, and one unsatisfactory item with an item-total correlation < .20 was removed, resulting in a sufficient alpha value of .76.

Cognitive ability

Cognitive ability in the developmental delay group was collected with the cognitive subscale of the Bayley Scales of Infant and Toddler Development[24](Bayley-III). The Bayley-III was administered in individualized testing in a playroom at the university by trained graduate students in clinical psychology or at a hospital by clinical psychologists, and the composite score was used to indicate cognitive ability (range = 50–120, M = 83.92, SD = 17.62).

Temperament

The Early Children Behavior Questionnaire (ECBQ)-Short form contains 107 items clustered into 18 scales[25], which are rated on a 7-point Likert-type scale (1 = never to 7 = always) by the parents of the children. The factors of surgency/extraversion were activity level, impulsivity, high-intensity pleasure, positive anticipation, and sociability. The factors of negative affectivity were discomfort, fear, sadness, shyness, anger/frustration, perceptual sensitivity, and motor activation. Effortful control was determined by calculating the average of inhibitory control, attentional shifting, attentional focusing, low intensity pleasure, cuddliness, and soothability. Cronbach's alphas of surgency/extraversion and effortful control were .67 and .74. Negative affectivity was initially .58, but after the removal of three unsatisfactory items with item-total correlations < 1.5, the alpha was a sufficient .66.

Procedures

Approval for the study was obtained from the Research Ethics Committee, and an informed consent form was signed by each parent. Most of parents rated children's mastery motivation and temperament while their children were administered the Bayley-III and returned the form in person after the session of developmental testing or by mail after completing it.

RESULTS

1. The levels of mastery motivation in children with developmental delay

For the three types of developmental delays included in this study, an analysis of motivational differences between groups was conducted. We found that there were no significant differences in all aspects of mastery motivation (Fs = 0.01– 1.93). ANOVA indicated that cognitive/object persistence, gross motor persistence, social persistence with adults, and social persistence with children were significantly lower in children with developmental delay than in children with typical development (Fs = 12.66–34.08, ps < .01; η^2 = .13–.29). Children with developmental delay had significantly lower scores on mastery pleasure, total negative reactions to challenges, and negative reaction–anger/frustration (Fs = 8.09–15.77, ps < .01; η^2 = .09–.16), but not negative reaction–sadness/shame, as compared with the typical development group (Table 1). Repeated ANOVA revealed significant differences in children with developmental delay (F(1,39) = 810.17, p < .001; η^2 = .95). Gross motor persistence was significantly higher than cognitive/object persistence and social persistence with children; social persistence with adults was higher than social persistence with children; mastery pleasure was higher than negative reactions to challenges (ps < .01).

2. Associations between children's temperament and mastery motivation in the developmental delay group

Surgency/extraversion positively correlated with children's gross motor persistence, social persistence with children, and mastery pleasure (rs = .38－.48, ps < .05). Negative affectivity had significant positive correlation with anger/frustration while facing challenges, and effortful control positively correlated with social persistence with children (rs = .31, .39, ps < .05) (Table 2).

Two-step hierarchical regressions were conducted to examine the predictive effects of three temperament factors on mastery motivation in children with developmental delay after controlling for the children's age and cognitive ability (Table 3, Table 4). The overall models of temperament explained 22%, 26%, and 29% (ps < .05) of the variance in gross motor persistence, social persistence with adults, and that with children, respectively. Surgency/extraversion had significant positive predictive effects on gross motor persistence, social persistence with adults, and that with children (βs = .33–.50; ps < .05). Effortful control had unique predictive effects on gross motor persistence and social persistence with children (βs = .39, .60; ps < .05). Negative affectivity had no significant predictive effects on the

instrumental domains of mastery motivation (βs = .18–.40; *ps* > .055). Temperament made no significant contribution to indicators of the expressive aspect, and surgency/extraversion had significant positive predictive effects on mastery pleasure (β = .40; $p < .05$).

DISCUSSION

We found group differences of mastery motivation between preschoolers with developmental delay and those with typical development on instrumental indicators and the expressive aspect. Preschoolers with developmental delay showed similar characteristics in their higher levels of gross motor persistence, social persistence with adults, and mastery pleasure, but lower levels of cognitive/object persistence, social persistence with children, and negative reactions to challenge. Surgency/extraversion and effortful control positively associated with gross motor persistence, social motivation, and mastery pleasure.

Children with developmental delay had lower levels than typically developing children in the domains of cognitive/object, gross motor, and social interaction with adults and with peers. These results are consistent with studies of school-aged children with cerebral palsy and toddlers with gross motor delay[8,9,11] and support the possibility that children with developmental delay are vulnerable in mastery motivation.

Preschoolers with developmental delay experienced lower levels of mastery pleasure than the typical group, which was consistent with previous studies of school-aged children with cerebral palsy[8,9]. However, this finding was not consistent with studies of toddlers with gross motor and language delay[6,11]. It may be that the preschoolers in this study were more conscious of success than the toddlers and thus expressed more mastery pleasure.

Children with developmental delay manifested intragroup motivation characteristics similar to those of typically developing children, with higher levels of gross motor persistence and social persistence with adults, followed by cognitive/object persistence and social persistence with children. These results were consistent with previous findings on toddlers with language delay[6]. The order of indicators of the expressive aspect from highest to lowest was as follows: mastery pleasure and negative reaction–sadness/shame, followed by a lower level of anger/frustration.

Turning to the discrete negative emotion while facing challenges, our study showed that preschoolers with developmental delay manifested higher levels of sadness/shame and lower levels of anger/frustration. This result was different from previous results on school-aged children with cerebral palsy, who were found to have lower levels of negative reaction–sadness/shame than children with typical development[8]. Children who express anger were more likely to persist in pursuing goals[26]; Sadness and shame activates the avoid motivational system[27 28].

In this study, negative reactions of anger/frustration correlated with most of the instrumental domains; however, sadness/shame significantly correlated with only cognitive/object persistence or social persistence with adults. It might imply the characteristics of higher sadness/shame to challenge which associated with children's lower level on instrumental aspect of mastery motivation.

Temperament factor of Surgency/extraversion positively associated with gross motor persistence, social persistence with adults, social persistence with children, and mastery pleasure, and these findings supported that the positive affect and the tendency to approach new stimuli were directly linked to children's persistence in pursuing goals and pleasure when successful[17 20].

Effortful control, which refers to the regulation of behavior and attention, had a direct predicting effect on gross motor and social persistence with peers. Our findings supported the idea that children's self-regulation has a positive association with mastery motivation[29] and the argument that effortful control has a direct predicting effect on mastery motivation, and especially on instrumental persistence of mastery motivation[15].

No significant predicting effect of negative affectivity on mastery motivation was found. Negative affectivity is a broad-band temperament factor composed of fear, anger, frustration, etc., and any possible direct associations with discrete emotion need to be examined. Negative affectivity and high effortful control have an interactive effect on children's level of negative emotions before and during achievement tasks[30], so the interaction effects of temperament factors on children's mastery motivation should be examined.

This study includes common categories of early intervention services and neurodevelopmental disorders in children with cognitive delay, language delay, and autism spectrum disorder. The research can expand the understanding of mastery motivation in children

with developmental delays and even in preschool-aged children with neurodevelopmental disorders, providing references for early intervention services to promote children's motivation. However, children with different developmental delays may have different motivational characteristics. Thus, whether the findings of this study on mastery motivation characteristics and the relationship between temperament and mastery motivation can be generalized to various types of developmental disorders requires further investigation. Considering the limitation of small sample size, future research can focus on larger samples to explore the mastery motivation characteristics of children with specific developmental delay and examine the relationship between temperament and mastery motivation in children with various developmental problems.

In this study, only half of the children in the typical developing group had cognitive ability scores, making it impossible to examine the relationship between temperament factors and mastery motivation after controlling for age and cognitive ability, as was done in the developmental delay group. Future studies can test whether the relationship between temperament and motivation found in this research is similar to that in typically developing children to better understand the connection between children's temperament and mastery motivation, and examine whether the relationship between temperament and mastery motivation in children with developmental delays has its unique characteristics

Clinical implications

Caregivers' perceptions of children's mastery motivation is important because these perceptions may influence parental practices in daily and intervention contexts. Children with developmental delay face intensive training and challenging tasks during early interventions. It is necessary to detect their mastery motivation and enhance their motivation to master skills according to their characteristics of mastery motivation. The relation of children's temperament to mastery motivation could be used to develop appropriate strategies to promote children's motivation. Increasing children's positive emotion and self-regulation on attention and behavior will benefit their mastery motivation.

CONCLUSIONS

Preschoolers with developmental delay showed vulnerable in mastery motivation, however, they also had their strengths in gross motor persistence, social persistence with adults, and mastery pleasure, and a weakness in social persistence with peers. Children's temperament, surgency/extraversion and effortful control were found to have important associations with their mastery motivation.

