

'Puppet' Children *A Report on Three Cases*

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THE association of mental retardation with abnormal physical development of congenital origin still includes a great variety of conditions whose causation is undetermined and which lack precise classification. The children described here possess such similarities as to justify combining them into a specific group, as yet of unknown cause. Their flat heads, jerky movements, protruding tongues and bouts of laughter give them a superficial resemblance to puppets, an unscientific name but one which may provide for easy identification.

Case 1 (Fig. 1)

A girl, born in July 1959, a normal birth of healthy parents, her birth weight being 5 lb. 3 oz. There are now 10 children in the family, the youngest being a mongol, but apart from this there is no family history of mental retardation or congenital abnormality. At birth her head circumference was 13 inches, but her skull was flattened anteroposteriorly and was indented with a deep horizontal furrow across the occipital region, as if one of her arms had pressed into her skull in utero. She sucked well after birth and appeared to be normal in other respects.

She was referred to the paediatric clinic when she was 15 months old because she was not yet sitting up. Her skull was small

and brachycephalic, the circumference being only 16½ inches, and the furrow across the occiput was still easily palpable. She could see and hear but no speech had developed, and her comprehension was extremely limited. There was a generalised hypotonia and unsteadiness, but her knee and ankle jerks were exaggerated, and she could reach out for an object with a crude tremulous grasp. There were frequent spasms of uncontrollable laughter. She was in a state of restless activity and frequent short fits were obviously occurring when her gaze became blank and she would sometimes shudder. Her eyes were imperfectly developed, showing poor choroidal development and some pallor of the optic discs, but no definite optic atrophy at that time. There were normal suture lines in the X-ray film of her skull and there was slight dilatation of the lateral and third ventricles in the air encephalogram. There was little evidence of normal resting rhythm in the EEG, there being many high amplitude bursts of 3 and 4 cycles per second activity, bilaterally symmetrical.

When 18 months old, she had some major fits but neither anticonvulsants nor steroids would control her numerous short fits, which resembled those of infantile spasms. She could sit up at 2 years and when 3 years old could stand without

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(a)



(b)



(c)



(d)

Fig. 1 (a) and (b). Case 1 at 3 years, showing tongue protrusion. (c) and (d) Recent photographs, when almost wholly blind, showing persistent tongue protrusion and some degree of prognathism.

support, her legs being hyper-extended owing to hypotonia. There had been little further growth of the skull, the circumference now being only 17½ inches, and she had remained speechless and in a profound state of amentia. Both hearing and vision had deteriorated. There had never been any proptosis or papilloedema, but there was poor development of retinal and choroidal pigment, so that the eyes transilluminated easily through the sclerae and the optic discs were pale and atrophied. There was a striking appearance about her eyes, the white sclerotics, light blue irides with clear-cut outlines and dark eyelashes giving them a 'colour-transparency' appearance, which was also evident in the other two children described. She was able to protrude an unusual length of her tongue, and she would keep practically the whole of her tongue protruded from between her closed lips for long periods, as shown in Fig. 1 (a) and (b).

Now, at the age of 5½ years, she is deaf and blind. She can stand holding on to a cot rail, and hold a biscuit in her hand and eat it. Her head circumference has remained stationary at 17½ inches, still markedly brachycephalic, with the occipital depression still present. Paroxysms of laughter still occur frequently. The cranial sutures are still visible on X-ray films, and a further air encephalogram shows a dilated right lateral ventricle and third ventricle, the basal cisterns being larger than normal, with some excess of air over the frontal regions of the brain, compatible with some cortical atrophy. Short fits occur frequently and the EEG shows bursts of poly spike and spike and wave activity.

Further Investigations (May 1965). Chromosome examination, blood-picture and c.s.f. normal. Urine chromatography shows amino-aciduria of 'central cluster' type, suggesting defect of renal tubular absorption.

Case 2 (Fig. 2)

A girl, born in July 1958 of healthy parents, her birth weight being 6 lb. 8 oz. Two other sibs are normal and there is no family history of mental retardation or congenital abnormality. She sucked poorly from birth and fluids sometimes regurgitated down her nose. At 1 year she still could not sit up and did not take much notice of her surroundings. Her head was brachycephalic and the circumference was only 16½ inches, but an X-ray film of her skull did not show any premature fusion of the sutures. In her case too there was a distinct horizontal depression across the occiput. Her muscles were hypotonic, but her knee-jerks were brisk and she could grasp objects in an ataxic and inco-ordinate manner. It was also evident that frequent short fits were occurring, sometimes associated with staring sideways and momentary shaking of her body. Her eyes were incompletely developed, with poor development of the chorio-capillaris, the larger choroidal vessels being easily visible throughout the fundi.

