

Correspondence

Enigmatic death of an infant

Sir,

The report of Hirschberger and Kleinberg (*Archives*, 1976, 51, 977) was stimulating; it is always a challenge to read about enigmatic cases. The authors describe an infant who failed to thrive and died at the age of 4½ months; on repeated occasions they found high urinary excretion of homovanillic acid (HVA) and vanillylmandelic acid (VMA). On microscopical examination of necropsy material the brain, lung, thyroid, liver, adrenal glands, and intestinal tract were normal. From their data (HVA and VMA, opsoclonus on one occasion, 'abnormal vertical eye movements'), even in the absence of a detailed report of neurological findings, we would like to suggest a diagnosis of *myoclonic encephalopathy of infants* (Kinsbourne, 1962).

Although failure to thrive, without accompanying diarrhoea, is not a usual symptom of myoclonic encephalopathy of infants, this could represent an age-specific manifestation. In their report the authors do not mention microscopical examination of the neural crest; therefore a possibly very small tumour (ganglioneuroblastoma) was not completely ruled out. However, even if the authors would agree with our diagnosis, there remains another enigma: as to the relationship between the hormones (HVA, VMA) and the clinical symptomatology—in this as well as in other patients. Nevertheless, in a future similar case, a therapeutic trial with ACTH would seem to be justified.

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Dr. Kleinberg comments:

We are grateful for the reference by Drs. Kopp and Burck to myoclonic encephalopathy, but hasten to point out that there are significant differences between our case and those presented in that report (Kinsbourne, 1962). Our case did not have myoclonic movements. There were occasional episodes of opisthotonic posturing and opsoclonus of the eyes, but myoclonus was simply not a feature of the neurological exam of our infant. Secondly, the youngest infant in Kinsbourne's series was 6 months old and almost all were considerably older. None presented with failure to thrive and none died. Lastly, of course, we are concerned about raised HVA and VMA levels which are not reported in Kinsbourne's paper.

Reference

Kinsbourne, M. (1962). Myoclonic encephalopathy of infants. *Journal of Neurology, Neurosurgery and Psychiatry*, 25, 271-276.

Sir,

I read with interest Hirschberger and Kleinberg's short report. There were some remarkable signs and symptoms in the infant described which I have personally noted in sudden infant death syndrome (SIDS) children; in fact I consider this infant a typical SIDS child.

In my studies of this syndrome I have come to the conclusion that the chief lesion in about 90% of SIDS children is a necrosis in the adenohypophysis or hypothalamus, caused by hypoxia or anoxia during fetal life, in cases of placental insufficiency. This finding was also reported by Sinclair Smith *et al.* (1976), who found retarded growth of the costochondral junctions of SIDS children. The child under discussion showed an absolute standstill in growth, which might have been caused by a lesion in the pituitary or hypothalamus. There was a reason for hypoxia during the mother's pregnancy (pneumonia in the seventh month). The lesions in the adenohypophysis have been imitated in rabbits by Lopes de Faria and Sokei (1973) by orthostatic collapse and were found by myself in an SIDS child (Visser, 1977). The authors do not mention examination of the pituitary at necropsy, nor the cerebral weight.

The neurological symptoms (opsoclonus and abnormal vertical eye movements) the infant showed during life point to a lesion of the brain stem described by Naeye (1976). He found astroglial proliferation in the brain stem combined with chromaffin hyperplasia in the adrenals in SIDS children. We found severe dislocation of the cerebellum and brain stem into the occipital foramen in an SIDS child of 11 months and considered it one of the causes of death in these children. In our case there was no cerebral oedema, yet the gyri of the cerebrum were flattened. The pituitary weighed 90 mg (normal for this age at least 120 mg). The stalk of the pituitary also showed damage caused by extrinsic pressure.

How are these brain lesions caused? Growth disturbances in infants, caused by deficiency of growth hormone, involve the skeleton, muscle tissue, internal and endocrine organs, but *not* the brain. Skull growth is retarded and the effect is a progressive noncorrelation of the brain mass and skull volume. The effect is dolichocephaly (seen in the photograph of Hirschberger and Kleinberg's patient) and progressive cerebral compression, which are responsible for the cerebral lesions and the typical neurological symptoms during life. Another relevant point is that at necropsy there were no signs of infection in any organ, yet blood culture yielded pneumococci. We have also found this phenomenon in SIDS children.

How are the increased levels of HVA and VMA explained in the infant under discussion despite the lack of a neural crest tumour? The only endocrine organ which might be responsible for the production of both these catecholamines is the pineal gland. It produces catecholamines, histamine, serotonin, glomerulotrophin, and