Case Report

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Failure to Thrive: A Rare Case Report

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Abstract

Neurofibromatosis type 1 (NF1) is an autosomal dominant disease with an incidence of about 1 in 2500–3300. Neurological manifestations may be due to involvement of the cerebrum, spine, cranial nerves and peripheral nerves. The severity of NF1 depends on the area of the brain involved. In children they may present with features of failure to thrive, when the lesion involves the hypothalamic area . We are presenting a rare case of diencephalic syndrome with involvement of hypothalamus, chiasm, suprasellar region, midbrain and cerebellum.

Keywords: Neurofibromas Type 1; Diencephalic Syndrome; Failure to Thrive; Optic Nerve Glioma; Unidentified Bright Objects.

Introduction

Failure to thrive is a common health and social problem for paediatricians. Diencephalic syndrome (DS) is a rare condition associated with central nervous system tumors presenting as failure to thrive with proper caloric intake and no structural impairment. Despite the importance of this syndrome, little is known of its pathophysiology. DS is a rare cause of failure to thrive in infants and young children. It is associated with neoplastic lesions of the hypothalamic-optic chiasmatic region. This syndrome is characterized by profound emaciation, despite a normal or slightly diminished calorie intake. Linear growth is usually maintained.

Case Report

A 4-year-old girl was brought to our OP department for evaluation of recent loss of weight. She was the only girl child born out of non-consanguinous marriage to a 37-year-old father with neurofi bromatosis and a 26-year-old mother. Her birth weight was 2.65 kg with adequate weight gain thereafter with developmental delay predominantly in the fine motor field (Development Quotient –35%) and with good gross motor and linguistic skills. She developed recent onset left eye squint with restricted lateral movement over the past one year. The child does not have polyuria, exertional dyspnea, generalized edema or abdominal distension.

On examination child was hyperactive with cachexia, thin triangular face with stable vitals, with left eye esotropia of 30^0. There were multiple café au lait spots with neurofibromas. Her height was between 10^{th} and 25^{th} centile and weight was below 3^{rd} centile. No signs of micronutrient deficiency. Cranial nerve examination revealed sluggish left eye pupillary reflex and left lateral rectus palsy with bilateral cerebellar signs. Other system examination was normal.

Laboratory tests were performed to evaluate the nutritive status of the patient. Complete blood cell counts, fasting blood sugar levels, and serum total protein/albumin levels were obtained. Thyroid hormone levels were examined to evaluate thyroid function. All test were within normal limits. Imaging studies were performed. There is isointense lobulated lesion in thalamus, hypothalamus, chiasm and suprasellar region with omit intense contrast enhancement (Figure 1) . The same lesion is hyperintense in T 2 image partially inverting on T 2

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FLAIR sequence. Both optic nerves are thickened. There is a isointense in left orbital cone extending from the left optic nerve. This is consistent with a diagnosis of optic nerve glioma involving the chiasm extending to thalamus, hypothalamus and left optic nerve. There is hyperintensity of right midbrain on T2 and FLAIR with no contrast enhancement in T1 weighted image. There is an area of hyperintensity in left cerebellum. These lesions are consistent with Unidentified Bright Objects (UBO) involving the left cerebellar hemisphere(dentate nucleus) and right midbrain. In addition there is right cerebellar hypoplasia (Figure 2).

