SOTOS SYNDROME; AN ENDOCRINE AND NEUROLOGICAL MAZE

Pages with reference to book, From 36 To 37

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Sotos syndrome is characterised by rapid growth in the first few years of life with advanced bone age, ultimate adult height being variable, with some cases having attained gigantic proportions. In addition these patients have a variable degree of mental retardation, behavioral problems, characteristic dysmorphic features, large hands and feet and motor clumsiness. We report a case of Sotos syndrome which presented with a bewildering array of symptoms, unlike most cases that have been described in the literature.

CASE REPORT

A 19 year old girl presented with a 4 years history of polyuria with tirgency, incontinence and enuresis. She drank water in excessive amounts and also complained of puffiness of her whole body. Her menarche was at the age of 15 years and since then she had infrequent and scanty menstruation. There was no history of galactorrhoea or hirsutism. She was the third amongst 7 off springs of a consanguineous marriage. All other siblings and both parents were normal. She was the product of an uneventful term pregnancy, born precipitously at home and was resuscitated after considerable delay. Her mother was 22 and father 28 years of a get the time of her birth. Her mother remembered her as a big baby though precise measurements were not taken. She began to walk at 10 months of age but her gait remained awkward and she had frequent falls. She began talking at 12 months with considerable stammering for 3 to 4 years followed by some improvement in her speech. She had to be taken out of school at 8 years of age because of excessive somnolence and failure to make any progress. She received no formal or informal education thereafter while all other siblings received formal education. There was no history of fits at any time. She was a very difficult girl, prone to temper tantrums, manipulative, uninhibited and at times had violent behaviour. Her participation in household chores was minimal. She was clumsy and incapable of doing anything that required fine movements. Physical examination revealed a tall girl with disproportionately large hands and feet, pes planus and a long puffy face with slight facial asymmetry, prognathism and a high-arched palate. Her eyes were deep-set and wide apart with a slight slant. Her height was 163.8 cms, her mother is 167 cms, the father being 172 cms tali. Her arm span was 163.9 cms. Heel to pubis measurement was 89 cms and pubis to crown measurement was 74.8 cms. Her head circumference was 59.6 cms and that of a 17 year old sibling was 58.3 cms. She was the tallest of all her siblings and of all of them she had the biggest hands and feet. She was also mildly obese with a weight of65 kg. She had no dependent edema. Neurological examination was normal a part from some degree of motor clumsiness. IQ testing showed a borderline performance. Cardiovascular, respiratory, gastrointestinal, genitourinary and gynaecologlcal examinations were all normal. Secondary sexual characteristics were normally developed. During her six weeks stay in the ward she had no incontinence of urine and no episode of enuresis. She did not drink large amounts gf water either. Her behaviour with her family was reported to have improved during this period. She bad no difficulty in relating to the ward staff. Her haematological investigations, urea, creatinine, electrolytes, fasting and 2 hours post-prandial blood glucose were all normal. Serum proteins, 24 hours urinary protein excretion and urinary specific gravity were also normal. Urinary volume in 24 hours was only 1.5 litres. Hormonal investigations revealed normal thyroid function with a T4 of 7.4 ug/dl (normal range 4.5-12.5) and aTSH of 1.8 ulU/ml (normal range 0.3-4.5). Growth

hormone was normal at 3.7 ng/ml (normal 1.0-7.0). Serum FSH and LH levels were also normal, FSH being 15.2 mIU/ml (normal upto 20) and LH 4.4 mIU/ml (normal upto 38 mIU/ml). Prolactin level was raIsed at 34 ng/ml(normal range 1.0-20.0). This was repeatedafteran interval of 4 weeks when the elevation was marginal at 22 ng/ml. No active treatment for hyper prolactinemia was given at this point. Ca, PO4 and cortisol levels were normal. X-rays of the skull showed a normal sized pituitary fossa. CT scan of the brain showed a normal pituitary gland and no significant dilatation of the ventricular system. X-rays of the hands and feet showed excessively long small bones, but no tufting of the terminal phalanges. An ultrasound examination of the uterus and ovaries was normal.

DISCUSSION

Sotos syndrome or cerebral gigantism was first described by Sotos and co-workers in 1964[1]. More than 105 cases have been reported since then. Despite the number of years that have elapsed since the first description of this syndrome and the number of cases reported so far, the aetiology and the pathogenesis of this rare disorder remain elusive. The 5 original cases reported by Sotos and co-workers[1] appeared to be sporadic and some intra-natal or peri-natal insult was present in each case. The case described here also appears to be a sporadic one with a definite history of peri-natal Insult. Zonana and coworkers[2], on the other hand, reported 3 families with multiple affected members which supported an autosomal dominant pattern of inheritance. Other workers have reported cases which support autosomal recessive mode of inheritance[3]. It stands to reason that a pen-natal insult cannot produce a large baby and a large head circumference at birth - features which have been consistently described in these cases. Some disorder of the hypothalamus has been postulated but no definite hormonal abnormality has been reported. In this case also there was some suggestion of a disorder of hypothalamic function, with a disturbance of sleep, thirst, satiety and possibly also of regulation of prolactin secretion. Whitaker et al studied the hypothalamus and pituitary in a 22 year old female with Sotos syndrome post mortem[4]. This patient also had a hyperprolactinemia of the same degree as our patient. Microanatomic study of the hypothalamus and immunocytochemical examination of the pituitary gland did not reveal any significant abnormality. Excessive growth cannot be explained on the basis of an excess secretion of growth hormone, although a paradoxical increase in growth hormone secretion after a glucose load has been described in two cases[4-6]. A study ofplasmasomatomedin activity in 22 children by Witet al[7] suggests that during the period of most excessive growth there are high levels of one or more of the somatomedins. The precise role of somatomedins in the pathophysiology of Sotos syndrome awaits further studies. In more recent years several cases of Sotos syndrome have been reported to have a fragile X chromosome[8-10]. The answer to the mystery of this syndrome may lie in this or some other chromosomal or genetic abnormality. The increased incidence of certain malignancies reported in cases of Sotos syndrome may also have a genetic or a chromosomal abnormality as its basis[11-13]. The unravelled mystery of this syndrome requires an enormous amount of work not only by paediatricians but also physicians, who will from time to time, encounter such cases in adults.

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