Etiologies of Central Diabetes Insipidus in Children : 15 Years Experience in Songklanagarind Hospital, Thailand

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Abstract

Central diabetes insipidus (DI) is a rare disease in children. The authors retrospectively reviewed the records of children with central DI identified at Songklanagarind Hospital from 1985 to 2000. Of the total 29 patients identified, 16 patients were males and 13 were females. All patients received computed tomography or magnetic resonance imaging of the brain to differentiate the etiologies of central DI. The median age at diagnosis was 6.6 years (range 1.5-14.9). The etiologies of central DI were intracranial tumors in 7 patients (24.1%), histiocytosis in 3 patients (10.3%), septo-optic dysplasia in 1 patient (3.5%), empty-sella syndrome in 1 patient (3.5%), pituitary abscess in 1 patient (3.5%), and idiopathic in 16 patients (55.1%). All patients with idiopathic central DI were followed-up for a median duration of 4.5 years (range 1.3-15.5). Three of 16 patients (18.8%) were found to have intracranial tumors at 1.3, 2.3, and 3.5 years of follow-up. It was also observed that the patients whose age at presentation was less than 5 years (histiocytosis was excluded) were less likely to have intracranial tumors than those older than 5 years, (0% *vs* 55%), with significant statistical difference ($p<0.01$). It is concluded that :

1) the common etiologies of central DI are intracranial tumor and idiopathic,

2) patients initially diagnosed with idiopathic central DI need to have long-term follow-up by magnetic resonance imaging to identify any occult intracerebral tumor.

Key word : Central Diabetes Insipidus, Diabetes Insipidus, Idiopathic Central Diabetes Insipidus, Intracranial Tumor, Neurogenic Diabetes Insipidus

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Central diabetes insipidus (DI) or neurogenic DI is a neuroendocrine disorder characterized by polyuria and polydipsia due to a deficiency of antidiuretic hormone from the hypothalamus or posterior pituitary. Previous studies of the etiologies of central DI have found that the two most common causes are intracranial tumors and idiopathic[1-6]. The remaining etiologies are histiocytosis, cerebral malformations, trauma, and familial[7-10]. Central DI is a rare disorder in children and adolescents and the reported case series are quite limited[1-6]. The authors wish to add more cases of central DI diagnosed between 1985 and 2000.

PATIENTS AND METHOD

The retrospective data bases of all patients who had documented cases of central DI between 1st January 1985 and 31st December 2000 at Songklanagarind Hospital were reviewed. The purpose was to identify the etiologies of patients initially presenting with central DI, therefore patients who developed central DI after intracranial surgery and those who developed central DI at the terminal stage of brain death or after severe head injury, were excluded.

There were 29 patients (16 males and 13 females) consistent with the diagnosis of central DI. The diagnosis was made by the standard water deprivation test in 21 patients. The rest of the patients were diagnosed by the clinical characteristics of polyuria accompanying hypernatremia and neurological symptoms (headache, impaired vision), for which cases the standard water deprivation test could not be done due to the alteration of consciousness and unstable vital signs. All 29 patients underwent computed tomography (before 1995, n=19) or magnetic resonance imaging (after 1995, n=10). Surgical tumor removal was performed in patients whose radiological imaging demonstrated intracranial mass (n=8; tumor in 7 patients and abscess in 1 patient). The definite diagnosis of intracranial tumor was based on the pathological findings. Structural brain anomalies were demonstrated in 2 patients which was septo-optic dysplasia in 1 patient and empty-sella syndrome in 1 patient. Langerhans' cell histiocytosis was diagnosed on the basis of clinical characteristics of exophthalmos, hepatosplenomegaly, skull defect and the tissue pathological section. The patients with no identifiable causes were considered as idiopathic central DI. Polyuria in all 29 patients improved after DDAVP administration.

Anterior pituitary function

Assessment of anterior pituitary hormone was performed in 21 patients (16 with idiopathic, 2 with brain tumors, 1 with pituitary abscess, 1 with empty-sella syndrome, and 1 with septo-optic dysplasia). Growth hormone (GH) status was evaluated by a clonidine test followed by an insulin tolerance test. Adrenocorticotropic hormone (ACTH) was assessed by an insulin tolerance test. All 29 patients were evaluated for free thyroxine (FT_4) and thyrotropin (TSH) levels.