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TABLES

Table1. Comparisons of Mastery Motivation between Preschoolers with Developmental Delay and Typical Development

	DD(n = 40)	TD (n = 45)			
Mastery motivation	*M* (*SD*)	*M* (*SD*)	*F*	η^2	Group difference
Cognitive/object persistence	2.70 (0.85)	3.31 (0.74)	12.66**	.13	DD < TD
Gross motor persistence	3.01 (1.02)	3.74 (0.67)	15.69***	.16	DD < TD
Social persistence with adults	2.92 (0.85)	3.74 (0.70)	23.99***	.22	DD < TD
Social persistence with children	2.56 (0.93)	3.54 (0.60)	34.08***	.29	DD < TD
Mastery pleasure	3.92 (0.96)	4.56 (0.48)	15.77***	.16	DD < TD
Total negative reactions to challenges	2.84 (0.88)	3.56 (0.76)	8.09**	.09	DD < TD
Negative reaction-anger/frustration	2.84 (0.89)	3.41 (0.91)	8.45**	.09	DD < TD
Negative reaction-sadness/shame	3.17 (1.04)	3.07 (0.71)	0.19	.00	-

** $p < .01$. DD = developmental delay group, TD = typical development group.

Table2. Correlations among Children's Variables and Mastery Motivation for Preschoolers with Developmental Delay

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13
1.Child's age	-												
2.Cognitive ability	-.35*	-											
3.Surgency/extraversion	-.09	.28	-										
4.Negative affectivity	-.29	.23	-.19										
5.Effortful control	.00	-.18	.09	**-.65*** **	-								
6.Cognitive-object persistence	-.03	.31	.25	-.00	.11	.-							
7.Gross motor persistence	-.20	**.38***	**.46****	.01	.20	**.54*****	-						
8. Social persistence with adults	-.09	.17	**.48****	-.01	.16	**.47****	**.72*****	-					
9. Social persistence with children	-.27	.05	.30	-.03	**.39***	.23	**.50****	**.61*****	-				
10. Mastery pleasure	-.10	.02	**.38***	.12	.05	**.52****	**.69*****	**.69*****	**.44****	-			
11.Total negative reactions to challenge	-.06	.10	.24	.24	-.16	**.44****	**.52****	**.57*****	.18	**.61*****	-		
12.Negative reaction–anger/frustration	-.01	.04	.21	.31	-.23	**.32***	**.45****	**.57*****	.20	**.64*****	**.92*****	-	
13.Negative reaction–sadness/shame	.11	-.16	-.08	.12	.00	**.40***	.17	.20	-.01	**.36***	**.53*****	**.38***	-
Mean	2.92	83.92	4.07	3.06	3.82	2.82	2.73	3.04	2.76	3.89	2.86	2.84	3.17
SD	0.76	17.62	0.96	0.79	0.88	0.74	0.86	1.01	0.82	0.98	0.90	0.89	1.04

* p < .05. ** p < .01. *** p < .001.

Table3. Predicting Effect of Temperament on Instrumental Domains in Preschoolers with Developmental Delay

	Cognitive/object persistence			Gross motor persistence			Social persistence with adults			Social persistence with children		
Predictors	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$
Step 1			.10			.14			.03			.08
Child's age	.08	.08		-.12	-.09		-.04	-.04		-.34	-.29	
Cognitive ability	.02	.34*		.02	.33*		.01	.16		.00	-.05	
Step2			.07			.22*		.26*				.29**
Child's age	.15	.14		.00	.00		.07	.06		-.18	-.15	
Cognitive ability	.02	.32		.02	.26		.00	.04		.00	-.07	
Surgency/ extraversion	.28	.19		.72	.41*		.74	.50**		.54	.33*	
Negative affectivity	.23	.18		.43	.28		.41	.32		.58	.40	
Effortful control	.42	.26		.73	.39*		.52	.33		1.06	.60**	
Total R^2			.17			.36			.29			.37

* p < .05. ** p < .01.

Table4. Predicting Effects of Temperament on Expressive Aspect in Preschoolers with Developmental Delay

	Mastery Pleasure			Total negative reactions to challenge			Negative reaction–anger/frustration			Negative reaction–sadness/shame		
Predictors	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$	*B*	β	$\triangle R^2$
Step 1			.			.01			.00			.04
		01										
Child's age	-.16	-.13		-.03	-.03		.00	.00		.05	.04	
Cognitive ability	-.00	-.07		.00	.09		.00	.04		-.01	-.20	
Step 2			.17			.14			.20			.05
Child's age	-.02	.02		.07	.06		.12	.11		.16	.12	
Cognitive ability	-.01	-.16		.00	-.05		-.01	-.12		-.01	-.20	
Surgency/extraversion	.68	.40*		.50	.32		.52	.33		.04	.02	
Negative affectivity	.54	.36		.47	.35		.59	.43		.48	.30	
Effortful control	.39	.22		.05	.03		-.01	.00		.31	.16	
Total R^2			.19			.15			.20			.09

* p < .05.

The Levels of Mastery Motivation in Preschoolers with Developmental Delay and Associations with Temperament

學齡前發展遲緩兒童精熟動機水準及與氣質之關聯

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中文摘要

背景與目的：精熟技能的動機與兒童能力及就學準備有重要關聯，發展遲緩兒童需要經常學習具挑戰性任務，了解發展遲緩兒童精熟動機特徵及影響動機的因素有助於促進學習。本研究目的為透過組間與組內差異比較，檢驗學齡前發展遲緩兒童的精熟動機特徵，以及檢驗氣質與精熟動機的關聯。**方法：**以 85 對親子為研究對象，其中 40 對為發展遲緩組，45 對為典型發展組(兒童年齡為 1.5 至 4.58 歲)。照顧者透過動機問卷評量所有兒童在認知物件、粗動作、社會互動領域及精熟愉悅、遇挑戰負向反應等動機指標；以個別化程序測量發展遲緩兒童的認知能力，並由照顧者以兒童早期行為問卷評量兒童的氣質。**結果：**發展遲緩兒童在大多數精熟動機指標皆顯著低於典型發展兒童；發展遲緩兒童展現較高的粗動作、與成人互動動機及精熟愉悅的組內動機優勢，兒童在外向騰動性及主動控制動的氣質，顯著正向預測這些動機優勢。**結論：**學齡前發展遲緩兒童有其精熟動機的脆弱性及內部優勢動機，而氣質與其精熟動機特徵有重要關聯。偵測發展遲緩兒童的動機與氣質將有助於發展促進其參與的策略。

關鍵字：發展遲緩、精熟動機、學齡前兒童、氣質

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Case Report

Possible Immunoglobulin G4-Related Hypertrophic Pachymeningitis Leading To Bilateral Visual Loss

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ABSTRACT

Immunoglobulin G4-related disease (IgG4-RD) is a fibro-inflammatory disorder affecting numerous organs. The most common sites of involvement are pancreas, lungs, thyroid gland, lymph nodes, bile duct, retroperitoneum, and lacrimal and salivary glands. Hypertrophic pachymeningitis is a very rare manifestation of IgG4-RD. He we describe an old man who suffered from painless, progressive bilateral visual loss. On ocular examination, his vision was hand motion in the right eye and no light perception in the left eye. Fundus examination showed severe papilledema with pre-retinal hemorrhage. Brain computed tomography revealed hydrocephalus. Lumbar puncture confirmed high intra-cranial pressure. Brain magnetic resonance imaging uncovered dural thickening at left hemisphere and tentorium. His serum IgG4 level was elevated. However, dural biopsy did not present the hallmarks of IgG4-RD features. As there was suspicion of IgG4-related hypertrophic pachymeningitis, he received oral low-dose steroid treatment. Unfortunately, his vision and thickened dura had not improved after 4 months of steroid treatment.

Keywords: Immunoglobulin G4, hypertrophic pachymeningitis

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is a rare, chronic inflammatory disease. It was first recognized in 20 patients with sclerosing pancreatitis in 2001[1]. After that, there had been reports of patients with affected organs, including the pancreas, lungs, thyroid gland, lymph nodes, bile duct, retroperitoneum, and lacrimal and salivary glands[2]. Hypertrophic pachymeningitis is a very rare form of IgG4-RD and was first discovered in 2009[3]. Here we report a case with bilateral visual loss due to possible IgG4-related hypertrophic pachymeningitis (IgG4-HP).

CASE REPORT

A 67-year-old man presented to our ophthalmologic department reporting painless visual loss for one month. He had cholecystectomy 5 years ago and colon cancer (stage I) operation 4 months ago. He also had hearing loss and chronic intermittent headache for years. The underlying causes for hearing impairment and headache are unknown after consulting with specialists. On ocular examination, his best corrected visual acuity (BCVA) was hand motion perception in the right eye and no light perception (NLP) in the left eye. Pupils were isocoric but with poor light reflex in both eyes; otherwise, the anterior segment was normal. Intraocular pressure was within normal range. Fundus examination showed bilateral grade IV optic disc edema with peri-papillary and pre-retinal hemorrhage (Figure 1). He had no fever. Neurologic and general examinations were normal. A computed tomography (CT) of the head was performed, and dilation of the ventricular system was discovered (Figure 2). At that time (two weeks after his first visit), his vision declined to NLP in both eyes.

He underwent an emergent lumbar puncture and the opening pressure was elevated to 40 cmH2O. Cerebrospinal fluid (CSF) analysis revealed a clear CSF with a WBC count 5 (100% lymphocytes). Glucose and lactate dehydrogenase levels were normal. The level of total protein was high (138.3 mg/dl). No oligoclonal band was identified. Gram stain, Indian ink stain, stain for cryptococcus, and CSF culture (including fungus and tuberculosis) were negative. Microscopic cytology showed some small and large lymphoid cells. No malignant cells were found.

He had ventriculoperitoneal (VP) shunt surgery 2 days later. A thorough workup to rule out infectious, inflammatory, or neoplastic sources was initiated. His white blood cell (WBC) count was 11,100/uL with left shift but no eosinophilia. Elevated level of C-reactive protein (CRP) (14.31 mg/L) and erythrocyte sedimentation rate (ESR)(59 mm/1 h) were found. Both serum IgG and IgG4 levels were elevated (2029 mg/dL and 474 mg/dl, respectively). IgA and IgM levels were normal. Testing for serum tuberculosis, syphilis, HIV, and blood culture were not informative. Chest X-ray, abdominal CT, and urine checkup were normal. Thyroid profile was unremarkable. Rheumatoid factor was elevated to 80.0 IU/ml and anti-ENA screen ratio was increased to 1.8. Further testing for MPO-ANCA showed elevated level (19 IU/mL), but the level of PR3-ANCA was normal. Anti-ENA smith, anti-ENA RNP, anti-ENA SSA, anti-ENA SSB were within normal range.

