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Radial aplasia and chromosome 22q11 deletion

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Abstract

We report on a neonate with deletion 22q11 (del22q11) presenting with facial dysmorphism, ocular coloboma, congenital heart defect, urogenital malformations, and unilateral radial aplasia. This malformation complex includes features frequently occurring in velocardiofacial syndrome as well as findings described in the CHARGE and VACTERL associations. To our knowledge, the present case is the first report of radial aplasia in del22q11. This observation further supports and extends the clinical variability of del22q11.

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Keywords: upper limb anomaly; radial anomaly; deletion 22q11; velocardiofacial syndrome

Deletion of chromosome 22q11 (del22q11) is a major cause of DiGeorge,[1] velocardiofacial,[1–3] conotruncal anomaly face,[4] and Opitz[5] syndromes. The acronym CATCH22 has been proposed to encompass the major clinical manifestations occurring in this disorder (C=cardiac defect, A=abnormal face, T=thymic hypoplasia, C=cleft palate, 22=22q11 deletion),[6] but the deletion spectrum has been progressively widened to include more than 100 symptoms.[7–14] Upper limb malformations have rarely been described in these patients. They include polydactyly, syndactyly, camptodactyly, thumb anomalies, and lobster claw deformity.[6 15–18]

We have observed a neonate with del22q11 presenting with a malformation complex characterised by facial dysmorphism, ocular colobomata, congenital heart defect, urogenital malformations, and unilateral radial aplasia. To our knowledge, radial aplasia has never been reported in association with del22q11.

Case report

The proband, a male, is the first child of healthy, non-consanguineous parents. The mother was 29 years old at the birth and the father 41. The baby was born by vaginal delivery at term after an uneventful pregnancy. Birth weight was 2800 g, length 49 cm, and head circumference 33.5 cm. Apgar scores were 7 and 9 at one and five minutes. Clinical examination showed horizontal palpebral fissures, flat nasal bridge, epicanthic folds,

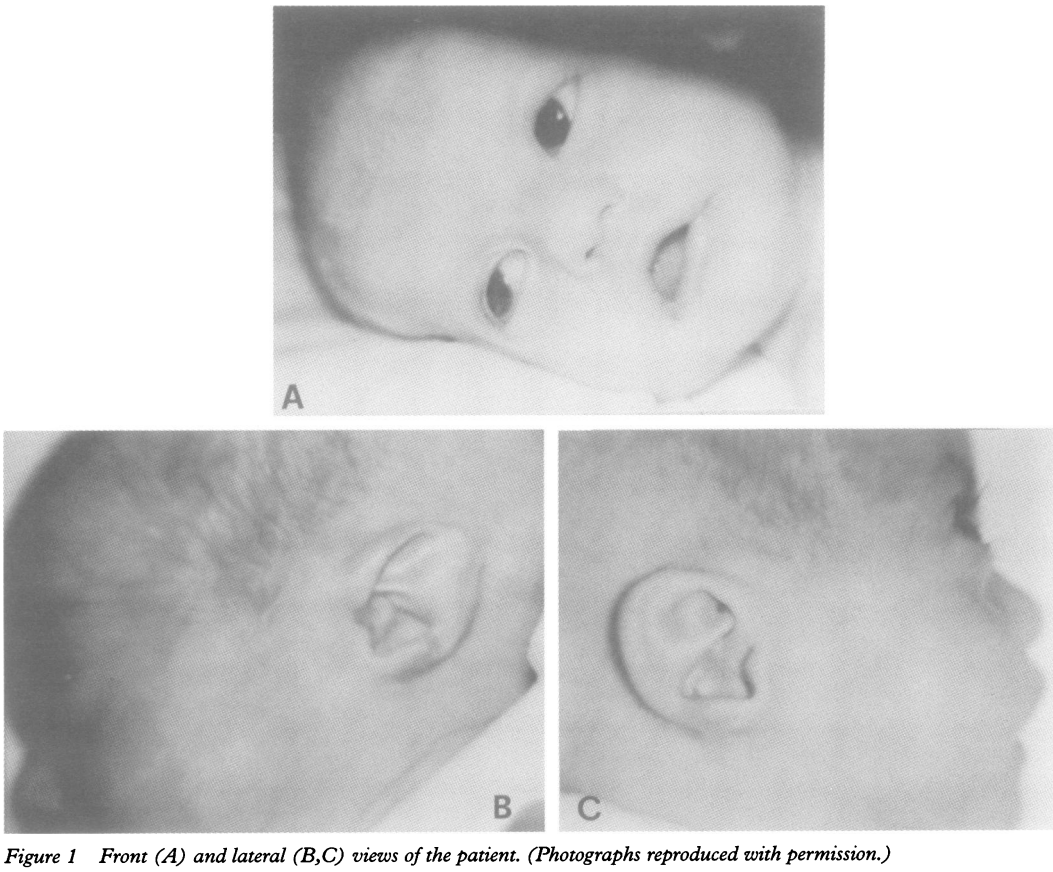

Figure 1 Front (A) and lateral (B,C) views of the patient. (Photographs reproduced with permission.)

