in one case in his article, described a neonate dying after 26 days and autopsy revealing cardiac anomalies.

Boue *et al.* described a translocation causing partial monosomy of chromosome 10 and partial trisomy of chromosome 1 in a spontaneous abortus. In the present case as parents refused to give blood for karyotyping, it may be difficult to comment on the inheritance of the translocation and whether it is a balanced one or not. Apparently, the dysmorphic features, mental and motor delay, talipes equinovarus could be related to the tandem translocation but definite correlation may not be possible. Though this is so, it is important from the point of view of studying position effect phenomenon in individuals with apparently balanced translocation with phenotypic consequences(5).

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Cerebral Gigantism (Sotos Syndrome)

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Sotos and colleagues in 1964 described a new syndrome characterised by excessively rapid growth with acromegalic features and a non-progressive neurological disorder in 5 patients(1). This disorder is now known as cerebral gigantism (Sotos syndrome) and is well-recognized by the presence of salient features such as advanced height, weight and bone age with distinctive facies characterised by large dolicocephalic head, hypertelorism, antimongoloid slant of the palpebral fissures, high arched palate, long arm span and large hands and feet(2). Most children are mentally retarded and clumsy with no gross neurological abnormalities. Radiological studies demonstrate ventricular enlargement in most of them. Over 150 patients have been reported in world literature since the original publication. On a survey of Indian literature, we could come across only two case reports of this condition

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(3,4). In this report, we document two further cases of cerebral gigantism.

Case Report

Case I: A 14-year-old girl was brought for evaluation of increasing head and body size observed since the age of 3 months. The child was born to non-consanguinous unaffected parents after a full term normal delivery. She weighed 3.6 kg at birth. The delivery and the immediate neonatal period were uneventful. Subsequently the infant was observed to be less active during the first three months. Her early milestones were delayed. In contrast, her teething started very early–the lower incisor teeth erupted by 3 months. By the end of one year she had 18 deciduous teeth. The permanent teeth started erupting by 4 years of age. The pubertal development was noticed at the age of 8 years as indicated by development of breast and menarche was attained at 10 years. Her clumsiness persisted in her early years and was associated with easy distractability. Her performance in the school was below par initially with speech problem. Inspite of her being a 'tall healthy' child, she could not participate in any school athletic event because of clumsiness. Subsequently, her mental function started improving and she successfully completed a Class X Board examination in first attempt.

On examination, she appeared tall, dull but friendly. She weighed 70 kg (expected 37.4±7.35 kg) with a height of 179 cm (expected 147.5±6.99 cm), arm span of 188 cm and a head circumference of 62.5 cm (expected 52.1±1.77 cm). The head showed dolicocephaly, with coarse facial features which included frontal bossing, flat nose bridge and hypertelorism. The palate was high arched with prominent lateral palatine ridges. The maxillary and mandibular regions were prominent with pointed chin. The hands and feet were large but the fingers did not show any distal tapering or tufting. The finger movements were clumsy with lack of fine motor control. There were no other neurological or systemic abnormalities.

Radiological evaluation showed macrocrania with normal sella without any evidence of raised intracranial tension. Hand *X*-rays were also normal with no tufting of phalanges. The bone age was 17 years and the heel pad thickness of right foot was 21 mm. CT scan of skull showed normal sized ventricles.

The endocrine biochemical investigations showed normal glucose tolerance curve. The growth hormone levels during basal state and during oral GTT were within normal range (1.9-16.5 ng/ml). The 24 hour urinary 17-ketosteroids levels were 4.5 mg and 17-hydroxysteroids were 4.25 mg (normal). The thyroid hormone levels and plasma cortisol levels were within normal range. The audiologic and ophthalmologic evaluations were within normal limits. The chromosomal karyotype was 46 XX. She was put on an estrogen-progesterone combination in cyclical doses in an attempt to reduce her height velocity.

Case II: A 2-year-6-months old girl was admitted with excessive linear growth and weight gain observed since the age of 6 months associated with mental retardation and delayed milestones. The girl was the second child of the parents who were non-consanguinous and unaffected. The antenatal period was uneventful, but the baby developed fetal distress and had to be delivered by a lower segment cesarean section. There was however no resuscitation problem at birth. Her birth weight was 3.5 kg.