Brain magnetic resonance imaging (MRI) coronal T1 sequence post-contrast uncovered dura thickening with enhancement at the left hemisphere and tentorium (Figure 3). Under the suspicion of IgG4-HP, dural biopsy was performed. Microscopically, section of the dura showed fibrous thickness containing hyalinized fibers with focal disarrayed pattern. Immunohistochemical studies of CD3, CD20, CD138, IgG and IgG4 were performed. Only several T lymphocytes (<10 cells/in total section) were demonstrated. The stainings for CD3, CD20, CD138, and IgG4 were all negative. No obliterative phlebitis was found (Figure 4).

Steroid treatment was suggested, but the patient's family only agreed to receive oral low-dose steroid. His papilledema subsided two months after VP shunt, and the optic discs turn pale. However, his vision and brain MRI showed no improvement after a 4-month course of treatment (20 mg/day)(Figure 5).

IgG4-RD is a fibro-inflammatory and lymphproliferative disorder involving nearly every organs. Although hypertrophic pachymeningitis (HP) could be attributed to infection (eg, neurosyphilis, tuberculosis, bacterial or fungal meningitis), inflammation (eg, Wegener, rheumatoid arthritis, and sarcoidosis), or malignancy, it has also been recognized as a manifestation of IgG4-RD[4]. The prevalence of IgG4-HP is approximately 2% of overall clinical manifestations of IgG4-RD[5]. IgG4-HP is also one of the leading causes of meningeal inflammatory disease[6]. The dura mater is the major meningeal layer involved in IgG4-RD. In a study by Levraut et al., the most common neurological symptoms in 60 patients with IgG4-HP are headache (65.4%), followed by cranial nerve palsies (29.1%), limbs motor weakness (29.1%), visual loss (29.1%), limbs sensory loss (16.4%), and seizures (12.7%)[6]. Mechanical compression of vascular or nerve structure has been proposed as the pathomechanism of neurological deficits. The thickened dura leading to increased intra-cranial pressure might account for the major cause of visual damage in our case.

The definite diagnosis of IgG4-HP requires confirmation through biopsy. The central histopathological features of IgG4-HP include lymphoplasmacytic infiltration of IgG4-positive plasma cells, storiform fibrosis,

and obliterative phlebitis. Our patient has elevated serum level of IgG4 (474 mg/dL, normal value < 135 mg/dL). Elevated serum IgG4 level is present in 70% to 90% of IgG4-RD patients. In a multi-ethnic study of patients with histologically confirmed IgG4-RD, Asians have a higher serum level of IgG4 than non-Asians, and the test sensitivity was higher in Asians (96%) compared to 67% in non-Asians patients[7]. Moreover, a study by Lu et al., found that 9% patients with IgG4-HP had hearing loss[8]. We were not able to confirm whether our patient's hearing impairment and prior gallbladder problems were attributed to IgG4-RD. Based on the elevated level of serum IgG4, clinical and radiological manifestations, and the absence of infection, inflammation and malignancy linking to the hypertrphic pachymeningitis, "possible IgG4-RD" can be diagnosed in our patient according to the 2020 revised comprehensive diagnostic (RCD) criteria despite the lack of histological evidences[9]. On the other hand, our patient meets the entry criteria of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) IgG4-RD Classification Criteria for international use (Characteristic clinical or radiologic involvement of a typical organ)[10]. However, the presence of elevated level MPO-ANCA excluded the definite diagnosis of IgG4-HP. According to a study comparing the performance of these two criteria, the 2019 ACR/EULAR criteria enable disease classification with high specificity without tissue biopsy, while the 2020 RCD criteria with high sensitivity in diagnosis[11].

This study was approved by Institutional Ethics Review Board (permission number: 20181002R).

DISCUSSION

IgG4-related visual loss is very rare[12]. Currently, a standard treatment protocol for IgG4-HP has yet to be established. Steroid remains the first-line of treatment; however, 42.1% patients experience disease relapse after discontinuance of steroid. Other immunosuppressants such as retuximab can be administered along or in combination with steroid. Surgery is another approach in some patients. Considering the old age of our patient and the side effects of steroid, the patient's family has only agreed to a low-dose steroid treatment. Unfortunately, his vision and hypertrophic meninges showed no improvement after 4 months of steroid treatment.

In conclusion, hypertrophic pachymeningitis is a rare manifestation of IgG4-RD. Only a few cases of visual loss resulted from IgG4-HP have been reported. Although our case fails to fulfill the ACR/EULAR IgG4-RD Classification Criteria for international use, clinicians should be familiar with this diseases because a prompt therapeutic approach may save a patients' vision and even his/her life.

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FIGURE AND FIGURE LEGENDS

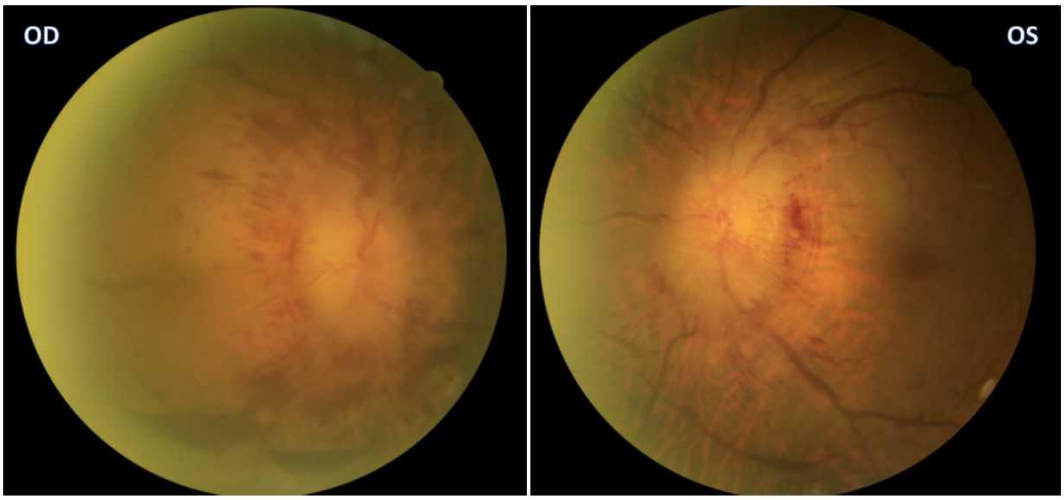

Figure 1. Fundus photograph showed bilateral optic disc edema with peri-papillary and pre-retinal hemorrhage.

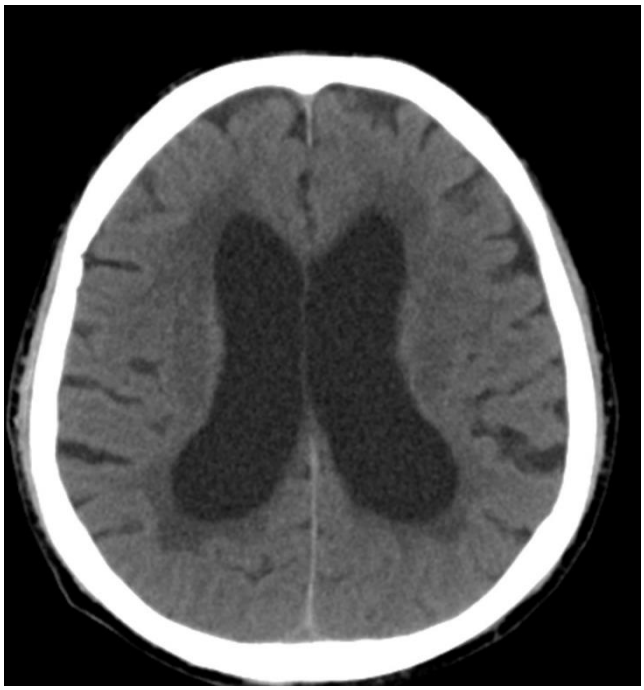

Figure 2. Computed tomography of head revealed the dilated ventricular system.

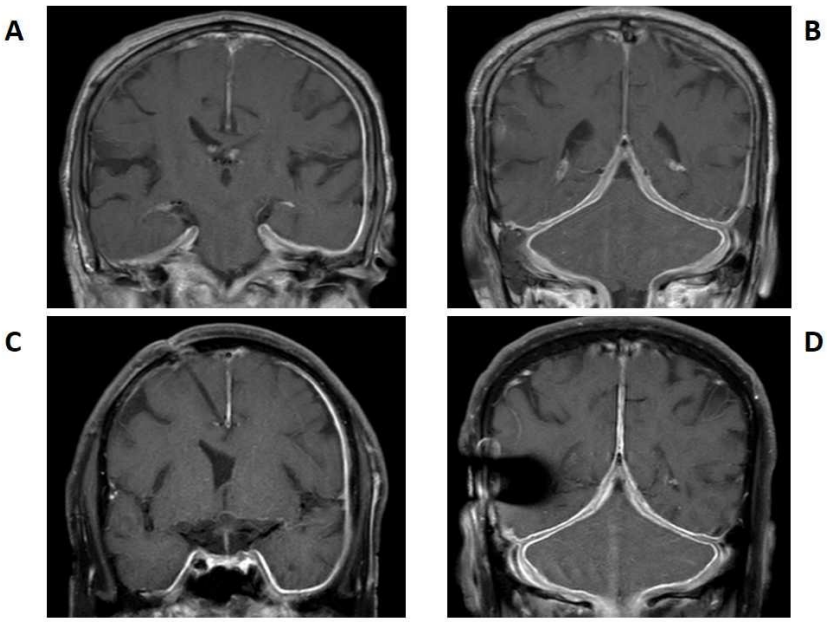

Figure 3. Brain magnetic resonance imaging (MRI) coronal view T1 sequence post-contrast showed linear dural thickening in the left hemisphere (A) and tentorium (B) before and after (C,D) steroid treatment.

