LETTERS TO THE EDITOR

Thalassaemia in Azerbaijan

A recent study referred to the incidence of molecular mutations and the clinical picture of thalassaemia in Azerbaijan (Kuliev *et al. J Med Genet* 1994;**31**:209–12). Unfortunately the section on α thalassaemia described in this report is incomplete. The incidence and clinical picture of α thalassaemia in this region of the former USSR have been extensively studied and published in Russian language publications between 1983 and 1985. Different forms of α thalassaemia have been identified in Azerbaijan. We studied the clinical picture and laboratory findings of different forms of α thalassaemia (haemoglobin H disease, α/β thalassaemia, and HbS/α thalassaemia) in 137 patients[1–3] and our data suggest considerable genetic heterogeneity of α thalassaemia in Azerbaijan. However, the clinical picture and laboratory findings were similar to the α thalassaemia found in the Mediterranean area. We also studied the frequency of α thalassaemia in two regions endemic for haemoglobinopathy (Kutkashen and Shaeki) and in the capital Baku by estimations of Hb Bart's in 1000 cord blood samples by electrophoresis and immunochemical methods.[4,5] In the Kutkashen region, among 200 cord blood samples, Hb Bart's was detected in 28 cases with a percentage ranging from 0·8% to 28%. In the Shaeki region, in 54 out of 600 cord blood samples, Hb Bart's from 0·8% to 25% was detected. In 10 out of 200 cord blood samples from the Gynecology and Obstetrics Department of Baku, Hb Bart's ranged from 0·8% to 9·5%. We found a trimodal distribution of Hb Bart's with values of 0·8% to 5%, 6% to 11%, and 25% to 28%. We consider that these values corresponded to genotypes of α thalassaemia 2, α thalassaemia 1, and α thalassaemia 1/α thalassaemia 2 respectively.[6,7] Our studies indicate that α thalassaemia 2 trait is more prevalent than α thalassaemia 1 trait in Azerbaijan (in Kutkashen 11·5% and 2%, in Shaeki 7·8% and 1%, in Baku 4% and 1% respectively).

DJAVID GAZIEV
Divisione Ematologica e Centro Trapianto Midollo Osseo di Muraglia, USL-3 Ospedale di Pesaro, Italy 61100.

1 Gaziev DjG. Alpha-thalassemic syndromes (in Russian). *Azerbaijan Med J* 1983;**8**:43–8.
2 Gaziev DjG, Abdullaev GM. Some clinico-laboratory peculiarities of different alpha-thalassemia types (in Russian). *Hematol Transfusiol* 1983;**5**:22–6.
3 Abdullaev GM, Gaziev DjG, Mamedova RG. Clinico-laboratory peculiarities of alpha-thalassemia and sickle-cell anomaly combination (in Russian). *Azerbaijan Med J* 1984;**2**:53–6.
4 Abdullaev GM, Tokarev YN, Gaziev DjG. Methods of alpha-thalassemia detection and identification (in Russian). *Methodical Recommendation, Baku*, 1983:1–27.
5 Levina AA, Andreeva AP, Cibulskaia MM, Tokarev JN, Gaziev DjG. Alpha-thalassemia diagnosis on a basis of immunochemical method of Bart's hemoglobin determination (in Russian). *Proceedings of II Congress of Hematology and Transfusiology of Usbekistan, Tashkent*, 1983: 164–5.
6 Gaziev DjG, Abdullaev GM, Tokarev YN. Bart's hemoglobin in Azerbaijan population (in Russian). *Hematol Transfusiol* 1983;**11**:47–53.
7 Gaziev DjG. Alpha-thalassemia in Azerbaijan (in Russian). *Hematol Transfusiol* 1985;**10**:8–10.

Blepharophimosis-mental retardation syndrome and terminal deletion of chromosome 3p

Three unrelated patients were published in *Journal of Medical Genetics* in 1987, 1988, and 1989[1–3] with an unknown syndrome whose symptoms included abnormal facies, hypothyroidism, postaxial polydactyly, and severe mental retardation. The author of the 1989 paper[3] concluded that these patients were affected by the same syndrome of unknown aetiology.