When 3 years old she had some major fits. Her head circumference had increased slightly to 17½ inches and she could stand when held, with her toes pointing downwards. She drooled a little and she too could protrude a long length of her tongue and keep it protruded for long periods in exactly the same manner as Case 1. She too had long and frequent paroxysms of laughter. Although she could see and hear, she could not utter any intelligible sound and comprehension was obviously severely limited. She had a habit of lying on her back and manipulating toys with her feet. Various anticonvulsants were tried for the fits without success. An EEG showed frequent high-amplitude occipito-parietal spike discharges, bilaterally synchronous and showing occasional correlation with some of the more obvious vacant attacks.

By 5 years she could walk a little with



(a)



(b)



(c)



(d)

Fig. 2. Case 2 at 5 years. (a) Normally. (b) In a fit. (c) Showing tongue protrusion. (d) Showing prognathism.

the aid of a walking chair, but was still ataxic with marked mental retardation. She would sit, holding a toy and laughing, but without any speech development or comprehension of speech. She had to be fed with a spoon. Her head circumference was now only 18 inches, her skull still brachycephalic, with the occipital furrow easily palpable. Frequent fits continued to occur and her eyes still showed thin choroids with some pallor of the optic discs. An air encephalogram revealed some increase in the cortical air pattern and a little dilatation of the 4th ventricle. Her latest EEG shows some asymmetry throughout the record, with spikes and paroxysmal theta in the left temporal cortex.

Further Investigations (May 1965). Chromosome examination, blood-picture and c.s.f. normal. Urine chromatography showed no increase in amino-acids.

Case 3 (Fig. 3)

A boy, born in November 1955, a normal birth, although his mother had some hydramnios during pregnancy. His birth weight was 6 lb. 4 oz. Both parents are healthy with no abnormal family history, and two other sibs are normal. After his birth the mother noted a depression in the back of his head. He sucked well after birth, but seemed abnormally quiet and slept a lot, and was still not sitting up at 18 months. He was seen at the paediatric clinic when 2½ years old because he was still not walking, although by that time he could sit up. He could see and hear but could not say any words, nor had he any comprehension of speech. He was incontinent and had to be spoon-fed, and his weight was only 24 lb. His head was small and brachycephalic and he too had a horizontal depression in the occipital region. He slobbered and was often in an almost convulsive state of laughter. He could reach out for objects in a very ataxic manner and there was a tremulousness in



(a)



(b)

Fig. 3 (a) and (b). Two views of Case 3 at 8 years.

his body like that of cerebellar disease. He had frequent short fits when his eyes would close, he would fall forward momentarily and then jerk back into a sitting position. Laughter often preceded and followed the fit. His muscles were hypotonic but his knee-jerks were exaggerated. Although his head circumference was only 18 inches, no sign of craniosynostosis was seen in the X-ray of his skull. An electroencephalogram showed bilateral atypical synchronous spike and wave forms in all areas. The frequency of the fits was not obviously affected by anticonvulsant therapy.

At 3 years, major epileptic attacks began and he was admitted to hospital in status epilepticus, from which it took him some time to recover. His condition had changed little over the years. When 6 years old he could walk unsteadily, holding on to the furniture. His head circumference was only 18½ inches and no improvement had occurred in his ability to comprehend. His eyes have shown faulty development, with thin peripheral choroids and some pallor of the optic discs. An air encephalogram reveals slight dilatation of the lateral and fourth ventricles, the appearances being suggestive of slight cortical atrophy with a little dilatation of the ventricular system. His latest EEG shows, as in previous tracings, almost continuous epileptic activity with spike and wave and poly spike and wave forms predominating. He would often have paroxysms of laughter before and after the fit, and spike and wave forms were present during the period of laughter.

Further Investigations (May 1965). Chromosome examination, blood-picture and c.s.f. normal. Urine chromatography showed very slight increase of amino-aciduria of the 'central cluster' type.