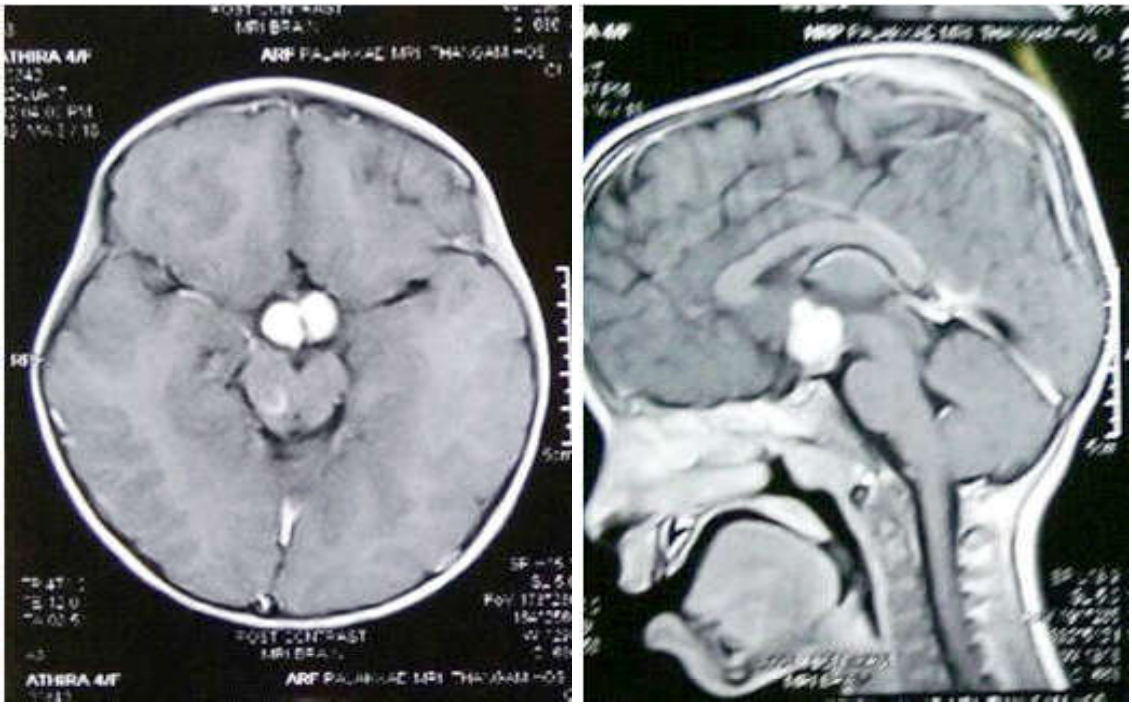

Fig. 1: Isointense lobulated lesion in thalamus, hypothalamus, chiasm and suprasellar region with intense contrast enhancement

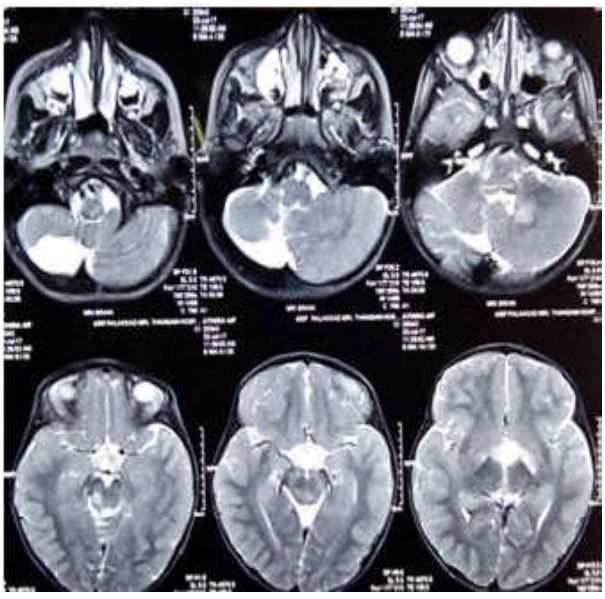

Fig. 2: Hyperintensity of midbrain on T2 and FLAIR with no contrast enhancement in T1 weighted image(UBO) and in left cerebellum. In addition there is right cerebellar hypoplasia

Discussion

Failure to thrive (FTT) can be defined as a syndrome characterized by failure of physical growth, malnutrition, and retardation of motor and social development. It may result from unfavorable environmental conditions, emotional deprivation, or organic disease. The underlying question in the presence of suspected FTT is the source of malnutrition. Diagnostic efforts should be directed toward determining whether the problem is secondary to inadequate intake, inadequate absorption, or excessive calorie requirement.

Diencephalic syndrome, or Russell's syndrome, was first described by Russel [1]. It is characterized by major features (severe emaciation despite normal or slightly decreased caloric intake, locomotor hyperactivity, and euphoria) and minor features (skin pallor without anemia, hypoglycemia, and hypotension). The tumors most often associated with the diencephalic syndrome are optic and hypothalamic astrocytomas.

