Iris coloboma, ptosis, hypertelorism, and mental retardation

Sir,

Drs Baraitser and Winter reported three patients with a new syndrome consisting of iris coloboma, ptosis, hypertelorism, and mental retardation (J Med Genet 1988;25:41–3). They correctly state that in Noonan’s syndrome no report of iris colobomas has been published. They partially used this fact to exclude the diagnosis of Noonan’s syndrome in their patients, although they felt the facial gestalt also differed.

I have seen a sporadic case of a patient with Noonan’s syndrome (figure) who had a left iris coloboma without retinal abnormalities. He was short and had mild psychomotor delay. He also had a dysplastic pulmonary valve, pectus excavatum, low set, thick ears, and malar flattening. I saw this patient in consultation with Dr Jacqueline Noonan, who also agreed with the diagnosis.

The iris coloboma may well be unrelated to the Noonan’s syndrome in the above patient: however, it can no longer be stated that colobomas have not been reported in a patient with Noonan’s syndrome.

BRYAN D HALL
Department of Pediatrics,
University of Kentucky,
Lexington, Kentucky 40536, USA.

Teratogenicity of ergotamine

Sir,

Hughes and Goldstein1 hypothesised on the basis of one case that ergotamine, acting either alone or in synergy with propranolol and caffeine, produced fetal vasoconstriction resulting in tissue ischaemia and subsequent malformation. This case report prompted us to check the database of the Hungarian Case-Control Surveillance of Congenital Anomalies, 1980–1986.2 This system has both prospective (prenatal care logbook) and retrospective (questionnaire) sources of data.

Within the group of mothers who delivered matched healthy newborns (the so called negative controls), 0-11% were treated with ergotamine during pregnancy (table 1). Additionally, 0-32% of mothers who delivered babies with Down’s syndrome (the so called positive controls) used this drug. (However, this figure relates to only one pregnant woman.) The rate of ergotamine use was 0-14% in the total sample of malformed index patients (p>=0-10). Of these 13 malformed babies, four had neural tube defects. Three mothers in the latter group were treated with ergotamine during the first trimester of pregnancy. Other groups of congenital anomalies did not show any significant increase of ergotamine treatment during pregnancy. These cases are available for further investigation concerning the occurrence of minor brain abnormalities including arrested cerebral maturation and paraplegia. After matching, the numbers of index patients and negative matched controls were 10:9 in the total samples but 4:0 in the neural tube defects cases (McNemar test: \( \chi^2 = 9-00, p<0-01 \)). The latter finding needs further study.
The data for propranolol were also analysed: 0.12% and 0.19% of mothers of matched healthy newborns and total malformed index patients, respectively, were treated (table 2). This figure was somewhat higher in the groups of cleft lip/cleft palate, neural tube defect, and hypospadias. However, a comparison with their matched controls did not indicate any significant difference.

Our database does not contain a pregnant woman who was treated with both ergotamine and propranolol during pregnancy.

Andrew Czeizel
Department of Human Genetics and Teratology, WHO Collaborating Centre for the Community Control of Hereditary Diseases, National Institute of Hygiene, Győri u. 2, 1966 Budapest, Hungary.

References

18p− syndrome with partial sacral agenesis

Sir,

We should like to present additional information regarding a patient with 18p− and a single central maxillary incisor who was originally reported in 1981.1 The patient, now aged seven years, was initially seen for evaluation of short stature, development delay, and unusual facial features, most notably a single central maxillary incisor. Growth hormone studies were unremarkable, but a lymphocyte karyotype showed 18p− in all cells examined. Karyotypes of the parents were normal.1

Toilet training was attempted but was not successful; this lack of success was ascribed to the patient’s developmental delay. Cognitive skills were in the range of borderline normal intelligence to mild mental retardation. A barium enema and intravenous pyelogram at the age of four years were reported to be normal, although spina bifida occulta (level not specified) was noted. Encopresis and enuresis persisted at the age of seven years. Because of the previously normal barium study and the normal neurological examination, it was felt that the encopresis and enuresis did not have an organic aetiology and a behavioural modification programme was instituted. This was not successful and, on further study, a radiograph of the lumbo-sacral spine showed partial agenesis of the sacrum. This was confirmed by a CT scan and myelogram of the sacrum, which also showed a high termination of the theca (at L4) and spinal cord (at T12 and L1), with no evidence of an intraspinal mass lesion.

Partial sacral agenesis with spinal cord abnormalities has not been described in the 18p− syndrome as far as we are aware. The neurological dysfunction