Growth hormone deficiency was defined by a peak GH level of less than 10 ng/ml after clonidine and insulin tolerance tests. ACTH deficiency was documented by a peak cortisol level of less than 20 μg/dl after the insulin tolerance test. TSH deficiency was defined by serum FT_4 of less than 0.7 μg/ml with a low TSH level.

Follow-up visit

All patients except those with histiocytosis were followed-up at the pediatric endocrine clinic every 3-4 months for adjustment of DDAVP dosage, neurological evaluation, growth monitoring, and hormonal evaluation. Patients with the initial diagnosis of idiopathic central DI were scheduled for magnetic resonance imaging every 1-2 years depending on the neurological evaluation.

RESULTS

The clinical characteristics of the 29 patients according to the etiologies of central DI are shown in Table 1. The median age at diagnosis was 6.6 years, ranging from 1.5 to 14.9 years. There was a significant difference of the age at presentation between patients with intracranial mass and those with idiopathic central DI (p=0.027). Of 8 patients with intracranial mass (7 with brain tumor and 1 with pituitary abscess), 5 patients had neurological symptoms and signs : headache in all and impaired vision in 3 patients. The duration of polyuria was significantly longer and the volume of urine was significantly greater, whereas, the serum sodium was significantly lower in patients with idiopathic than those with intracranial mass. The serum osmolality and growth parameters were not statistically different between the groups. For anterior pituitary hormone assessment, all 29 patients were evaluated for FT_4 and TSH, whereas, 21 patients (16 patients with idiopathic, 2 patients with cerebral malformation and 3

Table 1. Clinical characteristics of patients with central diabetes insipidus at initial presentation.

	Intracranial mass		Idiopathic	Histiocytosis	SOD	ESS
	Tumor	Abscess				
No of cases	7	1	16	3	1	1
Sex (M : F)	3 : 4	F	11 : 5	1 : 2	M	F
Age (years)						
Median	12.1	12.2	6.5[a]	2.9	2.5	5.9
Range	5.8-13.5	-	1.5-14.9	2.7-4.0	-	-
Duration of polyuria (months)						
Median	2	1	4[b]	1	6	3
Range	1-12	-	1-48	1-4	-	-
Neuro symptoms (cases)						
Headache	5/7	No	No	3/3	No	No
Impaired vision	3/7	No	No	1/3	No	No
Urine volume (ml/kg/h)						
Median	4.32	2.5	8.07[c]	6.5	10.0	15.8
Range	2.7-6.8	-	3.1-15.1	6.5-6.7	-	-
Serum Na (mmol/L)						
Median	150	148	143[d]	146	142	148
Range	144-159	-	132-154	144-146	-	-
Serum osmolality (mosm/L)						
Median	297	296	296	-	294	295
Range	287-320	-	283-310	-	-	-
Weight SDS						
Median	-1.95	+3.4	-1.65	-1.5	-3.47	-2.76
Range	(-0.85)-(-3.74)	-	(+0.55)-(-4.86)	(-0.14)-(-1.8)	-	-
Height SDS						
Median	-2.28	+0.65	-1.31	-0.67	-4.44	-2.82
Range	(-0.83)-(-4.54)	-	(+0.96)-(-5.6)	(-0.23)-(-1.2)		
GH deficiency	2/2	Yes	5/16	Not done	Yes	Yes
ACTH deficiency	2/2	No	3/16	Not done	No	No
TSH deficiency	2/7	No	1/16	No	No	No

SOD = Septo-optic dysplasia
ESS = Empty-sella syndrome
SDS = Standard deviation score