Discussion

It will be seen that all these children possess a number of characteristic features

in common and may be summarised as follows:

1. A horizontal depression in the occipital region of the skull, present at birth. Also brachycephaly associated with microcephaly, becoming more obvious as growth proceeds, but not due to premature fusion of the coronal sutures.
2. A varying degree of primary optic atrophy, associated with incomplete development of the choroid.
3. Abnormal air encephalograms indicating some degree of cerebral atrophy associated with ventricular dilatation.
4. Very frequent fits resembling a hypsarrhythmic state and a profound degree of mental retardation.
5. Easily provoked and prolonged paroxysms of laughter.
6. Ataxia, with weakness of the limbs and trunk resembling that seen in cerebellar deficiency.
7. Ability to protrude the tongue to an unusual degree.

All three children have been born with abnormalities of the brain, skull and eyes, a result of faulty embryological development. The shape of the skull is predominantly brachycephalic, and although they possess abnormalities of the brain and eyes which are often associated with craniosynostosis, premature fusion of the sutures is not visible radiologically in these cases. For a long time a sharp distinction has been made between craniosynostosis and microcephaly in the belief that in the former condition a small capacity skull restricts the growth of a potentially normal brain. McLaurin and Matson (1952), while advocating the operation of linear craniectomy, found that in cases of premature fusion of the coronal sutures there was a high incidence of associated abnormalities, and, in spite of early operation, mental retardation often resulted. The air en-

cephalograms of such children showed dilated ventricles and an excess of air over the cerebral cortex, and they regarded these cases as due to faulty embryological development. Freeman and Borkowf (1962) found that in cases of premature fusion of the coronal sutures operation made no difference to the mental status of the children. Moreover the optic atrophy in these cases is of the primary type and not preceded by papilloedema, which would have occurred if there had been increased intracranial pressure. Since the development of the brain and that of the skull are inter-related and proceed simultaneously, it seems probable that premature fusion of the sutures is just one facet of a generalised embryological defect of the central nervous system. The predominant factor determining the intelligence level seems not to be head size *per se* but the altered state of consciousness due to frequent fits.

No great emphasis has been placed on the form and development of the base of the skull in relation to head shape and brain development because the association must be just as close as that with the cranial vault and facial skeleton. Ingalls (1947) considered that the mongol's brachycephaly was due to failure of growth at the speno-occipital cartilage, with resultant lack of forward growth of the base of the skull. One striking feature of the radiographs of the skulls of the 'puppet' children is the marked vertical inclination

of the skull base, so that the pituitary fossa, instead of facing upwards, looks towards the occiput. One can imagine, therefore, that growth of the base of the skull proceeds not so much forwards as upwards, and in this way increases the height of the cranial vault and produces a high skull with a short anteroposterior measurement. The posterior fossa is small and this may have some relation to cerebellar deficiency. In Cases 1 and 2 the maxillae and frontal sinuses are small, in both cases giving an appearance of prognathism. Spitzer and Quilliam (1958) found that in mongols the maxilla and mandible are small, the frontal sinuses absent, and the metopic suture remains open. In all the present cases the metopic sutures were closed, and in all three there was no chromosome abnormality. A small maxilla and a vertical position of the base of the skull would explain the ease with which these children protrude their tongues. A marked horizontal furrow in the occipital region of the skull would also seem to indicate some intracranial abnormality.

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SUMMARY

Three unrelated children are described with similar physical abnormalities of congenital origin, reminiscent of puppet children, and profound mental retardation.

RÉSUMÉ

Enfants 'marionnettes'

L'auteur décrit trois enfants atteints d'anomalies physiques similaires d'origine congénitale et d'un retard mental profond.

ZUSAMMENFASSUNG

'Puppenkinder'

Drei Kinder werden beschrieben, mit einander gleichenden physischen Abnormitäten kongenitalen Ursprungs sowie schwerwiegender geistiger Zurückgebliebenheit.

RESUMEN

Niños 'muñecos'

Se describen tres niños con anormalidades físicas parecidas, de origen congénito, además de atraso mental profundo.

REFERENCES

- Freeman, J. M., Borkowf, S. (1962) 'Craniostenosis. Review of the literature and report of 34 cases.' *Pediatrics*, **30**, 57.
Ingalls, T. H. (1947) 'Pathogenesis of mongolism.' *Amer. J. Dis. Child.*, **73**, 279.
McLaurin, R., Matson, D. (1952) 'Importance of early surgical treatment of craniosynostosis.' *Pediatrics*, **10**, 637.
Spitzer, R., Quilliam, R. L. (1958) 'Observations on congenital anomalies in teeth and skull in two groups of mental defectives.' *Brit. J. Radiol.*, **31**, 596.