Diencephalic Syndrome: A Rare and Easily Overlooked Cause of Failure to Thrive

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Background : *Diencephalic syndrome (DS) is an uncommon cause of failure to thrive in infants and young children. The major manifestations are emaciation, hyperkinesia, and euphoria. Most patients have a tumor in the hypothalamic-optic chiasma region.*
Case Report : *Two children, aged 14 months and 5 years 9 months, who presented with classic features of DS at an onset of 2 and 3 months respectively, were reported. Neurologic examination was normal, except for papilledema in the second child. Imaging of the brain showed a suprasellar mass, identified as pilocytic astrocytoma in both cases. The first case was lost to follow up. The latter underwent partial resection of the tumor and received radiotherapy postoperatively. He gradually gained in weight and height.*
Conclusion : *DS should be a differential diagnosis in any children with emaciation despite adequate caloric intake and an inappropriately euphoric mood. Awareness of this syndrome, careful history taking, general detail as well as neurological examination including fundoscopic examination and appropriated investigations are crucial.*

Keywords : *Diencephalic syndrome, Failure to thrive*

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Diencephalic syndrome (DS) is a rare and easily overlooked cause of failure to thrive (FTT) in infants and young children. It is characterized by emaciation despite normal caloric intake, hyperkinesia and euphoria with minimal neurologic signs, that are attributed to hypothalamic dysfunction[1]. The majority of cases are due to a low grade astrocytoma in the hypothalamic or optic chiasma region[2,3].

The objectives of this paper were to describe two cases of DS caused by pilocytic astrocytroma and alert pediatricians who look after children with FTT to recognize this syndrome.

Case Report

Case 1

A 14–month–old boy had a 12-month history of failure to gain weight without vomiting or diarrhea. He was a full term newborn with a birth weight of 2,800 gm (at the 10th percentile) after an uncomplicated pregnancy. His developmental milestones were normal. At admission, his height, weight, and head circumference were 71 cm, 6 kg, and 43 cm, respectively (all below the 3rd percentile). Physical examination revealed a markedly emaciated and hyperactive child but the rest of the examination showed normal results including those for neurologic signs (Fig.1). Investigation revealed normal complete blood count,

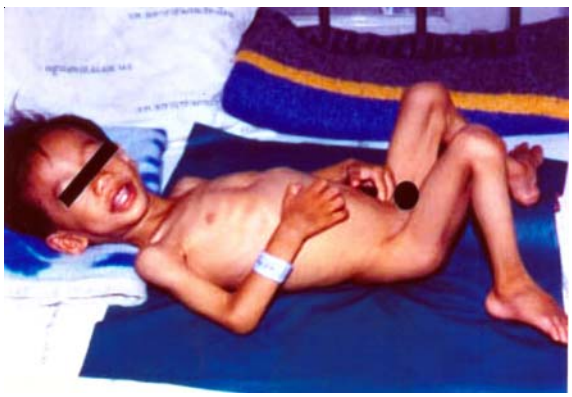

Fig. 1 Case 1: A 14-month-old boy with failure to thrive and an inappropriately euphoric mood

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electrolytes, stool examination, stool reducing substance, and renal and liver function. HIV antibody test was negative. Magnetic Resonance Imaging (MRI) of the brain showed a lobulated mass causing obstruction of the 3rd ventricle with seeding in the right ambient cistern. The patient underwent a craniotomy and the diagnosis of pilocytic astrocytoma was made. Unfortunately, he was too young to receive radiation therapy and was finally lost to follow up.

Case 2

A 5 year 9 month old boy had a history of vomiting 3-4 times per day since 3 months of age. Despite adequate caloric intake, he failed to gain weight. He had normal consistency of the stool and normal urine output. His developmental milestones were normal. His height and weight were 71 cm, and 6 kg, respectively (both below the 3rd percentile). Nevertheless, his head circumference was 52 cm (at the 75th percentile). In contrast to his emaciation, he was active, and had an inappropriately euphoric mood. Neurologic signs were normal, except for papilledema. Laboratory investigation including complete blood count, electrolytes, lipid profiles, and renal and liver function were normal, and HIV antibody test was negative. Preoperative endocrinologic evaluations including bone age were normal. Skull films revealed separated sutures and an enlarged sella turcica. Computer Tomography (CT) of the brain showed a round-shaped, inhomogeneous enhancing hypodense mass with no calcification in the suprasellar region, thus resulting in ventricular dilatation (Fig.2).

The patient underwent a craniotomy. Partial resection of the tumor with ventriculoperitoneal shunt was carried out. The histopathologic report revealed pilocytic astrocytoma. After surgery, he subsequently developed transient diabetes insipidus and cerebral salt wasting, which lasted for 2 weeks. After radiation therapy, he gradually gained in weight and height. At 10 months after treatment, his height and weight were 98.5 cm, and 12 kg, respectively.