[a] p=0.027 compared between tumor and idiopathic
[b] p=0.049 compared between tumor and idiopathic
[c] p=0.013 compared between tumor and idiopathic
[d] p=0.04 compared between tumor and idiopathic

patients with intracranial mass) were evaluated for GH and ACTH status. GH and ACTH deficiencies were documented in the 3 patients with intracranial mass and were suspected in another 3 patients who had short stature, but did not have the tests done. Secondary hypothyroidism was found in 2 out of 8 patients (25%) with intracranial mass. All 8 patients with intracranial mass underwent surgical mass removal and the pathological findings were germinoma in 4 patients, craniopharyngioma in 1 patient, pituitary adenoma in 1 patient, pinealoma in 1 patient, and pituitary abscess in 1 patient. For the patients with idiopathic central DI, 6 out of 16 patients (37.5%) had anterior pituitary hormone deficiency : 3 patients had GH and ACTH deficiencies; 2 patients had only GH deficiency and 1 patient had TSH deficiency. The two patients with cerebral malformations had GH deficiency without ACTH and TSH deficiencies.

All 16 patients with idiopathic central DI were followed-up for a median duration of 4.5 years (range 1.3 to 15.5 years). Three out of 16 patients were found to have an intracranial tumor after 1.3, 2.3 and 3.5 years of follow-up. Two of these 3 patients complained of headache for 1 month before cranial radiological imaging was performed (patients were followed-up for 1.3 and 2.3 years). For these 2 patients, the initial diagnosis of idiopathic central DI was made by the normal brain computed tomography before 1995, at which time magnetic resonance imaging was not available. Of these 2 patients, 1 patient (was followed-up for 1.3 years with age at initial evaluation 6.6 years) had GH deficiency and the other patient (was followed-up for 2.3 years

with age at initial evaluation 13.5 years) had TSH deficiency. The third patient who was followed-up for 3.5 years (the age at initial evaluation was 14.9 years) had neither neurological symptoms/signs nor endocrine abnormality, and cranial magnetic resonance imaging was performed as a routine follow-up. All 3 patients underwent surgical tumor removal and the pathological findings showed germinoma in 2 patients and lymphoma in 1 patient.

After the follow-up for a period of time, the patients who initially presented with central DI (histiocytosis was excluded) were documented to have intracranial mass in 11 out of 26 patients (42.3%). It was also observed that none of the children aged younger than 5 years at the time of evaluation were found to have an intracranial lesion whereas 11 out of 20 patients (55%) aged more than 5 years were associated with an intracranial lesion. This difference is statistically significant with p value<0.01.

DISCUSSION

The present study shows that the most frequent etiology of central diabetes insipidus is idiopathic, followed by intracranial tumors, histiocytosis, cerebral malformations and pituitary abscess. The present results were compared to previous studies as shown in Table 2. In the present series, the most common intracranial tumor is germinoma which is the same as in previous reports[1-6]. GH and ACTH status could be evaluated in only 2 patients with intracranial tumor and was found to be deficient in both patients. However, GH and ACTH deficiencies were suspected in another 3 patients with severe short stature or the deficiencies may be present in all patients with intracranial tumors, but the stimulation tests could not be done due to unstable clinical conditions at the time of evaluation. The measurements for insulin-like growth factor-1 and insulin-like growth factor binding protein-3 were not available at that time. One of the patients with an intracranial mass underwent surgery and was found unexpectedly to have a primary pituitary abscess which is an extremely rare condition in the pediatric age group[11]. The reported cases are mostly in adults and have an underlying condition such as sinusitis, dental problems, or pituitary apoplexy[12-16].

Idiopathic central DI is the diagnosis of exclusion after the radiologic imaging reveals a normal hypothalamus and pituitary gland. In the present study, 16 patients were diagnosed initially with central DI and all 16 patients had no neurological symptoms or signs. Six patients (37.5%) had other anterior pituitary hormone deficiencies: 3 patients had GH and ACTH deficiencies; 2 patients had only GH deficiency and 1 patient had TSH deficiency. Of these 6 patients associated with anterior pituitary hormone deficiency, there were 3 patients who had clinical features of hypopituitarism at the age of 2-3 years similar to that of septo-optic dysplasia but had neither ophthalmologic nor neuroimaging abnormalities.

The authors noticed that the clinical presentations of the patients with intracranial mass were different to those of patients with idiopathic central DI. The age at presentation of patients with idiopathic was significantly younger, the duration of poly-

Table 2. Etiologies of central diabetes insipidus from various reports.

