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.

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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 distractibility. 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 circum-
ference 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, dolico-
cephaly 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 ex-
cessive 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 fisure
s 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 oc-
curs only in about 85% cases. The charac-
teristic pattern of retardation appears to be
a delay of expressive language and motor
development in infancy followed by attain-
ment of normal intelligence later. Atten-
tion deficit is also a component of Sotos
syndrome(6). Our first case fits into this
pattern since she had delayed motor mile-
stones and attention deficit in early years
but progressively showed improvement in
mental function and school performance.
The second child had frank mental retar-
dation which could be attributed to cerebral
gigantism, and/or coexistent undetected
birth asphyxia. Hook and Reynolds(7) pos-
tulated 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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