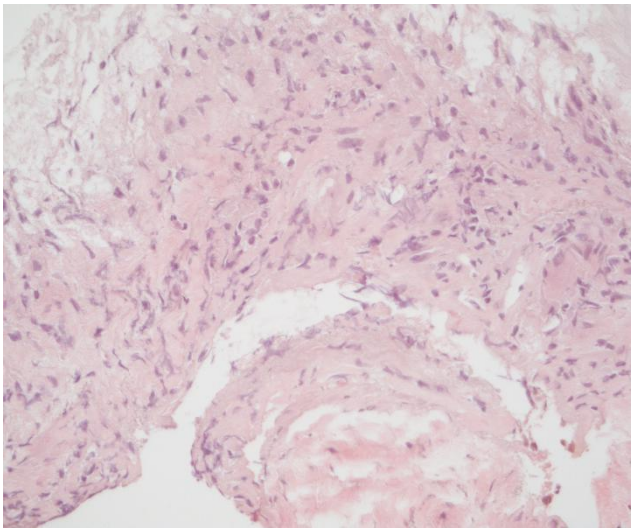

Figure 4. Dural biopsy showed fibrous change containing hyalinized fibers with only several T lymphocytes (hematoxylin & eosin stain, x 200). Immunohistochemical staining for CD3, CD20, CD138, IgG and IgG4 were negative.

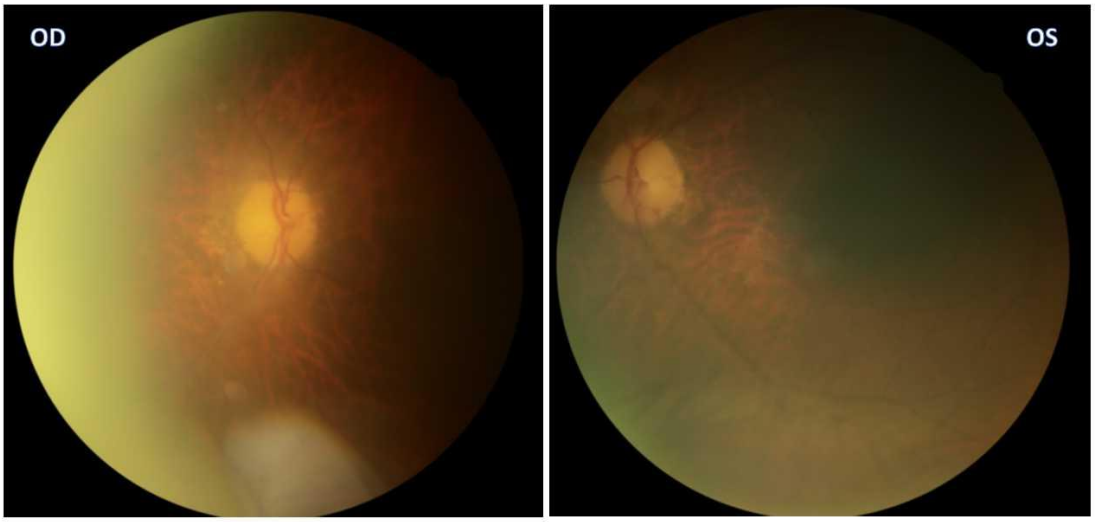

Figure 5. Fundus photograph two months after ventriculoperitoneal (VP) shunt showed resolution of papilledema, but the optic discs became atrophy.

Possible Immunoglobulin G4-Related Hypertrophic Pachymeningitis Leading To Bilateral Visual Loss

疑免疫球蛋白 G4-相關肥厚硬腦膜炎引起雙側視力喪失

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中文摘要

免疫球蛋白 G4-相關疾病是一纖維發炎性異常，影響許多器官，最常影響的部位包含有胰臟、肺、甲狀腺、淋巴結、膽管、後腹膜、淚腺、及唾液腺。 肥厚硬腦膜炎為其非常罕見的表現。我們提出一老年男性逐漸無痛性雙眼視力喪失，眼科檢查時右眼視力僅為見手動，左眼已無光覺。眼底檢查發現視神經盤水腫合併視網膜前出血。腦部電腦斷層顯示水腦，脊椎穿刺確定腦壓升高，腦部核磁共振發現左側大腦半球及大腦鐮硬腦膜增厚，血清免疫球蛋白升高，但是硬腦膜切片並無免疫球蛋白 G4-相關疾病的病理表現。由於懷疑是免疫球蛋白 G4-相關肥厚硬腦膜炎，他開始口服低劑量類固醇治療，可惜治療四個月後追蹤視力及硬腦膜增厚並無改善。

關鍵字：免疫球蛋白 G4、肥厚硬腦膜炎

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Case Report

Small cell neuroendocrine carcinoma of the renal pelvis – a case report and literature review

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ABSTRACT

Purpose: To present a rare clinical presentation of renal pelvis small cell neuroendocrine carcinoma. ***Case report:*** A 58-year-old female visited our urology department due to painless gross hematuria for two weeks. A renal ultrasound revealed right-side hydronephrosis with a mass lesion on the renal pelvis. Enhanced computerized tomography demonstrated a 3 cm localized enhanced mass on the right renal pelvis causing right hydronephrosis. A right nephroureterectomy with bladder cuff resection was performed. Microscopically, the tumor cells showed typical features of small cell neuroendocrine carcinomas, such as relatively small cells, a high N:C ratio, poorly defined cell borders, and scant cytoplasm. Immunohistochemical studies revealed that the tumor cells were positive for cytokeratin and GATA-3. Neuroendocrine differentiation demonstrated positive staining for synaptophysin, chromogranin A, and CD56. The patient was referred to the medical oncology department for adjuvant chemotherapy. Follow-up imaging at 9 months showed no signs of local recurrence or distant metastasis. ***Conclusion and Importance:*** There is no definite radiologic sign to differentiate renal pelvis small cell neuroendocrine carcinoma from other kidney tumors preoperatively at present due to limited case reports. Once diagnosed, postoperative adjuvant therapy is mandatory due to its vigorous growth pattern.

Keywords: hematuria, neuroendocrine, renal pelvis, small cell carcinoma

INTRODUCTION

Tumors of the renal collecting system account for 7% of renal malignancy, and most of these tumors arise from the urothelium (Rink et al., 2012). Non-urothelial renal collecting system cancer is rare. In 2021, Nagumo et al. reviewed 2567 upper urinary tract cancer patients with confirmed pathology findings, demonstrating urothelial carcinoma represented 94.8% of upper urinary tract tumors. The most common histological type of non-urothelial upper urinary tract carcinoma is squamous cell carcinoma, followed

by adenocarcinoma and small cell carcinoma (Nagumo et al., 2021).

Poorly differentiated neuroendocrine tumors, such as small cell carcinomas, mainly occur in the pulmonary system. Extrapulmonary small cell carcinoma is rare and it has been described in various organs such as the esophagus, stomach, pancreas, gallbladder, uterine cervix, kidney, urinary bladder, and prostate (Kim et al., 2004). Neuroendocrine small cell carcinoma (or so-called small cell carcinoma) of the genitourinary tract is very rare, with the most common site being the urinary bladder and sometimes concomitant with urothelial carcinoma. Neuroendocrine small cell carcinoma of the upper urinary tract is extremely rare, and due to its rarity, the available clinical information is also limited. Herein, we present and review a rare case of renal pelvis small cell neuroendocrine carcinoma. This study was approved by the IRB of St. Martin De Porres Hospital (23B-004).

CASE REPORT

A 58-year-old female presented at our urology department with painless gross hematuria for two weeks. Her mother is undergoing treatment and follow-up for superficial bladder urothelial carcinoma at our department. The patient is a non-smoker and generally in good health, with no systemic chronic disease. A renal ultrasound revealed right-side hydronephrosis with a mass lesion on the renal pelvis. Subsequently, enhanced computerized tomography (CT) demonstrated a 3 cm localized enhanced mass on the right renal pelvis causing right hydronephrosis (Fig. 1). Right upper urinary tract urothelial carcinoma was initially suspected due to her family history, and a right nephroureterectomy with bladder cuff resection was performed. The histopathological study revealed that the tumor was in the right renal pelvis and had invaded the muscularis propria (pT2). Microscopically, the tumor cells showed typical features of small cell neuroendocrine carcinomas, such as relatively small cells (<3 lymphocyte diameters), a high N:C ratio, poorly defined cell borders, and scant cytoplasm (Fig. 2). The nuclei exhibited finely granular nuclear chromatin (speckled; salt-and-pepper chromatin pattern) with small or absent nucleoli, and nuclear molding was frequently present. Tumor cells were mitotically active and showed conspicuous apoptosis and neuroendocrine features with large sheet-like, trabeculae, and solid growth patterns. Immunohistochemistry studies of the tumor cells were positive for cytokeratin (with a rim-and-dot–type pattern) and GATA-3 (Fig. 3) and negative for p63, p40, and CD10, while the Ki-67 index was 65−85%. Neuroendocrine differentiation was demonstrated by positive staining for synaptophysin, chromogranin A, and CD56 (Fig. 4). A chest-enhanced CT after the operation showed no evidence of tumor growth.

