Interstitial deletion of band 3q25

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Abstract

Interstitial deletions of the long arm of chromosome 3 are rare. We report a man with an interstitial deletion involving band 3q25. To our knowledge, this is the first patient to be described with this cytogenetic abnormality.

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Case report

The proband was referred to our service for reassessment at the age of 33 years when one of his sibs was planning a family and wished to know if there were likely to be any risks to her children. He was the second child of healthy, unrelated parents and had two sisters who have had no medical problems. There was no significant history in the extended family.

The proband was born at term after an uneventful pregnancy by normal vaginal delivery. Birth weight was 3300 g (25th centile). At birth, he was noted to be hypotonic and lethargic, although he did not require ventilation. He fed poorly during the first 48 hours of life but then improved. His mother became concerned when his milestones were slower than his older sisters. He sat independently at the age of 1 year and walked at the age of 2 years 3 months. He was said to have had several single words between the ages of 1 and 3 years, but this skill was lost after the age of 3 years.

Dysmorphic features were noted at paediatric assessment at the age of 2 years 10 months. He was said to have an unusual face with a low posterior hairline, developmental delay, and characteristic hand mannerisms. He also had a relatively small penis and undescended testes. Chromosome analysis was reported as normal.

He showed little developmental progress and, from the age of 5 years onwards, gradually developed autistic features, becoming withdrawn and constantly playing with a familiar object. From the age of 9 years, he clearly showed visual, tactile, and auditory avoidance with frequent manneristic vocalisations and finger movements. In his early teens, he showed marked distress at new situations and an obsessive need for a certain arrangement of familiar objects. He developed a self-mutilating habit and repeatedly banged the bridge of his nose. His only other medical problem has been a right corneal scar, which was noted at the age of 23 years and is thought to be the result of repeated self injury.

At the time of assessment he was 33 years of age and was independently ambulant but with no speech. He was able to feed himself with a fork and was continent during the day. His

Figure 1 The proband aged 33 years. The nasal bridge is narrow and the nasal tip prominent. The right corneal opacity secondary to self injury can be seen.

ritualistic behaviour was persistent and he disliked being touched. His interaction with other people apart from close family members was minimal. He walked with a stooped gait and his joints were hyperextensible.

On examination, head circumference was 53.5 cm (10th centile) and height was 166 cm (10th centile). He had a long, thin face with a narrow nasal bridge and a prominent nasal tip (fig 1). There were bilateral epicanthic folds and the traumatic opacity of the right cornea was noted. He had an open mouth with a thick, everted lower lip. He had a prominent jaw. The ears were prominent, simple, and low set. He had large hands and feet. The fingers were long, and the interphalangeal joints appeared relatively thickened. The first and second toes were unusually long compared to the other toes and there was less pronounced thickening of the interphalangeal joints of the toes. His feet were flat with loss of the plantar arch. His neck was short with a low posterior hairline. He had a pectus carinatum. The penis was small and there were no testes palpable in a small scrotum. There were no abnormal signs detected on cardiovascular or neurological examination.

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Figure 2 Karyotype of the proband showing interstitial deletion of band 3q25.

CYTOGENETIC ANALYSIS

Chromosome analysis was repeated at the age of 33 years and showed a small interstitial deletion of the long arm of chromosome 3 at band q25 (fig 2). The karyotype was 46,XY,del(3)(q25q25). Parental karyotypes were normal. Experiments with a whole chromosome painting probe for chromosome 3 showed no evidence of a translocation or chromosome rearrangement (data not shown).

Discussion

We have reported a 33 year old man with an interstitial deletion of the long arm of chromosome 3 at 3q25 as the cause of his severe learning difficulties, autistic behavioural traits, hypogonadism, and dysmorphic features.