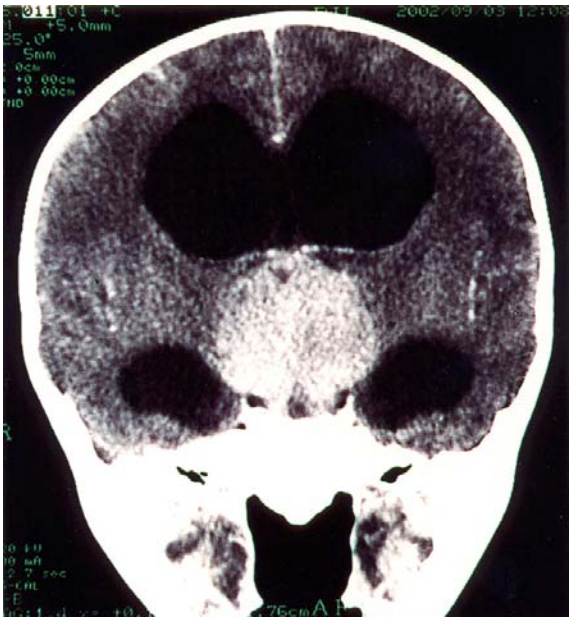

Fig. 2 Case 2: CT of the brain showed a suprasellar mass, measuring about 4.5x4.8x4.7 cm, which caused ventricular dilatation.

Discussion

DS is a relatively uncommon cause of FTT. It is characterized by emaciation despite adequate caloric intake, alert appearance, hyperkinesia and euphoria. These findings are in contrast to the features found in other causes of FTT[1-3]. Apart from emaciation and euphoric mood, general physical signs are usually normal. Fundoscopic and eye movement abnormalities were reported in approximately half of the patients[2-4]. Clinical features of DS that were presented in the presented patients are shown in Table 1[2]. Vomiting, with a reported range of 13-68%[2,4], was seen in the second case. Although papilledema is rarely found, it was also seen in the second patient[2]. Most cases of DS have the age of onset within the first year of life, which is similar to the presented patients. However, 15% of cases have onset of symptoms after 1 year old[2,3]. Although DS has been described in infants and young children, it has been reported in adolescents with dysgerminoma, and adults with craniopharyngioma[6,7]. The average lag time from the onset to diagnosis is 7 months[2], probably due to minimal physical and neurologic findings. Moreover, the diagnosis of DS is usually delayed until the common causes of FTT have been

Table 1. Clinical features of diencephalic syndrome[2]

Clinical features	% of total cases	Clinical features	% of total cases
Emaciation	100	Nystagmus	55
Alert appearance	87	Hydrocephalus	33
Hyperkinesis	72	Optic atrophy	24
Vomiting	68	Tremor	23
Euphoria	59	Sweating	15
Pallor	55	Papilledema	< 5

excluded. In the second patient, it took 5 years to make the diagnosis. This may be due to the lack of awareness of this syndrome.

Most patients with DS have a tumor in the hypothalamic or optic chiasma region. Eight percent of the patients have a tumor in the region surrounding the fourth ventricle. Approximately 80 % of tumors are low grade astrocytoma, or more precisely, juvenile pilocytic astrocytoma, as found in the presented patients[2]. On CT, low grade astrocytoma is isointense to slightly hyperintense, enhancing homogeneously. On MRI, the lesions are isointense to slightly hyperintense on T1 weighted images, and hyperintense on proton density- and T2 weighted images, enhancing homogeneously[4]. DS associated with ependymoma, ganglioglioma, dysgerminoma, epidermoid cyst and craniopharyngioma has been rarely reported[2,3,6-8].

Endocrinologic studies frequently show no diurnal variation in plasma cortisol, failure of response to metyrapone, occasionally central hypothyroidism, and abnormalities in growth hormone (GH) regulation. Basal GH was found to be elevated, and the paradoxical response to various stimuli was observed such as the exaggerated response of GH to L-DOPA, and partial suppression by the oral glucose tolerance test[5,9]. Endocrinologic investigation, performed pre- and postoperation in the second case, showed a normal thyroid function and morning cortisol level.

The pathophysiology of DS remains unclear. This might be due to distortion of the brain architecture resulting in abnormal brain function, increasing energy expenditure with a consequent hypermetabolic state, and abnormalities in hormonal regulation. Abnormal GH regulation might play a role in the pathogenesis of DS, and result in lipolysis and complete absence of subcutaneous tissue. β-lipoprotein (β-LPH) is another hormone that might play a role, as it has weak lipolytic activity and can increase GH release. Increased β-LPH, either secondary to the pressure effect of the tumor or due to excess secretion by the tumor, might explain both lipolysis and abnormal GH. Excess β-LPH and its morphinomimetic peptide might lead to the euphoria and alertness in DS[8,9].