This patient was referred to our medical oncology department, where she received four courses of Carboplatin + Etoposide adjuvant chemotherapy. She suffered from a severe coronavirus infection six months after her operation but recovered well. Imaging studies showed no signs of local recurrence or distant metastasis nine months after the operation.

DISCUSSION

Neuroendocrine neoplasms are epithelial neoplasms with predominant neuroendocrine differentiation. In the 5th edition of the WHO Classification of Tumors, neuroendocrine neoplasms are classified into two main categories: well-differentiated neuroendocrine tumors (NET) and poorly differentiated neuroendocrine carcinomas. The well-differentiated NET category includes NET grade 1, NET grade 2, and NET not otherwise specified (NOS). The poorly differentiated neuroendocrine carcinoma category encompasses large cell neuroendocrine and small cell neuroendocrine carcinomas (Rindi et al., 2022).

The diagnosis of neuroendocrine small cell carcinoma is mainly based on histopathologic findings, including small and oval spindle-shaped cells with absent or inconspicuous nucleoli, nuclear molding, scant cytoplasm, and increased mitotic activity (>11/10 hpf) (Morgan et al., 1996). Immunohistochemical staining also can be applied to confirm the diagnosis, with synaptophysin, chromogranin, and CD56 widely used neuroendocrine markers for small cell neuroendocrine carcinoma. Synaptophysin has a relatively reliable diagnostic potential whereas chromogranin is less sensitive, and CD56 is most sensitive but less specific (Kim et al., 2022).

Gross hematuria is the most common symptom of small cell neuroendocrine carcinoma, followed by pain (Pervez et al., 2013). Similar to pulmonary small cell carcinoma, renal small cell neuroendocrine tumor is aggressive with a poor prognosis. The median survival is 15 months, and the 1-, 2- and 3-year survival rates are 58.4%, 38.1%, and 23.8%, respectively (Ouzzane et al., 2011). Due to limited case reports, there is currently no standard treatment protocol. In a review of twenty-two reported cases, Majhail et al. (2003) demonstrated that 60% of patients with no evidence of distant metastases initially de-

veloped metastatic lesions during follow-up. They also found that 86% of patients who underwent nephrectomy had limited-stage disease, of which, 67% had distant relapse later. They suggested that there might be a high incidence of occult metastases on presentation in patients with localized disease and multiple modalities of treatment should be considered for these patients.

Due to the aggressive growth pattern and high incidence of occult lesions, some authors recommend adjuvant treatment once the pathologic diagnosis is confirmed after surgery. Platinum-based chemotherapy regimens, which are commonly used in small cell lung cancer, have been applied for small cell carcinoma of the kidney. In 2011, Ouzzane et al. reviewed the published data on thirty-nine patients with upper urinary tract small cell carcinoma, demonstrating that patients who received adjuvant chemotherapy had a higher median survival rate compared to those who did not receive chemotherapy but this difference was not statistically significant (24 vs. 12 months, $p = 0.56$). In a systemic review of twenty-two patients with kidney and renal pelvis small cell carcinoma, Majhail et al. (2003) revealed the use of platinum-based chemotherapy may improve the survival rate (median survival of 20 months in patients receiving a platinum-base regimen vs. 8 months in patients receiving non-platinum agents; $p = 0.02$). In a meta-analysis of seventy patients with upper urinary tract neuroendocrine carcinoma (68 small cell and 2 large cell) in 2018, Nakasato et al. concluded that adjuvant treatment with chemotherapy and radiotherapy significantly improved patient prognosis, particularly platinum-based chemotherapy. Our patient received Carboplatin + Etoposide systemic chemotherapy after nephrectomy and showed no evidence of tumor recurrence during follow-up.

CONCLUSION

The diagnosis of renal small cell neuroendocrine carcinoma is based on its pathologic findings but there is no definite radiologic sign to differentiate it from other kidney tumors preoperatively at present due to limited case reports. Once diagnosed, postoperative adjuvant therapy is mandatory due to its vigorous growth pattern.

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FIGURE AND FIGURE LEGENDS

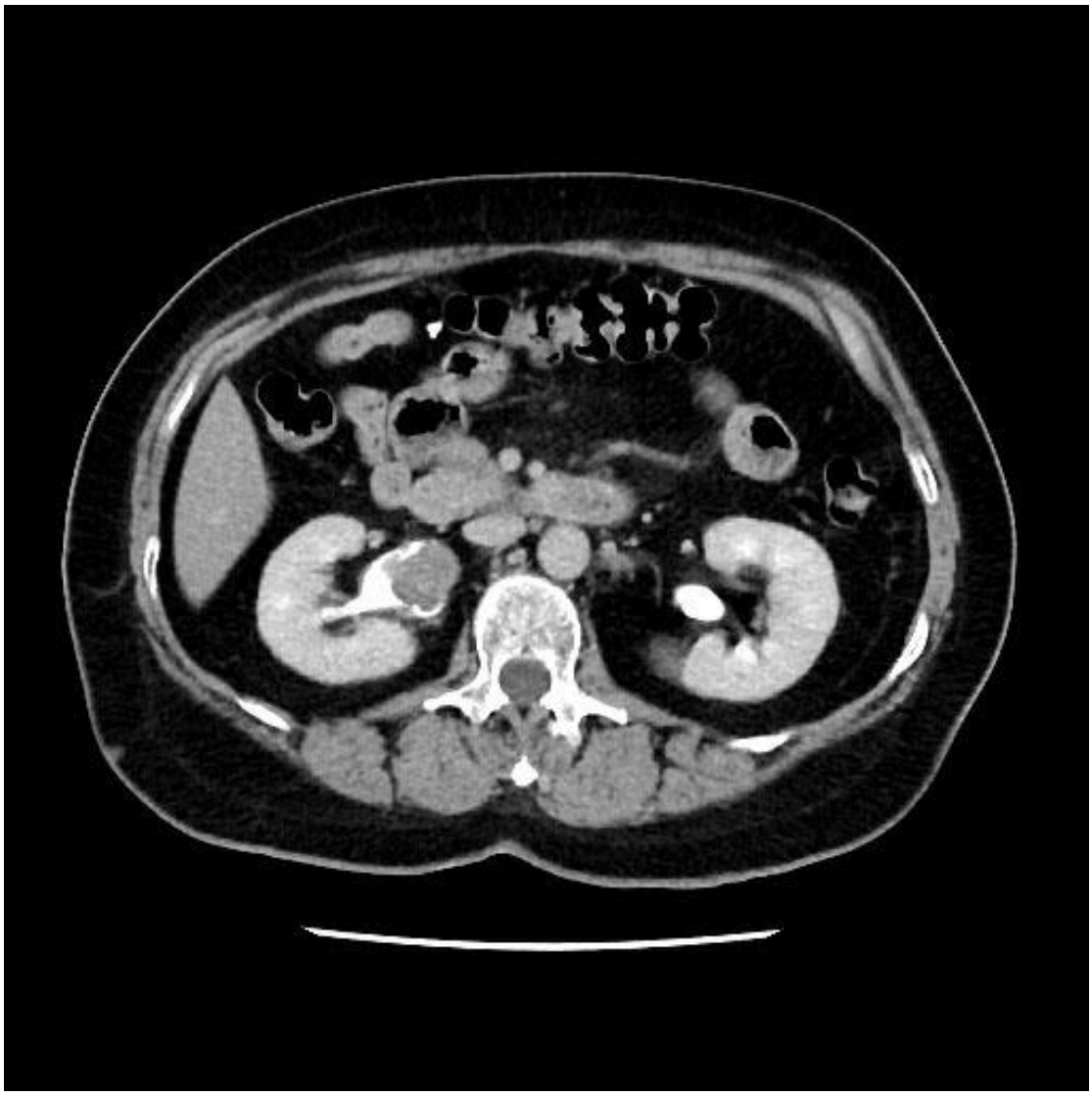

Figure 1. Enhanced computerized tomography demonstrated a 3 cm localized enhanced mass on the right renal pelvis causing right hydronephrosis.