On the third day, she developed jitteriness and peripheral cyanosis and was detected to be hypoglycemic. This was promptly corrected by glucose infusions. Subsequently, she was noticed to gain weight far in excess of what was expected from the age of 6 months. Her milestones were delayed from the beginning. The social smile appeared at 3 months, sitting without support at 11 months and walking without support only by 22 months. Her vocabulary is still limited to a few two letter words. She has not yet achieved toilet control. Dentition started at 6 months and at 2½ years she has 20 teeth. Her weight gain was obvious at 6 months and the weight was 21 kg at 2 years. She has excessive appetite and has a tendency for increased sleepiness.

On examination she weighed 21.5 kg (expected 9.5±1.74 kg) with a length of 89 cm (expected 80.2±5.89 cm). The arm span was 98 cm and the head circumference was 49 cm (expected 45.1±1.75 cm). The head appeared big and her face was puffy with a large tongue and prominent jaw. There were hypertelorism, anti-mongoloid slant of the eyes, dolicocephaly and high arched palate with prominent ridges. The hands and feet were big. Her systemic examination was normal.

X-ray of skull showed thick calvarium with a normal sella (*Fig. 1*). The bone age was advanced (6.6 yrs); CT scan of skull showed hydrocephalus and basal ganglionic calcification (*Fig. 2*). Endocrine evaluation showed normal glucose tolerance study. The growth hormone levels both basal and following insulin induced hypoglycemia and oral GTT were normal. The plasma cortisol and thyroid hormone levels were normal.

Discussion

The classic clinical features of Sotos syndrome include large size at birth or excessive growth in the first four years of life with advanced height, weight and bone age, macrocrania and distinctive dysmorphic features including a high forehead, frontal bossing, prominent jaw, hypertelorism and antimongoloid slant of the palpebral fissures as well as high arched palate(5). Some new additional findings have been described in literature but the distinctive nature of the primary constellation has remained intact.

Mental retardation was originally thought to be an invariable component of Sotos syndrome. Later review by Dodge *et al.*(5) showed that mental retardation occurs only in about 85% cases. The characteristic pattern of retardation appears to be a delay of expressive language and motor development in infancy followed by attainment of normal intelligence later. Attention deficit is also a component of Sotos syndrome(6). Our first case fits into this pattern since she had delayed motor milestones and attention deficit in early years but progressively showed improvement in mental function and school performance. The second child had frank mental retardation which could be attributed to cerebral gigantism, and/or coexistent undetected birth asphyxia. Hook and Reynolds(7) postulated that prenatal macrocrania and resultant difficult childbirth contributes to mental retardation in Sotos syndrome. But the specific pattern of development delay without ultimate intellectual impairment is obviously not due to perinatal birth trauma or asphyxia.

