

Neurotuberculosis as a Cause of Obesity

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Abstract

Childhood obesity, taking the form of pandemic in the present era owing to the food habits, lifestyle etc, is the main cause of adult onset diseases. Obesity is the major risk factor for insulin resistance and diabetes, hypertension, cancer, gall bladder disease, and atherosclerosis in adulthood. Obesity being multi-factorial various genetic, anatomic, environmental factors are implicated to its etiogenesis. While evaluating the causes of obesity in a child, in addition to the common causes, diseases involving hypothalamus should not be overlooked. We are discussing here a 9 year male child who reported to us for obesity and neurotuberculosis as the etiology was established.

Key Words

Obesity, Neurotuberculosis, Hypothalamus

Introduction

Hypothalamus, the most evolutionary conserved regions of mammalian brain involved in maintaining homeostasis of life, integrates sensory and hormonal inputs and provides coordinated responses through motor outputs to key regulatory sites. The patterned outputs to various effector sites result in coordinated endocrine, behavioral, and autonomic responses to maintain the homeostasis. (1,2) Leptin, an established mediator of body weight and other neuroendocrine functions, is secreted by adipose cells. Its high levels decrease food intake and increase energy expenditure. The childhood obesity which is taking the form of pandemic is multifactorial, i.e. various genetic, anatomic, environmental factors are implicated to this disease (1-4). While evaluating the cause of obesity in a child, in addition to the common causes, diseases involving hypothalamus should not be overlooked. We are discussing here 9 year male child who reported to us for obesity and neurotuberculosis as the etiology was established.

Case Report

A 9 year male child, 2nd in birth order, born to a consanguineous marriage, presented with history of significant weight gain, lethargy, vague pain in both lower limbs and loss of interest in the surroundings for last 6 months. There was history of hyperphagia along with physical inactivity. There was no history of fever, rash, swelling in any joint. History of contact with patient of pulmonary Koch's was present. There was no history of

abnormal weight gain in the family. Antenatal and perinatal history was normal. Milestones were consistent with age prior to illness. On examination the child was conscious, cooperative and well oriented. Vitals were normal. General physical examination was normal, no peculiar facies was noted. BCG scar was absent. Systemic examination did not reveal anything abnormal clinically. Tanner stage was, Pubertal 1, Gonadal 1 and Testicular volume-4-6ml. Eye examination including fundus and ENT examination were normal. Anthropometry: Weight 40 kg (as expected 25-27 kg), Height 125cm, Upper Segment: Lower Segment ratio 1:1, Head circumference 53cm, Chest circumference 77cm, Mid arm circumference 20cm, Body Mass Index(BMI) 25.64 Kg/Sq.m (greater than 95th percentile for the age)

Investigations revealed Hb 10gm%, Total Leucocyte Count- 9000/cu.mm, Differential Leucocyte Count - P68 L-30 E2, PBF- Normocytic normochromic, ESR 32 mm 1st hr. Urine /Stool Routine examination- normal, Urinary specific gravity of 1020 and 24hr urine volume was 1100ml (< 30ml/kg). 24 urinary cortisol (50µg/24hrs). 8 a.m cortisol was 18microgms/dl. Renal and Liver Function Tests, Lipid profile, Thyroid profile were within normal range. FSH (10.2mIU/ml), LH(11.3mIU/ml) were normal. X-ray chest- prominent hilar shadows with parenchymal lesion on right middle and lower lobes suggestive of consolidation. Mantoux reading 22 mm after 72 hours. Ultrasound abdomen revealed no abnormality.

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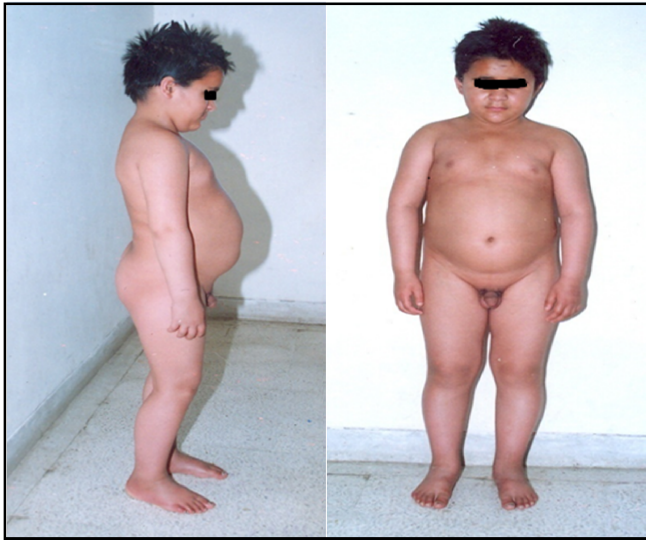


Fig.1 A 9 Year male Obese Child with Neurotuberculosis as the Etiology



Fig. 2 & 3 Contrast Enhanced MRI Study Showing Presence of Multiple Thick Walled ring Enhancing lesions in the Brain Surrounded by Edema and Presence of a Rounded Non –Enhancing Cystic Lesion in the Suprasellar Region

CSF exam: proteins-64mg%, glucose -56 mg%(Blood glucose-85mg%), 5 cells/hpf (lymphocytes), no AFB seen. Contrast enhanced MRI study revealed the presence of multiple thick walled ring enhancing lesions in the brain surrounded by edema and presence of a rounded non -enhancing cystic lesion in the suprasellar region. (Fig-2&3) The findings were highly suggestive of multiple granulomatous lesions (tuberculomas). In view of history and examination, investigations and radiological profile, a diagnosis of neurotuberculosis with obesity was made. The child was put on Anti tubercular Therapy (ATT) with steroids and supportive therapy. During the course of stay in hospital child's general activity improved, generalized body aches and lethargy decreased and appetite became normal.