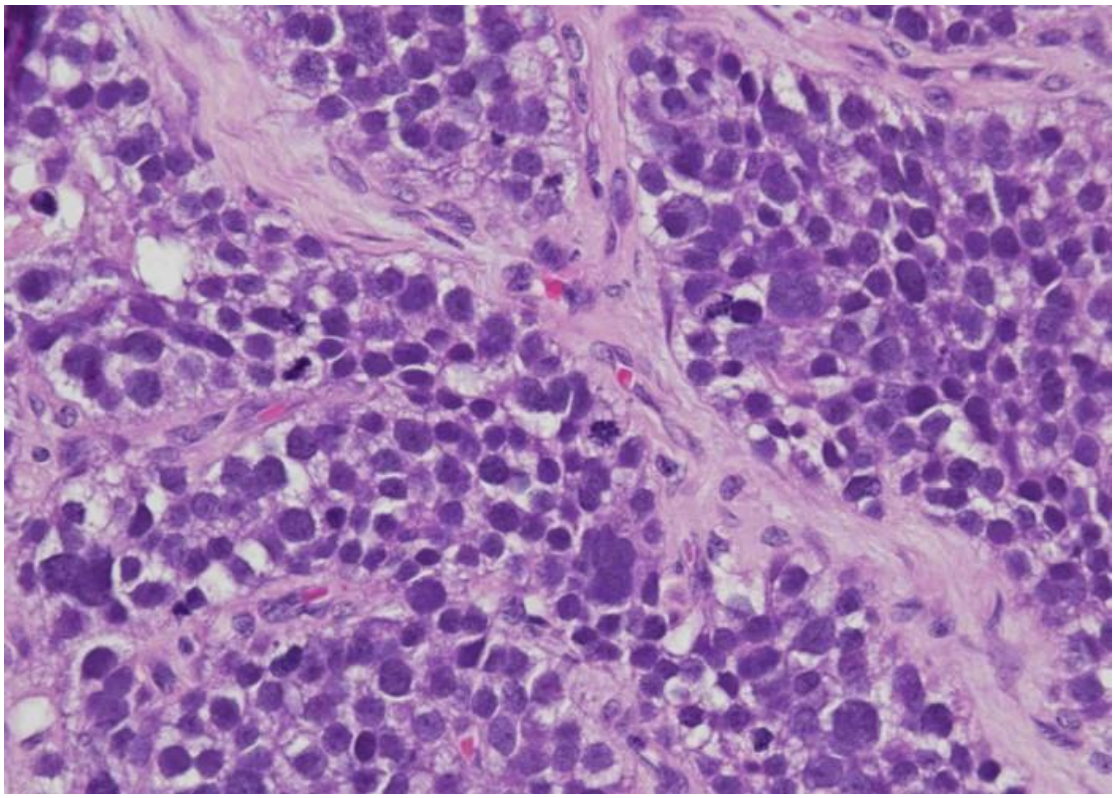

Figure 2. The tumor cells are densely packed and relatively small, with scanty cytoplasm, finely granular nuclear chromatin, nuclear molding, and inconspicuous nucleoli, and frequent mitoses are frequent (HE,400X).

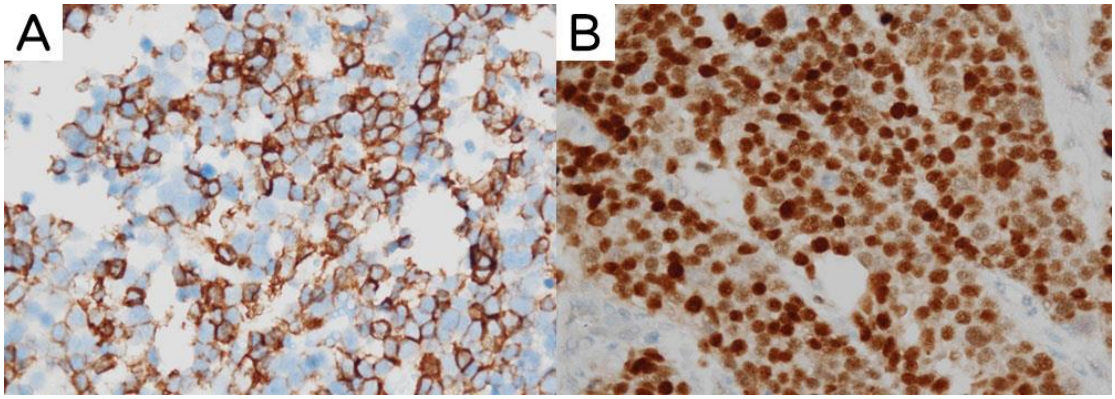

Figure 3. The tumor cells exhibit positive staining for pan-cytokeratin (A; 400X) and GATA-3 (nuclear staining) (B; 400X), indicating that the carcinoma originates from the urothelium.

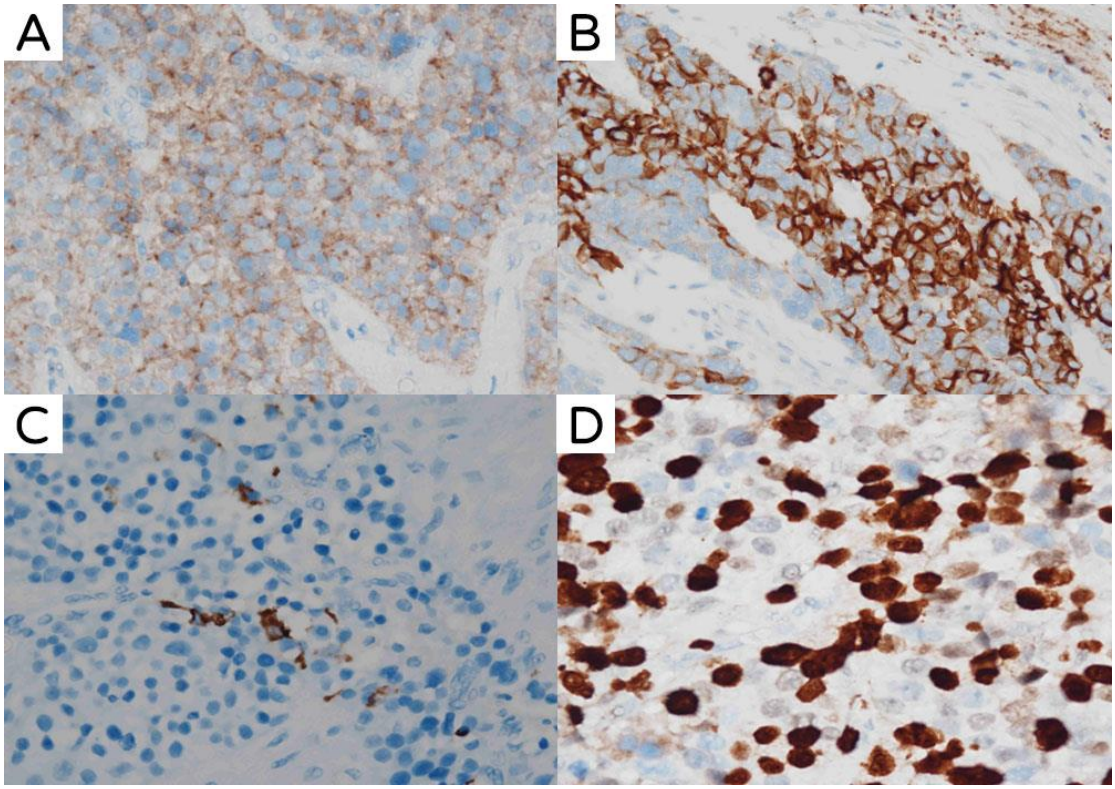

Figure 4. The tumor cells exhibit cytoplasmic staining for chromogranin A (A; 400X), membranous staining for CD56 (B; 400X), and focal positivity for synaptophysin (C; 400X). The high ki67 labeling index (>65%, D; 400X) indicates the tumor cells have an aggressive growth nature.

Small cell neuroendocrine carcinoma of the renal pelvis – a case report and literature review

腎盂小細胞神經內分泌癌：一病例報告及論文回顧

陳奕先[1]　翁啟倫[2,*]　周詠欽[3]

中文摘要

目的：報告一例罕見的腎盂小細胞神經內分泌癌。**病例報告：**一名 58 歲女性因持續兩週的無痛性肉眼血尿就診。診間腎臟超音波檢查顯示右側腎積水伴隨有腎盂部的腫塊。電腦斷層掃描顯示右側腎盂有一 3 厘米局限性腫塊，導致右側腎積水。病患接受了右側腎盂尿管切除術並膀胱袖口切除。在顯微鏡下觀察，腫瘤細胞顯示出小細胞神經內分泌癌的典型特徵，例如相對較小的細胞、高的核質比、不明顯的細胞邊緣和稀少的細胞質。腫瘤細胞的免疫組織化學研究顯示，細胞角蛋白和 GATA-3 染色呈陽性。神經內分泌鑑別顯示出突觸素、嗜鉻蛋白 A 和 CD56 染色呈陽性。她被轉介到我們的醫學腫瘤科進行輔助化療。手術後九個月的影像檢查未發現局部復發或遠處轉移的跡象。**結論和重要性：**由於案例報告有限，在手術前沒有明確的影像學徵象可以與其他腎腫瘤加以區分。一旦確診，由於其強侵襲性的生長模式，術後輔助治療是必要的。

關鍵字：血尿、神經內分泌、腎盂、小細胞癌

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Case Report

Atypical presentation of bilateral traumatic carotid-cavernous fistulas: a case report

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ABSTRACT

Carotid-cavernous fistula (CCF) is a rare sequela of head trauma, with potentially serious consequences. We report the case of a 24-year-old male patient who presented with bilateral CCFs two weeks after a traffic accident. He was found to have progressive proptosis, ophthalmoplegia without decreased vision, elevated intraocular pressure or conjunctival chemosis. Subsequent computed tomographic angiography confirmed a bilateral CCF. After the patient underwent two endovascular embolization procedures, the ocular symptoms were improved. Bilateral CCFs are extremely rare after craniofacial trauma. The most common signs of traumatic CCF include chemosis, elevated intraocular pressure, proptosis, impaired eye movement, and decreased vision. Untreated CCFs may result in severe consequences, therefore, a high index of suspicion must be maintained to establish a diagnosis and undergo an appropriate treatment.

Keywords: carotid-cavernous fistula, proptosis, ophthalmoplegia

INTRODUCTION

Carotid-cavernous fistula (CCF) is a rare complication of craniomaxillofacial trauma, occurring in only 0.17% to 0.27% of cases[1]. Untreated CCFs can lead to progressive ocular symptoms and eventually to total loss of visual acuity. Therefore, early diagnosis of CCFs is very important. However, it is possible to make a misdiagnosis without classical triad of pulsatile exophthalmos, bruit, and conjunctival chemosis[2]. We present a case of atypical manifestations of bilateral carotid-cavernous fistulas in a 24-year-old male two weeks after a traffic accident.