All children with cerebral gigantism

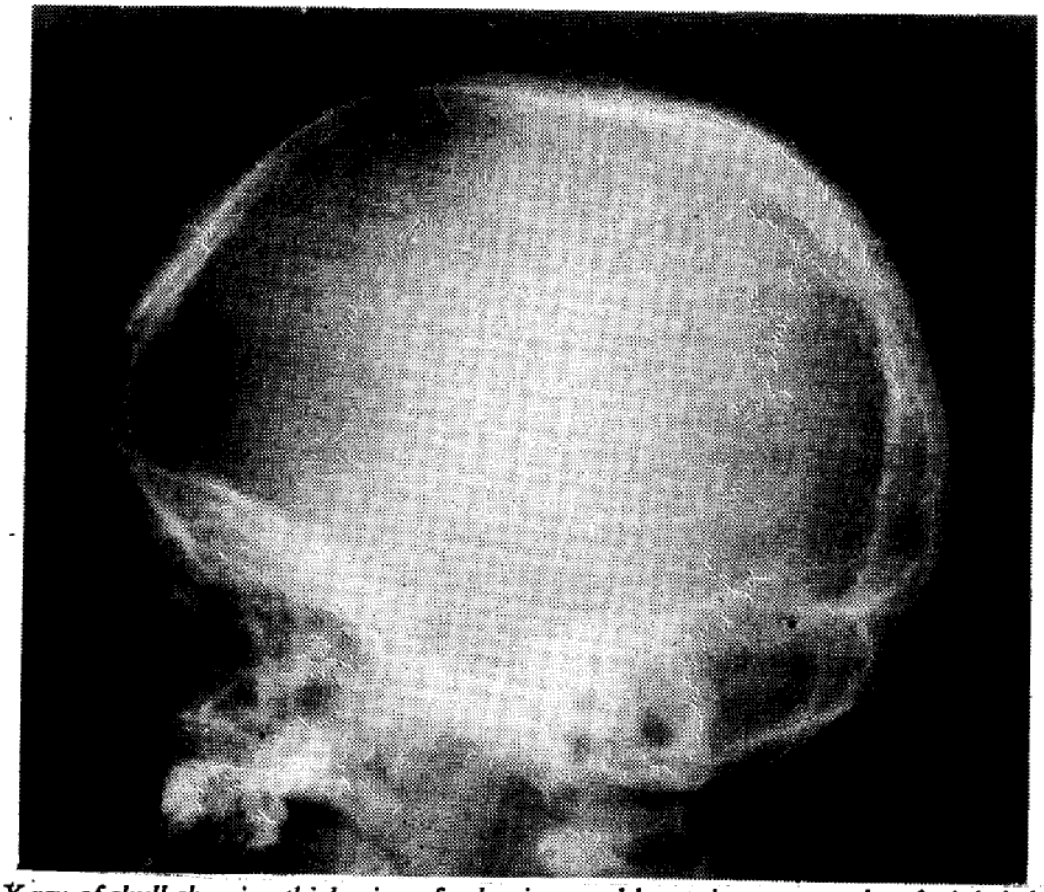

Fig. 1. X-ray of skull showing thickening of calvarium and large size compared to facial skeleton. Sella is normal.

