Internuclear ophthalmoplegia in pernicious anaemia

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We report a case of internuclear ophthalmoplegia in association with vitamin B₁₂ deficiency, which has not to our knowledge been described in Europe.

Case report

A 44 year old man presented in July 1987 with a one year history of progressive numbness of his feet, paraesthesia of his hands, a tendency to trip, and urgency of micturition. His mother suffered from pernicious anaemia. On examination he had ataxic nystagmus on right lateral gaze and bilateral pyramidal signs in the legs, consisting of increased tone, exaggerated knee jerks, and extensor plantar responses. Ankle jerks were unobtainable, and there was mild proprioceptive loss in the toes.

Recording of visual evoked responses, examination of cerebrospinal fluid (including oligoclonal bands), cervical myelography, and magnetic resonance imaging all yielded normal results. Haemoglobin concentration was 158 g/l with a mean corpuscular volume of 106 fl. A blood film showed a macrocytic, normochromic picture with hypersegmentation of neutrophils. Serum concentration of vitamin B₁₂ was 19 ng/l (normal 170-900), and serum folate concentration was normal. Antibodies to gastric intrinsic factor

were absent. Results of a Schilling test were consistent with a diagnosis of pernicious anaemia.

Subacute combined degeneration of the cord was diagnosed, and the patient was treated with intramuscular hydroxocobalamin, 1 mg daily for five days and three monthly thereafter. The ataxic nystagmus had completely resolved two months after treatment started, but the myelopathy persisted with little change in its severity.

Comment

Two patients with pernicious anaemia who had defects of upward gaze have been reported.^{1,2} Gamstorp and Kupfer found this to be due to denervation of the extraocular muscles as shown by electromyography.¹ Also, a Japanese patient with Addison's disease complicated by pernicious anaemia and medial longitudinal fasciculus syndrome has been reported.³ Our patient had an internuclear ophthalmoplegia and myelopathy in association with vitamin B₁₂ deficiency. The myelopathy of B₁₂ deficiency is known not to improve much with treatment, but this patient's internuclear ophthalmoplegia resolved entirely.

- 1 Gamstorp I, Kupfer C. Denervation of extraocular and skeletal muscles in a case of pernicious anaemia. *Neurology* 1961;11:182-4.
- 2 Sandyk R. Paralysis of upward gaze as a presenting symptom of vitamin B₁₂ deficiency. *European Neurology* 1984;23:198-200.
- 3 Matsumoto T, Togawa K, Yamamoto M, Yamagami Y, Ogata E. A case of idiopathic Addison's disease complicated with alopecia universalis, vitiligo vulgaris, superficial mycosis, pernicious anaemia and bilateral medial longitudinal fasciculus syndrome. *Nippon Naika Gakkai Zasshi* 1977;66:1588-94.

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Are all infants of diabetic mothers "macrosomic"?

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Macrosomia has been defined as a birthweight exceeding an arbitrary limit—for example, 4000 g or the 90th centile for gestation. The condition is of interest because of the difficulties of delivering a large infant. Fetal size has been used as an indication of the degree of control of diabetes during pregnancy, and the infants are often referred to as either "macrosomic" or "non-macrosomic," implying a bimodal distribution of birthweights.

In this study we examined details of the deliveries of 280 infants to diabetic mothers to determine whether there are two populations according to birthweight.

Patients, methods, and results

We reviewed the case notes of 280 women who were diabetic when pregnant and who gave birth at this hospital in 1976-85. Those with pre-existing diabetes (247) were treated with insulin during pregnancy, whereas most (25) of the 33 women with gestational diabetes were managed by restricting their intake of carbohydrate. The mean (SD) maternal weight (67.5 kg (12.3)) and height (161 cm (7.3)) did not differ significantly from those of 3959 non-diabetic mothers (64.9 kg (13.2) and 160 cm (7.1)) who gave birth at the hospital during the same period.

The birth weights were expressed as the number of standard deviations by which they differed from the mean birth weights for gestational age of a reference range constructed from 3959 consecutive singletons born in the hospital during the study. In all cases gestational age had been confirmed by measuring the

biparietal diameter and the length of the femur by ultrasound early in the second trimester.²

The birthweights of the 280 infants of diabetic mothers formed a unimodal normal distribution (mean +1.23; SD 1.35; Anderson-Darling test of normality 0.65, p=0.18). This distribution was shifted significantly to the right of the reference range (p<0.0001) by 1.23 standard deviations (roughly 500 g) (figure 1).

The distribution of birthweights (standard deviations from the normal mean for gestational age) for 280 infants of diabetic mothers and 3959 infants of normal mothers

Comment

The findings of this study dispute the classification of infants of diabetic mothers as either "macrosomic" or "non-macrosomic." Such classification ignores the continuous distribution of birthweight and may conceal any correlations between the biochemistry of the infants and fetal size. The data suggest that every infant of a diabetic mother, irrespective of actual birth weight, is growth promoted and exceeds its genetic