CASE REPORT

A 24-year-old man visited our outpatient department for bilateral frozen and progressive bulging of eyes for one week. (Fig 1) By tracing back his history, he suffered a traffic accident causing his bilateral mandible fracture 2 weeks before his symptoms occurred. On ophthalmic examination, his best corrected visual acuity (BCVA) was 6/6 (OD) and 6/6.7 (OS); intraocular pressure (IOP) was in the normal range. Slit lamp biomicroscopy revealed entropion of bilateral lower lids, and punctate epithelial erosions of bilateral corneas without conjunctival chemosis or corkscrew vessels. (Fig 2) Limitation of extraocular muscles in all directions, absence of pupillary light reflex of both eyes and bilateral ptosis were also noted.

Hertel exophthalmometry was 22 millimeters (mm) and 23 mm respectively. Laboratory results ruled out thyroid eye disease and ocular myasthenia gravis. Computed tomography (CT) was arranged for suspected retrobulbar lesions, which showed bilateral exophthalmos with engorged superior ophthalmic veins (SOVs). (Fig. 3) Brain computed tomographic angiography (CTA) further revealed bilateral direct carotid-cavernous fistulas, draining anteriorly to the SOVs, and posteriorly via the inferior petrosal sinus (IPS). (Fig. 4) Transcatheter arterial embolization (TAE) was then performed with detachable coils. After TAE, his extraocular motion (EOM) significantly improved, except for slightly underaction of left lateral gaze. However, lateral gaze limitation progressed within 1month with recurrent ptosis in the left eye. The follow-up cerebral angiography revealed bilateral CCFs with residual flow, and was more severe on the left side with flow into intercavernous sinus and cavernous sinus. (Fig 5) After the second TAE and transvenous embolization (TVE) for the residual CCFs of left side, the symptoms were improved. Hertel exophthalmometry was 16 mm in the right eye and 18 mm in the left eye after TAE. He had only 18 prism diopters of left eye esotropia at the visit after one month. (Fig 6) Eye movement was normal in his both eyes after six months. (Fig 7) His BCVA was 6/6 in both eyes and there was no sequelae in the macula and optic nerve. (Fig 8)

DISCUSSION

Carotid-cavernous fistulas (CCFs) are abnormal communications between the carotid artery and the cavernous sinus. According with Barrow's classification, CCF could be classified in two groups: A) direct and B) indirect[3]. Direct fistulas show a direct communication between the internal carotid artery and the cavernous sinus. They are usually caused by craniomaxillofacial trauma and exhibit a high flow rate, instead indirect fistulas are usually spontaneous and exhibit a low flow rate. Invasive treatment usually is not required in most cases of indirect, low-flow fistulas, as these may close spontaneously. However, untreated direct CCF may disrupt normal cerebral or ocular venous drainage routes. This can lead to cerebral hemorrhage, venous congestion, or deterioration of ocular symptoms. Therefore, emergent intervention is required and may improve patient outcome[4,5]. Any symptoms of proptosis or ophthalmoplegia after trauma should always be carefully studied to rule out vision-threatening conditions and emergencies. Among the various differential diagnoses, CCF is a rare complication[6]. It is usually unilateral, and bilateral traumatic CCFs are extremely rare[7]. In fact, only 0.3% of craniomaxillofacial traumas are associated with CCFs[2]. The clinical symptoms and signs are influenced by the size of the fistula, the rate of the blood flow, and the drainage route, especially if the drainage route of the fistula is posterior, anterior, or both[6]. In this case, bilateral fistulas drain partially and posteriorly into the inferior petrosal sinus; therefore, produce no classic signs of tortuous corkscrew vessels. CT scanning was arranged due to suspected retrobulbar lesions, and the correct diagnosis was made until CT angiography was performed. Patients in whom a CCF is suspected require neuroimaging that may include non-invasive computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). Both techniques have high sensitivities for both direct and indirect CCFs that cause visual manifestations[4]. Endovascular embolization is the preferred treatment modality, offering a high rate of cure and low rate of complications[5]. More than 80% of patients who undergo endovascular treatment for direct and indirect CCFs will experience a complete cure.

In conclusion, any patient who develops a red eye, chemosis of the conjunctiva, EOM limitation, or proptosis after trauma would lead us to consider the diagnosis of CCF. However, the diagnosis with atypical symptoms represents the main clinical pitfall that warrants a careful neurovascular evaluation to ensure the appropriate management. We reported a case of bilateral traumatic CCFs with proptosis, ptosis, and complete ophthalmoplegia as the initial presentation. The differential diagnosis of CCF should always be kept in mind for patients having trauma history as the clinical presentations may be atypical without congestion of eyes nor elevation of intraocular pressure (IOP). Close follow-up after intervention was suggested and any progression of EOM limitation can be an early sign of recurrence or residual flow of CCF.

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FIGURE AND FIGURE LEGENDS

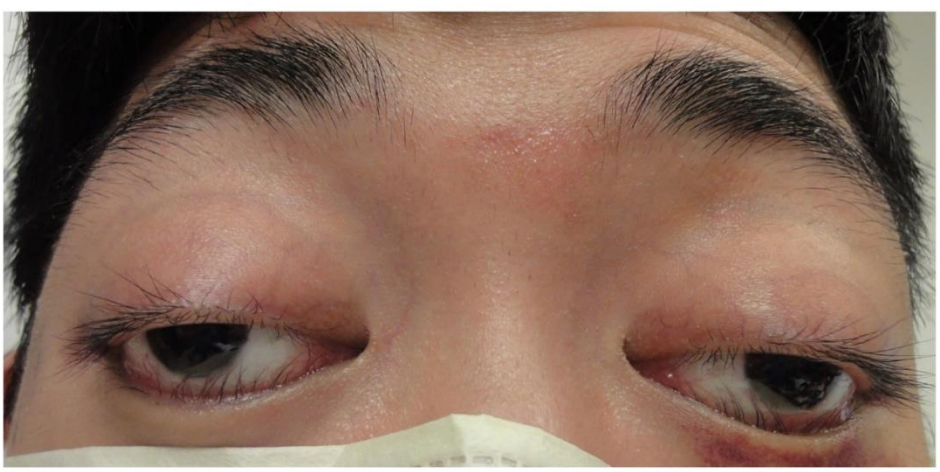

Figure 1. External photograph taken at time of initial presentation, showing bilateral ptosis and bulging eyes

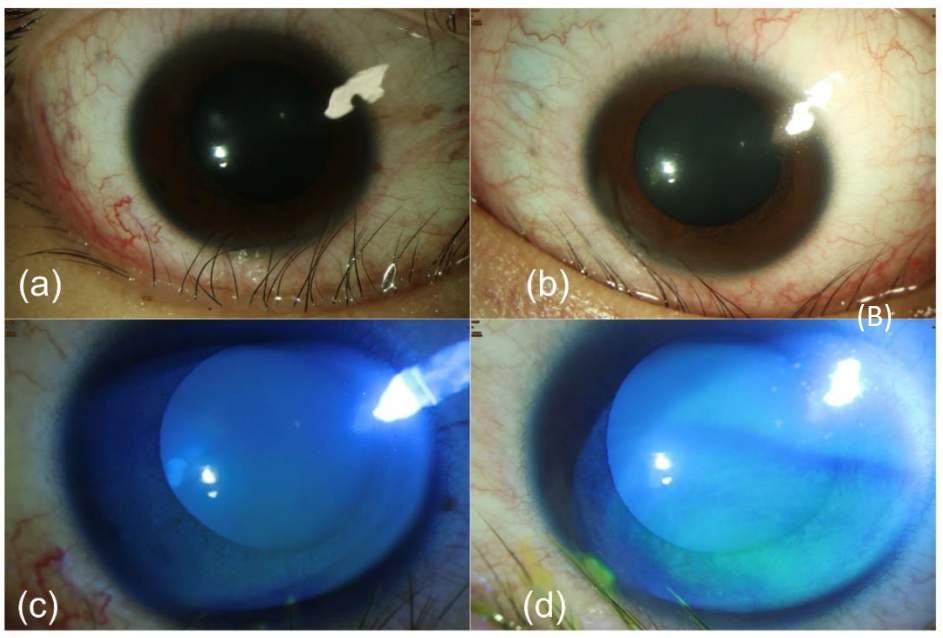

Figure 2. Slit-lamp photograph (left column, OD; right column, OS) showing entropion of bilateral lower lids, absence of pupillary light reflex without conjunctival chemosis or corkscrew vessels of both eyes (a,b). Punctate epithelial erosions of bilateral corneas were noted (c,d)

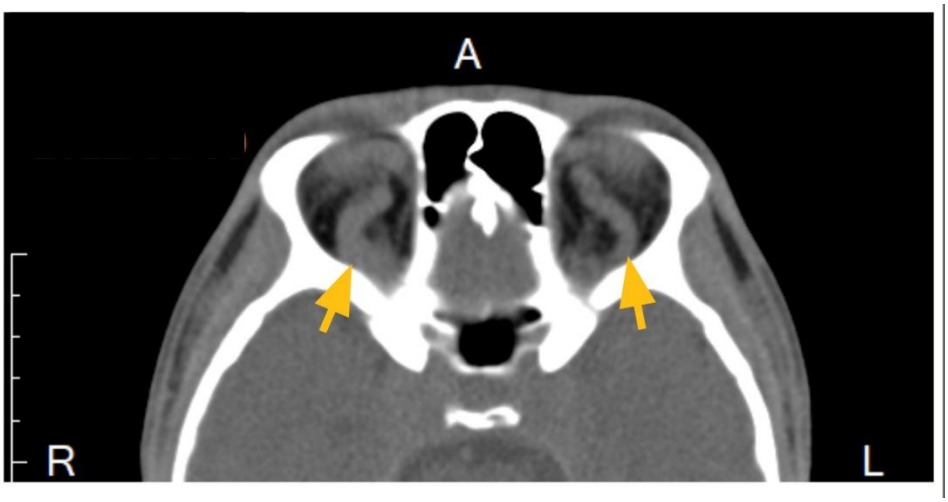

Figure 3. Computed tomography showed bilateral engorged superior ophthalmic veins (SOVs)