We recently examined a 5 month old boy referred because of hypotonia and growth retardation (−3 SD). He was microcephalic and severely hypotonic. He exhibited facial dysmorphism with blepharophimosis, ptosis,

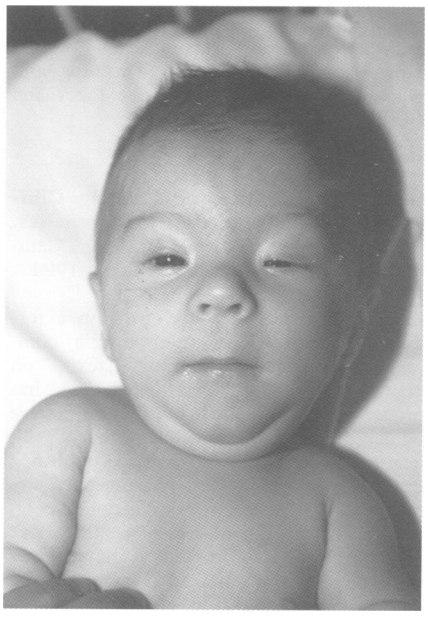

Figure 1 Facial features of the proband at 7 months. Note the blepharoptosis, bulbous nose, long philtrum, and thin upper lip.

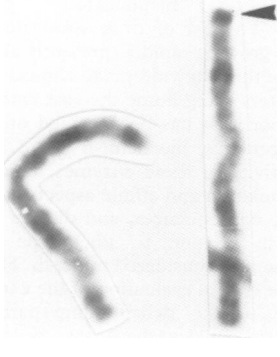

Figure 2 High resolution R banded chromosomes 3 of the patient. The right shows del(3)(p25-3pter).

hypertelorism, upward slanting palpebral fissures, short nose with a broad nasal tip, long philtrum, micrognathia, bilateral preauricular pits, and postaxial polydactyly on the left hand (fig 1). Chromosome analysis was performed using R banding and was found to be normal.

However, a patient reported in *Atlas des Maladies Chromosomiques*[4] with a 3p25-pter deletion showed a striking resemblance to our patient.

The clinical features so closely resembled those of 3pter deletion that we carefully checked this region on the R banded karyotype and found the expected 3p25-3pter deletion, which was then confirmed by high resolution banding (fig 2). Without the clinical indications, this deletion would have remained undetected.

On the basis of this finding, we suggest that similar patients reported by Young and Simpson,[1] Fryns and Moerman,[2] Cavalcanti,[3] and Buntinx and Majeswski[5] could also have 3pter deletions. The clinical features of these patients and our case are compared in the table. All of them share severe pre- or postnatal growth retardation, hypotonia, and the same facial dysmorphism: microcephaly with blepharophimosis, ptosis, epicanthus, a broad nasal tip, and micrognathia. It is just possible that these deletions may have been missed on standard chromosome analysis if they were as small as the one which we observed.

Sixteen published cases with 3pter deletions had a larger deletion including the whole of band 3p25-pter.[6] Growth retardation, mental retardation with neonatal hypotonia, blepharophimosis, blepharoptosis, epicanthus, hypertelorism, and thin upper lips are consistent features. Microcephaly is present in 70% of cases, postaxial polydactyly in 50%. Less frequently observed anomalies are congenital heart defect, renal malformation, cryptorchidism, and rocker bottom feet. Hypothyroidism was diagnosed in one patient with 3p deletions as well as hearing loss (table).

We think that 3pter deletions can be diagnosed clinically and should be confirmed by high resolution banding or FISH using markers in this region[7] when a standard karyotype is normal.

Blepharophimosis-ptosis-epicanthus syndrome with normal intelligence is associated with 3q23 microdeletion.[8–10] Blepharophimosis and developmental delay were reported together by Bieseker in 1991.[8] She reported a child with blepharophimosis, simple ears, hypoplastic teeth, developmental delay, and hypotonia. This patient was very similar to a previous report by Fujita *et al*[11] and Bieseker suggests that all cases have a distinctive syndrome named Ohdo syndrome. Recently Clayton Smith *et al*,[12] Melnyk,[13] and Maat-Kievit *et al*[14] have reported six new cases with this syndrome describing additional clinical features. We suggest that some patients are very concordant for 3p- deletions. We recommend that clinicians keep in mind the 3p localisation when examining patients with mental retardation and blepharophimosis.

The author wishes to thank Dr M Baraitser for critical review of this letter.

ANNE MONCLA
NICOLE PHILIP
JEAN FRANÇOIS MATTEI
Centre de Génétique Médicale, Hopital des Enfants-Timone, 27 Boulevard Jean Moulin, 13385 Marseille Cedex 05, France.

1 Young ID, Simpson K. Unknown syndrome: abnormal facies, congenital heart defects, hypothyroidism, postaxial polydactyly, and

Thalassaemia in Azerbaijan.

D Gaziev

J Med Genet 1995 32: 245
doi: 10.1136/jmg.32.3.245

Notes