Etiologies	Bode and Crawford[1] (1969)	Pomarede et al[2] (1980)	Greger et al[4] (1986)	Wang et al[5] (1994)	Maghnie[6] (2000)	Jaruratanasirikul (2001)
Intracranial tumors	21	46	34	19	18	7
Idiopathic	7	21	9	5	41	16
Histiocytosis	-	15	6	-	12	3
Malformation	3	1	10	7	-	2
Trauma	2	2	2	1	2	-
Infection	0	2	8	3	-	1
Familial	2	6	-	-	5	-
Autoimmune polyendocrinopathy	-	-	-	-	1	-
Terminal event	-	-	2	-	-	-
Mixed etiologies	-	-	2	-	-	-
Total	35	93	73	35	79	29

uria was longer and the urine volume was greater than those with an intracranial mass. The longer duration and greater amount of polyuria in patients with idiopathic is probably due to unnoticed polyuria by the parents, particularly in young children. The shorter duration of polyuria in patients with intracranial mass can be explained by the early detection by the patients themselves since they are old enough to notice this unusual polyuria. Moreover, the presence of neurological symptoms such as headache and impaired vision makes both the patients and their parents concerned and medical treatment is sought. The significantly higher serum sodium concentration in patients with intracranial mass is also explained by the less compensated polydipsia from the impaired neurological symptoms.

All 16 patients with an initial diagnosis of central DI were followed-up clinically every 3-4 months and radiologically every 12-24 months. The authors found 3 patients who were later detected to have an intracranial mass after a follow-up of 1.3, 2.3 and 3.5 years. However, 2 patients were diagnosed before 1995 at which time the neuroimaging study was computed tomography. The occult intracranial tumor or the thickened pituitary stalk might not be detected at that time. The delayed diagnoses of intracranial tumors in patients who were initially diagnosed as idiopathic have been reported[3,17-19]. The delays in neuroimaging have been mostly reported to be within 4 years after the initial presentation of diabetes insipidus[3,19]. However, delays as long as 11 and 21 years have also been reported [17,18]. Therefore, the authors emphasize that the diagnosis of central diabetes insipidus should be based on long-term and repeated neuroradiologic imaging. It is known that magnetic resonance imaging with contrast enhancement is the most useful investigation to detect subtle lesions in the brain, particularly the thickened pituitary stalk[19]. Therefore, contrast-enhanced magnetic resonance imaging should be performed yearly for at least 5 years after the initial diagnosis. A period of follow-up for at least 4-5 years without any detectable abnormality of the pituitary and the stalk seems to be reasonable in making certain diagnosis of idiopathic central DI[3, 19]. However, a yearly neuroimaging study is still recommended to detect the delayed manifestation of the occult intracranial tumor[17,18].

The most common intracranial tumor associated with central DI is craniopharyngioma, followed by germinoma[3,5,6]. However, most reported craniopharyngioma patients developed central DI after surgical tumor removal[4,5]. In the present report, the patients who developed central diabetes insipidus after intracranial surgery were excluded. From the present study, 6 patients with germinoma, whereas, only 1 patient with craniopharyngioma manifested initially with central DI. The studies of the natural history of germinoma have found that most germinoma patients usually present first with central DI at which time the tumor may not be detected by the neuroradiologic imaging resulting in the misdiagnosis as "idiopathic"[18-21]. The clinical course of the 3 patients in this study who were initially diagnosed as idiopathic and were later found to have germinoma and lymphoma emphasizes the difficulties in making the diagnosis of these occult tumors, and also emphasizes the necessity of close neurological evaluation and neuroimaging study.

Another significant observation from the present study is that all 11 patients with intracranial mass-associated DI were older than 5 years of age at the time of initial presentation. The youngest patient with intracranial tumor-associated DI was 5.7 years. The patients with nontumor-associated DI (idiopathic, cerebral malformations) were significantly younger at initial presentation. Of the 6 patients with nontumor-associated DI who were younger than 5 years old at initial presentation, none were found to have an intracranial tumor after follow-up for 5-15 years. However, 11 out of 20 patients (55%) whose age at initial presentation was older than 5 years did develop an intracranial mass ($p<0.01$).