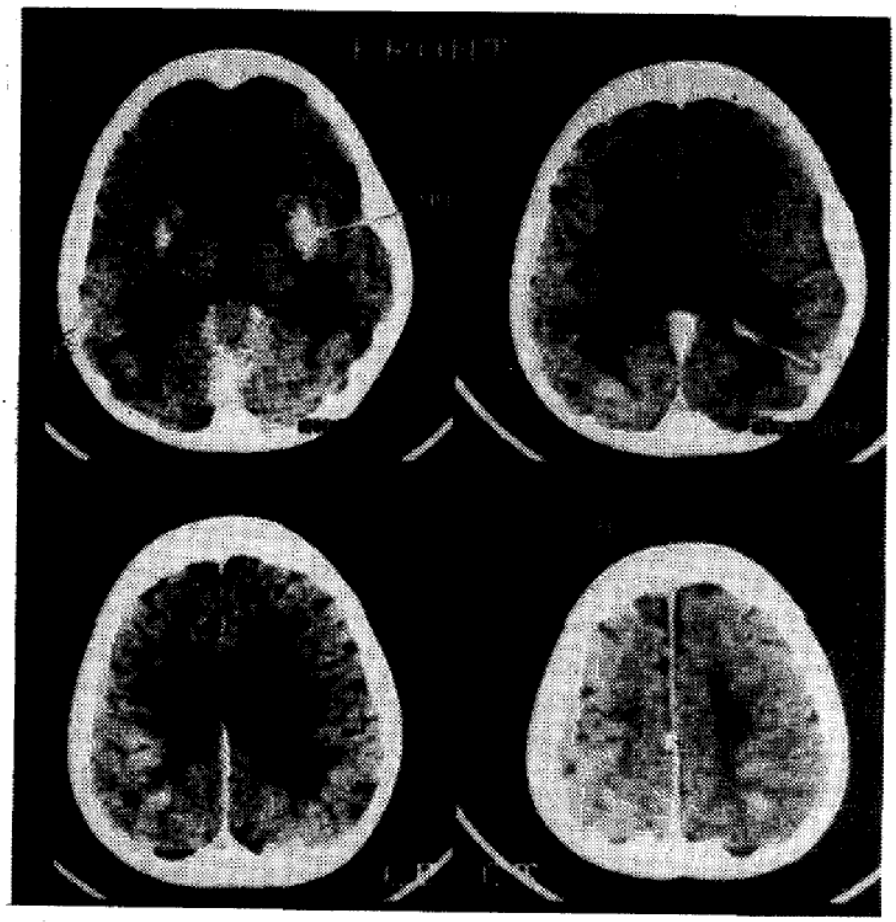

Fig. 2. Contrast enhanced CT scan shows moderate hydrocephalus and basal ganglionic calcification.

have increased head size but the characteristic acromegalic features including the pointed chin may not be very obvious. Our first case showed increase in head size and gigantic proportions with pointed chin as well as maxillary prominence. Cephalometric studies by Bale *et al.*(10) demonstrated that mandibular prominence is a frequent finding in Sotos syndrome but is obscured by concomitant maxillary prominence. They also noted that dolicocephaly was not present in 2 patients indicating that it may not be an essential feature of Sotos syndrome.

Endocrine basis for the development of cerebral gigantism has been postulated in earlier years but lately consensus has emerged that no major endocrine abnormalities are present in this syndrome. The most common abnormality observed is the presence of glucose intolerance in about 14% cases(5). Transient hypoglycemic episodes have been reported (as in our second case) but the significance of this is doubtful. Growth hormone (GH) secretion and activity were normal in most series. There is no rise in GH levels in response to hyperglycemia but patients who had paradoxical rise in GH have been reported indicating probable hypothalamic dysregulation(7,8). However, pituitary function in response to other hormones has been normal and biochemical evidence for a hypothalamic defect have not been consistently described. A recent neuro-anatomic and immunocytochemical study also failed to detect any abnormality in the pituitary and hypothalamus(9). Studies on somatomedins and other growth factors have been unremarkable(10). Parathyroid, adrenal, testicular and ovarian functions are normal and some patients are even fertile. Studies on thyroid function have been reported as normal, hypothyroid and hyperthyroid(2,11).

In literature most reported cases are sporadic in nature. Both autosomal dominant and recessive patterns have been described(5). A genetic defect leading to abnormal organogenesis has been postulated as the possible causative agent for the malformation and increased predisposition to cancer in these children(12). Beemer *et al.* have recently shown the association of fragile X sites to this syndrome(13). Inspite of increasing evidence for a genetic cause, the pathophysiology of Sotos syndrome still remains obscure.

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Tuberculosis Meningitis–How Early Can it Occur?

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Tuberculous meningitis (TBM) is fairly common and a dreadful complication of primary complex in pre-school children in our country. Early onset of the disease indicates high prevalence of pulmonary tuberculosis in the community and carries a high mortality and morbidity(1). Early onset could either be because of congenital or post-natally acquired infection.

It takes about 6-8 weeks for a primary complex to develop(1). It is after 6-12 months of primary infection that the tuberculous meningitis, secondary to hematogenous spread, occurs. The commonest age group for tuberculous meningitis is 9 months to 3 years(2-6). Tuberculous meningitis (TBM) is very rare before 4 months of age. TBM is a very sensitive index of prevalence of pulmonary tuberculosis in the community(1). When tuberculosis starts declining, the decline is first seen in younger age group and in respect of those manifestations which are seen secondary to hematogenous spread(2). Recently, we came across a case who had tuberculous meningitis who became symptomatic at 3½ months of age. We feel it is the earliest age at which post-natally acquired TBM can manifest.

Case Report

A four-month-old infant was brought to the Chacha Nehru Bal Chikitsalaya Avam Anusandhan Kendra, Indore with the complaints of cough, cold, breathlessness, off feeds, dullness and loose motions since 15 days. He was born full term and was delivered normally at home. The birth weight was not known and perinatal history was uneventful. He had one brother 1½ year old who was healthy. The parents belonged to low socio-economic status and were laborers. The infant was mainly breast fed and was unimmunized. There was no history of contact with tuberculosis in the family. Before this illness, the development of baby was normal.

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