Interstitial deletions involving the second band of the long arm of chromosome 3 (3q2) are rare.^{1 2} A recognisable phenotype associ-

ated with interstitial deletions of 3q2 has been suggested, comprising developmental delay, growth retardation, microcephaly, blepharophimosis, ptosis, large and abnormal ears, and a prominent or beaked nose.¹ However, the most specific features of this phenotype, blepharophimosis and ptosis, are also findings in the blepharophimosis, ptosis, epicanthus inversus (BPES) syndrome, which has been localised to band 3q23.³⁻⁶ The distinctive clinical findings in the BPES syndrome allow patients with 3q23 deletions to be differentiated from those with more distal 3q2 deletions, such as our patient.

Several subjects with larger interstitial deletions involving band 3q25 than our patient have been described (table 1; the patient of Willner *et al*⁸ is excluded, as the clinical features of this patient were not specifically stated in the abstract). With the exception of blepharophimosis and ptosis, most of the dysmorphic features are non-specific, such as developmental and growth delay, epicanthic folds, displaced and dysmorphic ears, and congenital heart disease. Reports of interstitial and terminal deletions distal to 3q25 have also not yet resulted in a distinct 3q deletion phenotype, possibly owing to the paucity of documented cases.⁷⁻⁹

It is interesting that our patient has pronounced autistic and obsessive behavioural traits, a finding that has not to our knowledge been described in any of the other reported patients with deletions involving or distal to 3q24^{1 2 7-15} or in the BPES syndrome.⁵ The significance of the autistic traits in the context of this chromosome deletion in our patient is uncertain. However, specific behavioural phenotypes (for example, obsessive behaviour) are recognised features of chromosomal deletion syndromes.^{16 17}

Our patient has a short neck and a low posterior hair line. Short neck was a common dysmorphic finding among cases with 3q2 deletions^{1 2 9 12 13} and cases with breakpoints within this band.⁶ The patient also has thickening of the interphalangeal joints of his fingers and toes, a rarer physical sign that has previously been described with other digital anomalies in a patient with an interstitial deletion of 3q23q25.¹⁴

Conclusion

We describe a 33 year old man who has severe learning difficulties, autistic and obsessive behaviour, hypogonadism, and dysmorphic features including a short neck, low posterior hairline, and thickening of the interphalangeal joints of the fingers and toes. He has a de novo interstitial deletion involving band 3q25, the first patient to be reported with this cytogenetic abnormality. A specific 3q deletion syndrome apart from the BPES syndrome and deletions of 3q23 has yet to be identified, perhaps because of insufficient published reports. The patient has marked autistic and obsessive behavioural traits, findings that have not previously been associated with deletions in this chromosome region, although they are recog-

Table 1 Summary of cases with interstitial deletions involving band 3q25

Clinical findings	Franceschini <i>et al</i> ¹¹	Martolf and Ray ¹²	Al-Awadi <i>et al</i> ¹⁴	Alvarado <i>et al</i> ¹	Present case
Deleted segment	3q23→q26	3q23→q25	3q23→q25	3q23→q25	3q25
Gestation		35 wk		39 wk	Term
Birth weight		2041 g	1900 g	2280 g	3300 g
Motor delay	++	+	+	+	+
Speech delay	++		+		Severe
Growth delay	Short stature	<3rd centile	3rd centile	+	10th centile
Microcephaly		<3rd centile	<3rd centile	+	10th centile
Blepharophimosis	-†	-	+	+	-
Ptosis	-†	+	+	+	-
Telecanthus		+		+	-
Epicanthic folds	-†	+	+		+
Large/relatively prominent ears			+	+	+
Abnormally set ears		R low set	Low set	Posteriorly rotated	Low set
Dysplastic ears		Asymmetrical		+	+
Nasal bridge	Broad	Broad	Flat	Broad	Narrow
Nasal tip	Prominent†			Prominent	Prominent
Neck		Short		Short	Short
Posterior hair line		Low			Low
Heart		VSD	VSD	VSD	-

+Presence of feature, -absence of feature, spaces in the table have been left blank where no information is available.
*The patient was described as having severe mental retardation.
†Evaluated using published clinical photographs.
VSD = ventricular septal defect.

nised in other chromosomal deletion syndromes.

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