Discussion

Obesity as defined by BMI exceeding 95th Percentile, age gender specific , represents a heterogeneous group of conditions with multiple causes (1-4). Body weight is determined by complex interaction between genetic, environmental, and anatomic factors.

Aetiology of obesity may be attenuated or exacerbated by non-genetic factors which may include both infective and non-infective causes.

Leptin which is produced by adipose tissue plays a central role in the long-term maintenance of weight homeostasis by acting on the hypothalamus by decreasing food intake and increasing energy expenditure. Leptin suppresses expression of hypothalamic neuropeptide Y, a potent appetite stimulatory peptide, and it also increases the expression of MSH, which acts through the MC4R melano-cortin receptor to decrease appetite. Thus, leptin activates a series of downstream neural pathways that alter food-seeking behavior and metabolism (1-4). Diseases infective/non infective involving hypothalamus cause dysregulation of the Leptin pathway and consequently food seeking behavior like hyperphagia as was seen in this particular child.

Tuberculosis, a major global public health issue owing to its resurgence due to HIV pandemic in both developing and developed countries, has been estimated approximately 10% for CNS involvement. In developing countries CNS tuberculosis is a disease of younger age group, usually childhood (5). Most tuberculous infections of the CNS are caused by Mycobacterium tuberculosis. Less frequently, other mycobacteria may be involved. It is believed that the bacilli reach the CNS by the haematogenous route secondary to disease elsewhere in the body. Initially small tuberculous lesions (Rich's foci) develop in the CNS, either during the stage of bacteraemia of the primary tuberculous infection or shortly afterwards (6). These initial tuberculous lesions may be in the meninges, the subpial or subependymal surface of the brain or the spinal cord, and may remain dormant for years after initial infection. Later, rupture or growth of one or more of these small tuberculous lesions produces development of various types of CNS tuberculosis. Rupture into the subarachnoid space or into the ventricular system results in meningitis. The type and extent of lesions that result from the discharge of tuberculous bacilli into the cerebrospinal fluid (CSF), depend upon the number and virulence of the bacilli, and the immune response of the host.

It has been suggested that with a sizeable inoculation or in the absence of an adequate cell-mediated immunity, the parenchymal cerebral tuberculous foci may develop

into tuberculomas.(5-8) Tuberculomas are firm, avascular, spherical granulomatous masses, measuring about 2-8 cm in diameter. They are well limited by surrounding brain tissue which is compressed around the lesion and show oedema and gliosis. The inside of these masses may contain necrotic areas composed of caseous material, occasionally thick and purulent, in which tubercle bacilli can be demonstrated.

Intracranial tuberculomas can occur at any age. In developing countries young adults and children are predominantly affected while in developed countries they are more common in older patients. The symptoms produced by tuberculoma are related to their location. Low-grade fever, headache vomiting, seizures, focal neurological deficit, and papilledema are characteristic clinical features. Hypothalamic-pituitary dysfunction develops in a single/multiple supratentorial tuberculomas. Infra-tentorial tuberculomas are more common in children and may present with brainstem syndromes, cerebellar manifestations, and multiple cranial nerve palsies.(5)

On CT scan, tuberculomas are characterised as low or high-density lesions, rounded or lobulated masses and show intense homogenous or ring enhancement after contrast administration. They have an irregular wall of varying thickness. Moderate to marked peri-lesional oedema is frequently present. Tuberculomas may be single or multiple and are more common in frontal and parietal lobes, usually in parasagittal areas. On CT scan, the 'target sign', a central calcification or nidus surrounded by a ring that enhances after contrast administration, is considered pathognomonic of tuberculomas(6-9). In developing countries like India, tuberculomas are frequently confused with cysticercus granuloma. Stereotactic diagnostic biopsy can help in establishing an accurate diagnosis in significant proportion of patients who had tuberculomas in childhood. Because early diagnosis and appropriate replacement therapy can be of great benefit to these patients, and prevent them from development of hypopituitarism.(10)

Obesity, hypogonadism, Frolich syndrome, sexual precocity, diabetes insipidus, and growth retardation have been reported after tubercular meningitis. Hypothalamus also controls the regulation of food intake. The lateral area of tuber cinereum acts as a center for hunger or appetite, while the ventromedial nucleus of the thalamus is considered with satiety. Damage to the latter affects satiety with the result that the child develops voracious appetite and obesity. This is seen long after steroid therapy is omitted in a child with TBM and may appear even after months.(6,9,11) This might be the possibility in our

case in development of obesity following neurotuberculosis.

Conclusion

Any child coming for evaluation of obesity, neurotuberculosis as the cause of obesity should be kept in mind and accordingly investigated. The varied manifestations of CNS tuberculosis, a common neurological disorder in developing countries, have now become relevant in other parts of the world, as the whole spectrum of these disorders is now being reported worldwide. The increasing problem of drug resistance has added a new challenge. The early recognition and timely treatment of the disease is critical as the considerable mortality and morbidity associated with the condition can be prevented.

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