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hypoplastic left nostril, unilateral choanal stenosis, flat philtrum, thin upper lip, downturned corners of the mouth, a high palate, and circular, flat, and retroverted dysmorphic ears (fig 1). The genitalia were hypoplastic with a small penis and bilateral undescended testes. The left arm was short with an absent radius and hypoplastic ulna. The left hand was deviated at the wrist, with a hypoplastic first ray, ulnar deviation of the second finger, and camptodactyly of the third and fourth fingers. *X* ray examination of the left arm and hand (fig 2) showed an absent radius, hypoplastic ulna, short first metacarpal bone, hypoplastic phalanges of the first finger, and clinodactyly of the second finger. No additional skeletal abnormalities were detected on total body examination. Cerebral CT scan was unremarkable. An ophthalmological examination disclosed bilateral retinal colobomata. Fibrolaryngoscopy showed anterior laryngomalacia. A normal thymic shadow was detected on chest *x* ray. Chest *x* ray with barium swallow and echocardiography showed double aortic arch, which was repaired at 40 days of age. Renal ultrasonography showed a slight left pelvic ectasia. Transient hypocalcaemia (7.7 mg/dl) was detected on the second day of life. T lymphocyte numbers were slightly below the normal range.

Standard and high resolution chromosome analysis of peripheral blood lymphocytes disclosed a normal male karyotype. Fluorescent in situ hybridisation (FISH) analysis with Sc11.1,[19] co23,[20] and D22S75 and D22S39 (control, ONCOR) probes showed 22q11.2 hemizygosity.

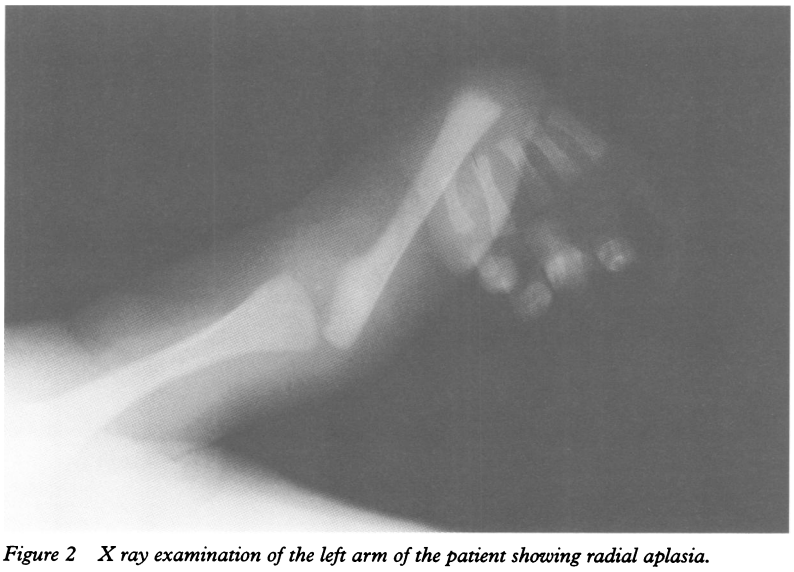

Figure 2 X ray examination of the left arm of the patient showing radial aplasia.

Table 1 Clinical manifestations of our patient compared with cardinal features of velocardiofacial syndrome (VCF), DiGeorge syndrome (DG), CHARGE, and VACTERL associations

Clinical feature	*Present case*	*VCF/DG*	*CHARGE*	*VACTERL*
Facial dysmorphism (quite distinct in different disorders)	+	+	+	+
Ocular colobomata	+	+	+	−
Choanal stenosis	+	−	+	−
Cleft palate	−	+	+	−
Cardiac defect	+	+	+	+
Tracheo-oesophageal fistula	−	−	−	+
Vertebral defects	−	+	−	+
Radial ray defects	+	+	−	+
Renal anomalies	+	+	+	+
Genital defects	+	+	+	+
Hypocalcaemia	+	+	+	−
Thymic hypoplasia	−	+	−	−

Discussion

Upper limb malformations described in patients with the CATCH22 phenotype include preaxial and postaxial polydactyly, syndactyly, camptodactyly, club hands, thumb hypoplasia, and lobster claw deformity.[6 15-18] To our knowledge, the present case is the first report of radial aplasia in del22q11, although other types of radial ray defects have been found previously.[15] In addition, it is interesting to note the unilateral nature of the limb defect in the present case. The malformation complex presented by our patient includes findings frequently occurring in velocardiofacial syndrome, such as facial dysmorphism, high palate, neonatal hypocalcaemia, aortic arch defect, and urogenital anomalies[21] (table 1). Ocular coloboma has also been reported in velocardiofacial syndrome.[22] The association of this defect and choanal stenosis is suggestive of the CHARGE association[23] (table 1). The clinical overlap between velocardiofacial syndrome and CHARGE association has been noted previously.[24] Del22q11 has been reported in a few CHARGE patients,[25] but extensive molecular analyses have failed to show this hemizygosity.[26] A clinical diagnosis of VACTERL association was suggested in our patient because of the combination of aortic arch defect and radial aplasia,[27] but was not supported by the absence of vertebral, anal, and tracheoesophageal anomalies (table 1).

The present observation further supports and extends the clinical variability of del22q11, and adds radial aplasia to the list of symptoms associated with CATCH22 patients.

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