A case of deletion 14(q22.1→q22.3) associated with anophthalmia and pituitary abnormalities

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Abstract

An interstitial deletion of the region q22.1→q22.3 of chromosome 14 is described in a child with bilateral anophthalmia, dysmorphic features including micrognathia, small tongue, and high arched palate, developmental and growth retardation, undescended testes with a micropenis, and hypothyroidism. Interstitial deletions of the long arm of chromosome 14 are extremely rare, but this case seems to confirm that the region q22 is specifically concerned with pituitary and eye development.

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Deletions of the long arm of chromosome 14 appear to be very uncommon from published reports, and mapping the regions associated with specific clinical features has been difficult for this reason. We describe a case which seems to localise certain specific features, including bilateral anophthalmia and pituitary abnormalities, to deletion of the region 14q22→q23.

Case report

The patient, now 4 years old, is the carrier of a de novo microdeletion of the region q22.1→q22.3 of chromosome 14. He is the first child of healthy parents and has been blind since birth because of bilateral anophthalmia. The pregnancy was normal, although there was some heart beat irregularity at 36 weeks and the patient was born at term weighing 2740 g. He was in special care for the first month with a collapsed lung, but was feeding satisfactorily on discharge. At the age of 2 years, the fontanelle was not closed and his primary dentition was notably delayed as he had only four teeth by then. His weight (9 kg), length (78 cm), and head circumference were below the 3rd centile and his muscle tone was very hypotonic; he could roll over but not crawl, and could only just sit. He was not speaking, although his hearing seemed normal. Dysmorphic facies were now noted, with micrognathia, an extremely small tongue, and a high arched palate. The genitalia were hypoplastic with the left testis palpable but not the right (fig 1). A diagnosis of primary hypothyroidism was confirmed by thyroid function tests and 25 µg thyroxine was prescribed daily. There was some improvement in his third year and he was able to stand with help and to play happily with his 1 year old brother. He still could not speak or feed himself, although he could hold a beaker, and he did not increase in weight. His fourth year showed a little more development in that he could say one or two words, but he began to suffer from chronic blepharitis and also had grommets fitted as he had glue ears. Chromosome analysis carried out when the child was 2 years old indicated a very small deletion in the long arm of chromosome 14 (46,XY,del(14)(q22.1→q22.3)) (fig 2). This was confirmed by flow karyotyping using a fluorescence activated chromosome sorting system (FACS) and the deleted chromosome

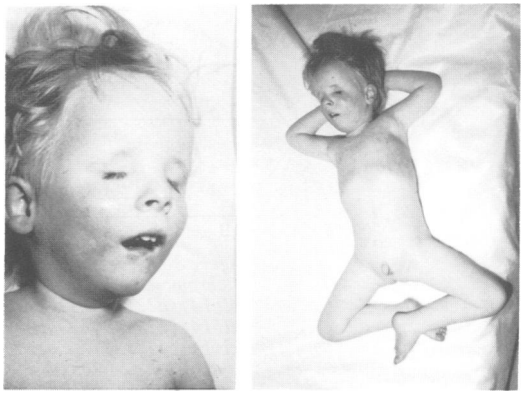

Figure 1 The patient at 4 years 5 months.

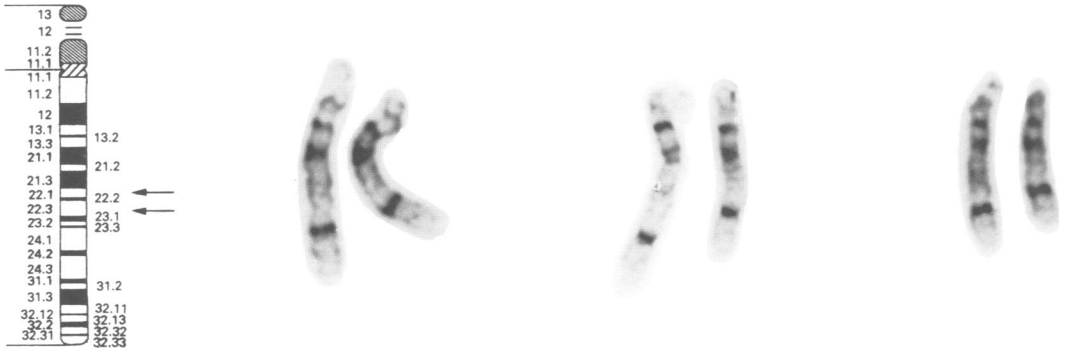

Figure 2 G banded partial karyotype. Deleted chromosome 14 is on the right. Arrows indicate the breakpoints.

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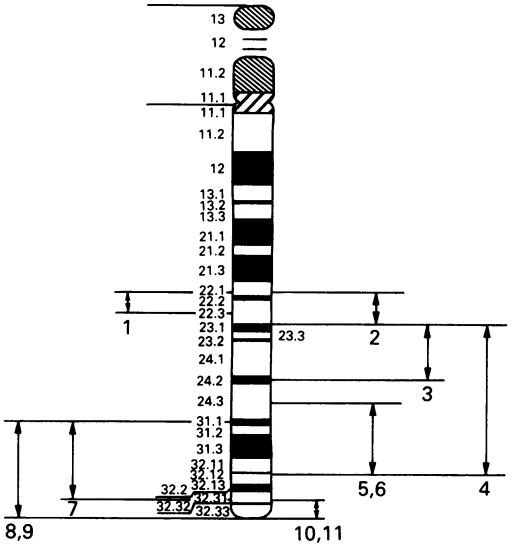

Figure 3 Schematic diagram showing deleted segments of chromosome 14 in reported cases. Case 1: del(14)(q22.1q22.3), present case. Case 2: del(14)(q22q23).[1] Case 3: del(14)(q23q24.2).[2] Case 4: del(14)(q23q32).[2] Case 5: del(14)(q24.3q32.1).[3] Case 6: del(14)(q24.3q32.1).[4] Case 7: del(14)(q31q32.3).[5] Case 8: mosaic del(14)(q31qter).[6] Case 9: del(14)(q31.1qter).[7] Case 10: del(14)(q32.3qter).[8] Case 11: del(14)(q32.3qter).[9]

was shown to be paternal in origin. At present there is no cell line established for this patient.

Discussion

Our case is the second to be published involving an interstitial deletion at 14q22. The previous case[1] was a female fetus with a deletion at q22→q23, which had similar dysmorphic features to our patient including bilateral anophthalmia, micrognathia, and underdeveloped external genitalia. The pituitary fossa was absent in the fetus.

Nine other reports of patients with interstitial or terminal 14q deletions[2–9] had breakpoints more distal than those of the present and previously described cases (fig 3). A recent review by Gorski *et al*[5] showed that there is no consistent clinical picture in these patients.

The similarities between our case and that of the fetus with a similar deletion are very striking as both had bilateral anophthalmia and micrognathia. In the fetus there was no pituitary fossa and in our patient there appears to be a pituitary abnormality resulting in hypothyroidism. The growth retardation is probably caused, at least in part, by the lack of thyroxine. The hypogonadism is likely to be associated with the hypopituitarism, but the gonadatrophin levels have not been measured. This case seems to confirm that the region 14q22 is specifically concerned with eye and pituitary development.

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