Because the diencephalic tumor is slow to disclose its presence by positive neurologic signs, nystagmus—horizontal or rotatory and usually beginning unilaterally—may be the earliest and the only neurologic finding in DS. Other optical findings may be pallor of the optic nerve or optic nerve atrophy, but these are late findings. Papilledema is noted only rarely, despite the location of the tumor.

The mechanisms of failure to thrive in diencephalic syndrome are not fully explained. Pathogenesis of weight loss in diencephalic syndrome was proposed in previous studies. It has been suggested that increased level of Growth Hormone (GH) may explain the extreme loss of subcutaneous fatty tissue, which may be the result of lipolysis stimulated by increased GH(2). Another hypothesis for the severe wasting seen in DS may be the disruption of normal appetite control by the tumor, because the satiety center is located in the ventromedial hypothalamus. An elevated GH level with a paradoxical response to a glucose load, partial GH resistance, and excessive β-lipotropin (a lipolytic peptide) secretion, resulting in increased lipolysis and subsequent loss of subcutaneous adipose tissue also lead to failure to thrive [3]. Furthermore, an increase in energy expenditure which affected growth and weight has also been reported in DS.

The natural course of DS is varied. Without treatment, average survival is approximately 6 months to 2 years after the diagnosis, although survival for 8 to 12 years after diagnosis has been reported [3]. The ideal treatment of patients with DS is total surgical excision of the tumor. It has been shown that total excision of the tumor yields a 25-year survival rate in excess of 90% [4]. However, the deep, midline location of the tumor usually makes total surgical excision impossible. Radiotherapy has its own set of adverse effects on growth, endocrine function, and most important, neuropsychiatric development [5]. It has been found that the neuropsychiatric effects of radiation were most significant in patients less than 5 years of age [6]. Because of the concerns about the severe adverse effects of radiation in infants, chemotherapy has become an option for the treatment of young patients with diencephalic tumors [7].

Neurofibromatosis type 1 (NF1) results in the appearance of hyperintensities on T2-weighted images in the brain; these hyperintensities are referred to as unidentified bright objects [8]. The exact nature of UBOs remains unclear. Histological analysis has shown that UBOs result from a vacuolar or spongiotic alteration in the white matter caused by intramyelinic edema. These cerebral microstructural changes are transient, as has been shown by longitudinal MRI studies of patients over the first decades of life. UBOs in NF1 were more commonly found in the basal ganglia followed by the thalamus and cerebellum, with the brain stem being the least involved. However, after the first decade, although some lesions remained unchanged, most lesions will disappear or decrease in size [9].

Other intracranial manifestations of NF1 include , characteristic NF1 "spots" and low-grade neoplasms. The NF1 "spots" are regions of signal abnormality involving the basal ganglia, thalami, dentate nuclei, cerebellar peduncles, optic radiations, and brainstem in children and adolescents; they are thought to represent regions of myelin vacuolization [9]. They are hyperintense on T2 sequences and typically iso-to mildly hyperintense on T1 images.

The most common CNS neoplasm associated with NF1 is a low-grade optic pathway glioma [10]. The presence of bilateral optic nerve gliomas is considered pathognomonic for NF1. The tumors cause enlargement, elongation and "buckling" of the optic nerve, resulting in the "dotted i" appearance on axial images. Low-grade cerebellar, brainstem, tectal plate, and basal ganglia gliomas are also common and have an increased incidence in the setting of NF1; the vast majority are pilocytic astrocytomas, although high-grade gliomas may occasionally be seen as well. Sphenoid wing dysplasia is a characteristic finding of NF1 but is relatively uncommon [11].

A delay in diagnosis may occur because brain tumor is not considered early. Therefore, DS should be considered as a differential diagnosis in any child with failure to gain weight with normal linear growth, and imaging studies should be performed even if there are no additional neurological symptoms.

Diencephalic syndrome is rare but potentially morbid and general pediatricians should have a high and early index of suspicion of CNS neoplasms as a cause of unexplained failure to thrive in early childhood.

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