CENTRAL PRECOCIOUS PUBERTY FOLLOWING DIENCEPHALIC SYNDROME: A CASE REPORT

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The diencephalic syndrome (DS) is one of the rare causes of failure to thrive (FTT) in pediatric age group. It is manifested by progressive emaciation in an apparently alert and cheerful young child. This syndrome is almost exclusively seen in infants and young children and most patients have a space-occupying lesion of the hypothalamic region. We present a case of DS, a 3-year-old boy who was initially admitted to our hospital because of severe FTT that began at the age of 4 months. Computerized tomography scan and magnetic resonance imaging demonstrated a large tumor occupying the hypothalamic region. After surgical removal of the tumor, radiotherapy with 5,000 rads of linear accelerator (LINAC) was directed at the tumor site. He was readmitted at the age of 5 with signs of precocious puberty. The interesting point with this case was that central precocious puberty was associated with diencephalic syndrome.

Keywords • diencephalic syndrome • failure to thrive • precocious puberty

Introduction

Failure to thrive (FTT) is a common problem in pediatric practice and accounts for 1% to 5% of all referrals to children’s hospitals or tertiary-care centers. It may result from unfavorable environmental conditions, emotional deprivation, or organic disease. The causes of organic FTT are numerous and malfunction of any organ system in the body can be responsible for FTT. When the differential diagnosis of organic FTT is considered, diencephalic syndrome (DS) stands near the bottom of the list.

We are reporting here, a case of FTT due to DS. He developed central precocious puberty 2 years after treatment. Precocious puberty following DS has rarely been noted in the medical literature.

Case Report

A 3-year-old boy was initially admitted because of severe FTT and emaciation (Figure 1) to the Department of Pediatric Endocrinology of Mashhad University of Medical Sciences, Mashhad, Iran.

He had been born following a normal pregnancy and delivery weighing 2.7 kg at birth. At 3 months of age, his weight was 5.3 kg. At 4th month, he began to become emaciated despite breast feeding and adequate food intake. On admission, he weighed 6.5 kg while several laboratory studies including gastrointestinal and urinary tracts investigations had already been done for evaluation of his FTT. The family history was not remarkable. A physical examination revealed a severely emaciated, alert, and pale child with a horizontal nystagmus. Laboratory data showed that blood cells counts, renal and liver function tests, and the levels of plasma glucose and electrolytes were normal. Brain computerized tomography (CT) scan without contrast media demonstrated a large tumor in hypothalamic region with suprasellar extension and marked dilatation of the lateral ventricles (Figure 2A). Magnetic resonance imaging (MRI) of the brain showed a contrast-enhanced mass (Figure 2B).

The tumor was shown to be astrocytoma on
Central precocious puberty following diencephalic syndrome

histopathologic examination. Surgical removal of the hypothalamic pilocytic astrocytoma and radiotherapy with 5,000 rads of linear accelerator (LINAC) led to satisfactory results.

Thereafter, the parents refused to follow up the patient. He was readmitted, however, at the age of 5 years because of precocious puberty. He was found to have a Tanner stage II-III testis, penile enlargement, and pubic hair.

On the latter admission, his weight and height were 15.5 kg and 101 cm, respectively. Endocrinologic studies were as follows: basal plasma level of growth hormone (GH): 16.2 mIU/mL, luteinizing hormone (LH): 12 mIU/mL, follicle-stimulating hormone (FSH): 5 mIU/mL, testosterone: 9.5 nmol/L, cortisol: 21.5 ng/dL, T4: 7 mg/dL, thyroid-stimulating hormone (TSH): 1.5 mIU/mL, and dehydroepiandrosterone sulfate (DHEAS): undetectable.

Luteinizing hormone-releasing hormone (LHRH) test showed an over-response of LH and FSH. On admission, brain MRI was normal. Treatment with a long-acting LHRH agonist was started and 2 months later, serum testosterone was 0.4 nmol/L while the basal levels of LH and SH were 0.2 and 0.1 mIU/mL, respectively.

**Discussion**

The diencephalic syndrome is a rare disorder of infancy characterized by severe emaciation and FTT despite apparently normal calorie intake. DS is well described in literature and the majority of cases are due to low-grade gliomas of the anterior hypothalamus or optic nerve. Pilocytic astrocytoma is a slowly growing low-grade astrocytoma, which most commonly arise in children and adolescents with a pick incidence around 10 – 12 years of age. This tumor is characteristically located in midline structures (e.g., cerebellum, third ventricular region, optic chiasma/nerves, and brainstem). Compared with other astrocytomas, pilocytic astrocytoma is well circumscribed with limited tendency to infiltrate the surrounding brain tissue, having a more favorable outcome than that of diffusely infiltrating lesions. On microscopic examination, the tumor is composed of bipolar cells with long, thin “hair-like” processes that are glial fibrillary acidic protein-positive (GFAP-positive). Rosenthal fibers, microcysts, and an increase in the number of blood vessels are often present.

The most striking clinical finding of DS is FTT due to depletion of subcutaneous fatty tissue, frequently abnormal eye movements, alert appearance, euphoria, irritability, and vomiting.

Cases of precocious puberty following diencephalic syndrome associated with a hypothalamic tumor are quite rare in the literature. The mechanism by which hypothalamic-pituitary (HP) lesions induce premature activation of the HP gonadal axis is unknown. The role of the increased pressure on the HP area has been discussed and chronic minimally increased intraventricular pressure may be involved in its induction.

Central precocious puberty in boys is almost invariably secondary to central lesions. However, in this case, precocious puberty may be due to central nervous system (CNS) surgery or irradiation.

The ideal treatment of DS is total surgical excision of the tumor; nevertheless, total removal of the tumor is usually impossible given its difficult anatomic location. Consequently, partial resection of the tumor followed by radiation therapy or irradiation alone has been performed most frequently. Gropman et al recommended chemotherapy with a carboplatin and vincristine regimen for DS.

Markesebery et al described a patient with DS who survived 12 years following subtotal removal and cobalt irradiation.
Finally, with widespread use of CT and MRI in medical practice today, DS is diagnosed more quickly and easily. Close endocrinologic investigations should be considered in following up the cases.

References