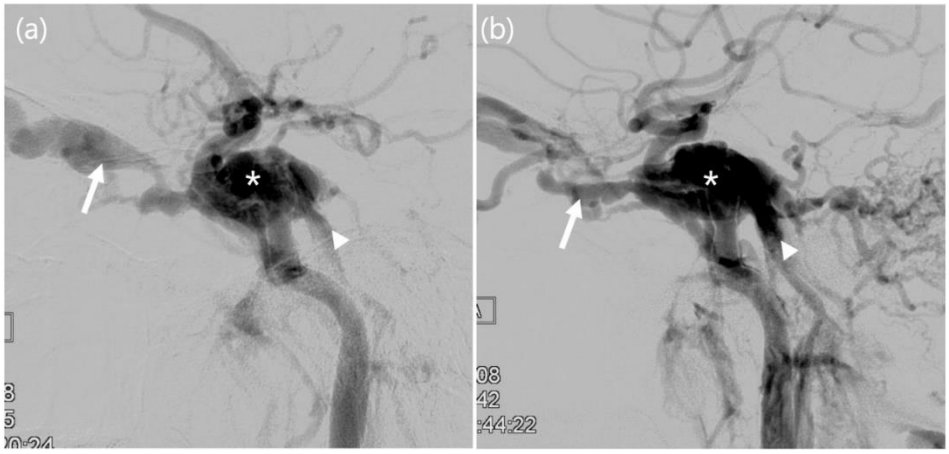

Figure 4. Brain CT angiography revealed (a) right side (b) left side direct carotid-cavernous fistulas (asterisks), draining anteriorly to the SOVs (arrows), and posteriorly via the inferior petrosal sinus (arrowheads)

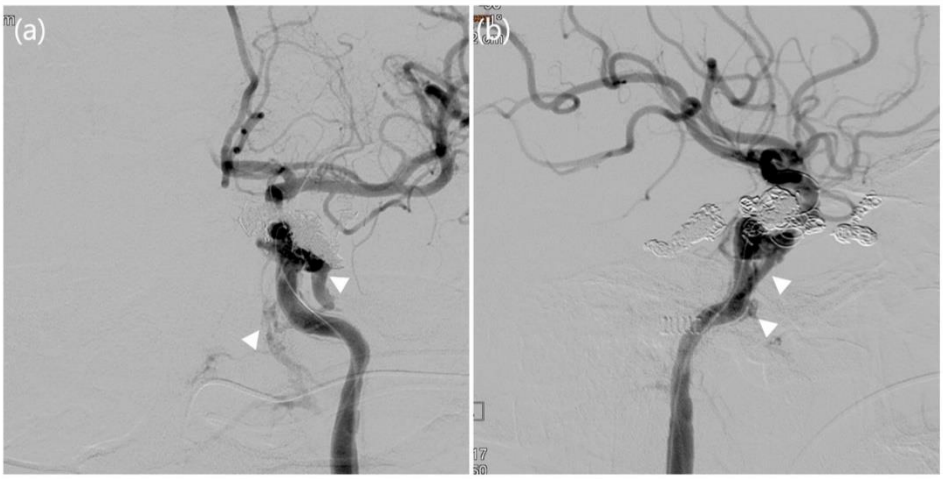

Figure 5. Post TAE cerebral angiography demonstrated (a) anterior view (b) lateral view of left residual CCFs, with drainage into intercavernous sinus and cavernous sinus.

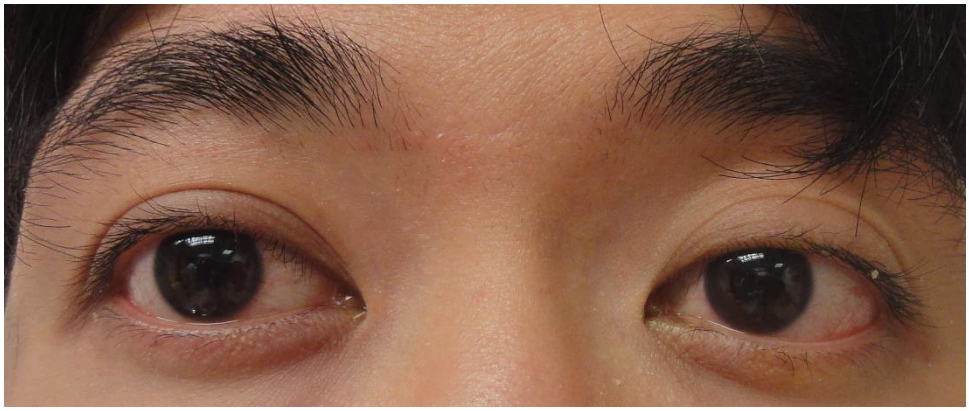

Figure 6. External photograph after TAE showed esotropia in the left eye.

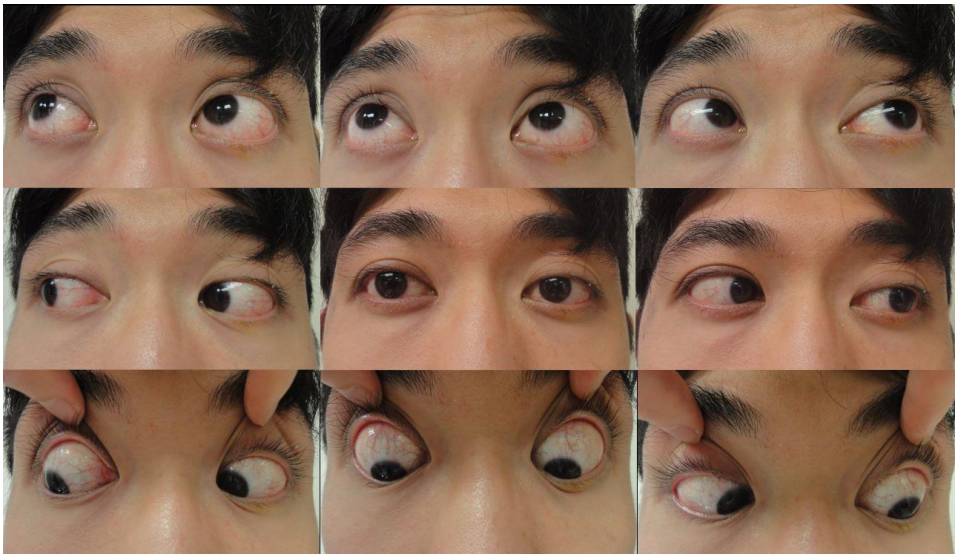

Figure 7. Nine-gaze direction photograph after TAE showed normal eye movement in all gazes.

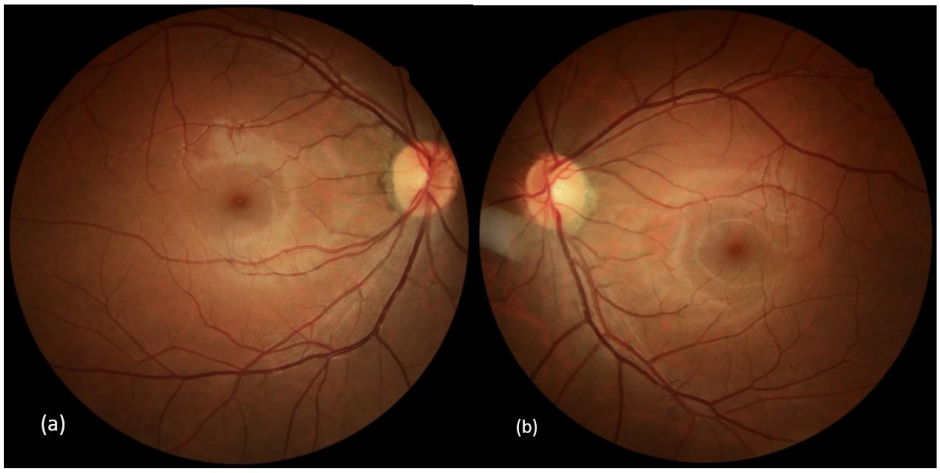

Figure 8. Color fundus photograph showed normal macula and optic nerve (a) right eye (b) left eye

Atypical presentation of bilateral traumatic carotid-cavernous fistulas: a case report

非典型表現之雙側創傷性頸動脈海綿竇瘻管：病例報告

林惠真[1,2]　唐甄蔚[1,2,*]　陳彥如[1]　施玫如[1]　鄭成國[1,2]

中文摘要

頸動脈海綿竇瘻管是頭部外傷後罕見的併發症，會引起相當嚴重的結果。我們報告了一位 24 歲男性在車禍兩星期之後出現了雙眼突出及眼球轉動異常的症狀，病患雙眼視力及眼壓正常，結膜沒有充血及水腫，經由電腦斷層血管攝影診斷為雙側頸動脈海綿竇瘻管，病患進行了兩次血管內栓塞治療後，眼部的症狀獲得改善。雙側外傷性頸動脈海綿竇瘻管是相當罕見的疾病，常見的症狀包括結膜充血水腫、眼壓上升、眼球突出、眼球轉動異常、視力下降，沒有及時治療的頸動脈海綿竇瘻管將會導致嚴重的後果，因此頭部外傷後出現以上任一症狀，都應該保持高度警覺，讓病患能早期獲得正確的診斷與適當的治療。

關鍵字：頸動脈海綿竇瘻管、眼球突出、眼球轉動異常

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