In summary, the two most common etiologies of central DI in children and adolescents are intracranial tumor and idiopathic. Patients who are diagnosed initially as "idiopathic" should be closely followed-up both clinically and neuroradiologically to detect the delayed appearance of an occult intracranial tumor. Patients who present initially at an age older than 5 years are more likely to have an intracranial mass than idiopathic.

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REFERENCES

1. Bode HH, Crawford JD. Disorders of posterior pituitary in children. In : Gardner LI, ed. Endocrine and genetic diseases in children. Philadelphia: WB Saunders, 1969: 126-38.
2. Pomarede R, Czernichow P, Rappaport R, Royer P. Le diabete insipide pitressosensible de l'enfant. II Etude de 93 cas observes entre 1955 et 1978. Arch Fr Pediatr 1980; 37: 37-44.
3. Czernichow P, Pomarede R, Basmaciogullari A, Brauner R, Rappaport R. Diabetes insipidus in children. III. Anterior pituitary dysfunction in idiopathic types. J Pediatr 1985; 106: 41-4.
4. Greger NG, Kirkland RT, Clayton GW, Kirkland JL. Central diabetes insipidus : 22 years' experience. Arch Dis Child 1986; 140: 551-4.
5. Wang LC, Cohen ME, Duffner PK. Etiologies of central diabetes insipidus in children. Pediatr Neurol 1994; 11: 273-7.
6. Maghnie M, Cosi G, Genovese E, et al. Central diabetes insipidus in children and young adults. N Engl J Med 2000; 343: 998-1007.
7. Maghnie M, Arico M, Villa A, Genovese E, Beluffi G, Severi F. MR of the hypothalamic-pituitary axis in Langerhans cell histiocytosis. Am J Neuroradiol 1993; 13: 1365-71.
8. Cacciari E, Zucchini S, Ambrosetto P, et al. Empty sella in children and adolescents with possible hypothalamic-pituitary disorders. J Clin Endocrinol Metab 1994; 78: 767-71.
9. Yagi H, Nagashima K, Miyake H, et al. Familial congenital hypopituitarism with central diabetes insipidus. J Clin Endocrinol Metab 1994; 78: 884-9.
10. Gagliardi PC, Bernasconi S, Repaske DR. Autosomal dominant neurohypophyseal diabetes insipidus associated with a missense mutation encoding $Gly^{23} \rightarrow Val$ in neurophysin II. J Clin Endocrinol Metab 1997; 82: 3643-6.
11. Schwartz ID, Zalles MC, Foster JL, Burry VF. Pituitary abscess : An unusual presentation of "aseptic meningitis". J Pediatr Endocrinol Metab 1995; 8: 141-6.
12. Jain KC, Varma A, Mahapatra AK. Pituitary abscess : A series of six cases. Br J Neurosurg 1997; 11: 139-43.
13. Jadhav RN, Dahiwadkar HV, Palande DA. Abscess formation in invasive pituitary adenoma : Case report. Neurosurgery 1998; 43: 616-9.
14. Kashiwagi N, Fujita N, Hirabaki N, et al. MR findings in three abscesses. Case reports. Acta Radiol 1998; 39: 490-3.
15. Sabbah P, Bonardel G, Herve R, et al. CT and MRI findings in primitive pituitary abscess. A case report and review of literature. J Neuroradiol 1999; 26: 196-9.
16. Somali MH, Anastasiou AL, Goulla DG, Polyzoldes C, Avramides A. Pituitary abscess presenting with cranial nerve paresis. Case report and review of literature. J Endocrinol Invest 2001; 24: 45-50.
17. Sherwood MC, Stanhope R, Preece MA, Grant DB. Diabetes insipidus and occult intracranial tumors. Arch Dis Child 1986; 61: 1222-4.
18. Stanhope R, Preece MA, Grant DB, Brook CGD. Is diabetes insipidus during childhood ever idiopathic? Br J Hosp Med 1989; 41: 490-1.
19. Mootha SL, Barkovich AJ, Grumbach MM, et al. Idiopathic hypothalamic diabetes insipidus, pituitary stalk thickening, and the occult intracranial germinoma in children and adolescents. J Clin Endocrinol Metab 1997; 82: 1362-7.
20. Ramelli GP, von der Weid N, Stanga Z, Mullis P, Buergi U. Suprasellar germinomas in childhood and adolescence : Diagnostic pitfalls. J Pediatr Endocrinol Metab 1998; 11: 693-7.
21. Ono N, Kakegawa T, Zama A, Nakamura M, Inoue HK, Tamura M. Suprasellar germinomas : Relationship between tumor size and diabetes insipidus. Acta Neurochir 1992; 114: 26-32.