Without treatment, the majority of patients die within 12 months after the onset of symptoms. However, patients who stayed alive while untreated for 2 to 4 years have been reported[2,3]. This is similar to our second patient who survived untreated for 5 years before the diagnosis. Treatment including surgical excision of the tumor, chemotherapy and radiation therapy depends on the patient's age and clinical status. Total surgical excision would be the ideal treatment of hypothalamic glioma, but it is usually impossible to perform. Radiotherapy alone, or partial resection of the tumor followed by radiation therapy improve clinical status and survival for longer than 5 years. However, radiotherapy in children younger than 5 years of age results in cognitive impairment, hypopituitarism, and secondary malignancy. Despite the benign nature of this tumor, chemotherapy consisting of carboplatin and vincristine results in weight gain, tumor shrinkage, and relative lack of toxicity. It also significantly delays the need for radiation therapy[10,11].

Conclusion

Although DS is rare and may be easily overlooked as a cause of failure to thrive, it should be a differential diagnosis in any children with emaciation despite adequate caloric intake and an inappropriately euphoric mood. Awareness of this syndrome, careful history taking, general detail as well as neurologic examination including fundoscopic examination, and appropriate investigations (CT or MRI of the brain) are crucial.

References

1. Russel A. A diencephalic syndrome of emaciation in infancy and childhood. Arch Dis Child 1951; 26: 274-9.
2. Burr IM, Slonium AE, Danish RK, Gadoth N, Butler IJ. Diencephalic syndrome revisited. J Pediatr 1976; 88: 439-44.
3. Addy DP, Hadson FP. Diencephalic syndrome of infantile emaciation: Analysis of literature and report of further 3 cases. Arch Dis Child 1972; 47: 338-43.
4. Poussaint TY, Barnes PD, Nichols K, Anthony DC, Cohen L, Tarbell NJ, et al. Diencephalic syndrome: Clinical features and imaging findings. Am J Neuroradiol 1997; 18: 1499-505.
5. Ertem D, Acar Y, Alper G, Kotiloglu E, Pehlivanoglu E. An uncommon and often overlooked cause of failure to thrive: Diencephalic syndrome. J Pediatr Gastroenterol Nutr 2000; 30: 453-7.
6. Moreno VJM, Fernandez CF, Gallego FME, Munoz GA, Manzanares LMJ, Rodrigo AM. Diencephalic syndrome: An uncommon cause of malnutrition. An Esp Pediatr 2002; 56: 466-71.
7. Sharma RR, Chandy MJ, Lad SD. Diencephalic syndrome of emaciation in an adult associated with a suprasellar craniopharyngioma - a case report. Br J Neurosurg 1990; 4: 77-80.
8. Greenes D, Woods M. Case report: A 4 month old boy with severe emaciation, normal linear growth, and a happy effect. Curr Opin Pediatr 1996; 8: 50-7.

9. Drops SLS, Guyda HJ, Colle E. Inappropriate growth hormone release in diencephalic syndrome of childhood: case report and 4 year endocrinological follow up. Clin Endocrinol 1980; 13: 181-7.
10. Arita K, Kurisu K, Sugiyama K, Itoh Y, Hotta T, Sogabe T, et al. Long term results of conventional treatment of diencephalic pilocytic astrocytroma in infants. Childs Nerv Syst 2003; 19: 145-51.
11. Gropman AL, Packer RJ, Nicholson HS, Verzina LG, Jakacki R, Geyer R, et al. Treatment of Diencephalic syndrome with chemotherapy. Cancer 1998; 83: 166-72.

กลุ่มอาการไดเอนเซปฟาลิก (Diencephalic syndrome) สาเหตุของภาวะทุพโภชนาการที่ถูกมองข้าม

ประไพ เดชคำรณ, สุรชัย ลิขสิทธิ์วัฒนกุล, เกวลี อุณจักร

รายงานผู้ป่วยกลุ่มอาการไดเอนเซปฟาลิก 2 ราย อายุ 14 เดือน และ 5 ปี 9 เดือนตรวจร่างกายระบบประสาทปกติ ยกเว้นในผู้ป่วยรายที่ 2 พบจอประสาทตาบวม ภาพรังสีของสมองพบเนื้องอกบริเวณเหนือต่อเซลลา ผลชิ้นเนื้อเป็น Pilocytic astrocytoma ผู้ป่วยรายแรกขาดการติดต่อ รายที่สองอาการดีขึ้นหลังการรักษาด้วยการตัดเนื้องอกและรังสีรักษา

กลุ่มอาการไดเอนเซปฟาลิกเป็นสาเหตุของภาวะทุพโภชนาการในเด็กที่พบไม่บ่อย เกิดจากเนื้องอกในสมองส่วนไฮโปทาลามัสและเส้นประสาทตา ทำให้การทำงานของสมองผิดปกติ โดยมีอาการซูบผอมทั้งที่ได้รับสารอาหารเพียงพอ และมีอารมณ์ดีร่าเริงโดยไม่สมเหตุผล ซนไม่อยู่นิ่ง ควรนึกถึงโรคนี้ในผู้ป่วยที่มีอาการดังกล่าว