สาเหตุของโรคเบาจืดในเด็ก : ประสบการณ์ 15 ปีในโรงพยาบาลสงขลานครินทร์

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โรคเบาจืดชนิด central diabetes insipidus (DI) เป็นโรคที่พบน้อยในเด็ก ผู้วิจัยได้ทำการศึกษาย้อนหลังจากเวชระเบียนผู้ป่วยที่ได้รับการวินิจฉัยโรคเบาจืดชนิด central DI ในโรงพยาบาลสงขลานครินทร์ตั้งแต่ พ.ศ. 2528 ถึง พ.ศ. 2543 พบมีจำนวนผู้ป่วยทั้งสิ้น 29 ราย เป็นเพศชาย 16 รายและเพศหญิง 13 ราย ผู้ป่วยทุกรายได้รับการตรวจทางรังสีวิทยาโดยวิธี computed tomography หรือ magnetic resonance imaging ของเนื้อสมองเพื่อตรวจค้นสาเหตุ อายุกึ่งกลางของผู้ป่วยขณะได้รับการวินิจฉัยคือ 6.6 ปี (พิสัย 1.5 – 14.9 ปี) สาเหตุของ central DI มีดังนี้คือ เนื้องอกในสมอง 7 ราย (ร้อยละ 24.1), histiocytosis 3 ราย (ร้อยละ 10.3), septo–optic dysplasia 1 ราย (ร้อยละ 3.5), empty–sella syndrome 1 ราย (ร้อยละ 3.5), ฝีในต่อมใต้สมอง 1 ราย (ร้อยละ 3.5) และไม่ทราบสาเหตุ 16 ราย (ร้อยละ 55.1) ผู้ป่วย central DI ที่ไม่ทราบสาเหตุทุกรายได้รับการติดตามอย่างสม่ำเสมอโดยมีระยะเวลากึ่งกลางของการติดตาม 4.5 ปี (พิสัย 1.3–15.5 ปี) ผู้ป่วย 3 รายจากทั้งหมด 16 ราย (ร้อยละ 18.8) พบมีเนื้องอกในสมองหลังจากติดตามเป็นเวลานาน 1.3, 2.3 และ 3.5 ปี ตามลำดับ สิ่งที่น่าสังเกตจากการศึกษานี้คือ ผู้ป่วยที่มีอายุต่ำกว่า 5 ปี ขณะเริ่มมีความผิดปกติ (ทั้งนี้ไม่นับรวมผู้ป่วย histiocytosis) มีโอกาสที่จะพบเนื้องอกในสมองได้น้อยกว่าผู้ป่วยที่มีอายุมากกว่า 5 ปี (ร้อยละ 0 และร้อยละ 55 ตามลำดับ) โดยมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ($p<0.01$)

จากผลการศึกษา สามารถสรุปได้ดังนี้ 1) สาเหตุที่พบบ่อยของโรคเบาจืดชนิด central DI คือ เนื้องอกในสมองและไม่ทราบสาเหตุ 2) ผู้ป่วยโรคเบาจืดที่ไม่ทราบสาเหตุควรได้รับการติดตามระยะยาวโดยการตรวจ magnetic resonance imaging ของสมอง เพื่อวินิจฉัยเนื้องอกในสมองที่ในระยะแรกตรวจไม่พบ

คำสำคัญ : เบาจืด, เบาจืดที่ไม่ทราบสาเหตุ, เบาจืดที่มีสาเหตุจากระบบประสาทส่วนกลาง, เนื้องอกในสมอง

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