A rare case of a de novo dup(19q) associated with a mild phenotype

M Qorri, P Oei, H Dockery, J McGaughran

CASE REPORT
The proband was a female, born at 39 weeks of gestation to non-consanguineous, Caucasian parents. She was delivered by caesarean section for maternal reasons. Birth weight was 3355 g (>50th centile), length 52 cm (90th centile), and OFC 33.3 cm (>10th centile). Her Apgar scores were 9 at one minute and 10 at five minutes. She was the couple’s first child. Clinical examination at birth was normal. She had some difficulty breast feeding but managed well with bottle feeding. At 6 months of age there were concerns about her development. She was referred for assessment at the age of 11 months. Although she had good head control, she was able to sit supported, and take weight on her forearms, she could not weight bear and had no head control. She appeared to respond appropriately to visual and auditory stimuli. At 14 months, she was able to stand and eat pureed food. She had constipation, which required treatment with a laxative. Otherwise she was a healthy child with no behavioural problems and no history of seizures. On examination, her height was 85.9 cm (>25th centile), weight 13.9 kg (>75th centile), and OFC 46.5 cm (25th centile). Her neck was short and downturned, and he had micrognathia. His neck was short and downturned, and he had micrognathia. His head was small. His palate was slightly higher than normal. The remainder of the examination was unremarkable except for a crease running from between the two toes under his ear. 

Figure 1 Partial karyotype of a dup(19)(q13.1q13.3) de novo direct duplication. Arrows indicate the region of duplication.

DISCUSSION
Pure duplications of 19q are rare; two of the four previously reported cases were live born and one was an abortion. Two cases were detected prenatally and there is minimal phenotypic information. In the case described by Cotter et al, a dup(19)(q13.2q13.4) was found on chorionic villus biopsy performed for advanced maternal age. Following the discovery of a cystic hygroma on scan, a suction termination of pregnancy was carried out at 13 weeks. No phenotypic characterisation was possible. The second case found prenatally was described by Tercanly et al. During the index pregnancy, an ultrasound scan had shown the presence of a single large cystic dysplastic kidney. There were congenital heart anomalies including a ventricular septal defect, aortic coarctation, and an anomaly of the aortic arch. A chorionic villus biopsy was performed and the fetus found to have dir dup(19)(q13.1q13.3) de novo. The final karyotype was interpreted as 46,XX,dir dup(19)(q13.1q13.3) de novo.ish dir dup(19)(q13.1q13.3) (wcp19+).

METHODS AND RESULTS
Cytogenetic G banded studies undertaken on stimulated peripheral blood lymphocytes using conventional techniques showed a de novo, non-mosaic duplication of chromosome 19 between bands q13.1 to q13.3 (fig 1). The 60 cells examined included 5% mosaicism with 95% confidence. Parental chromosomes were normal. Fluorescence in situ hybridisation (FISH) studies with a whole chromosome 19 paint (wcp19) probe (Boehringer Mannheim) confirmed the G banding analysis. The final karyotype was interpreted as 46,XX,dir dup(19)(q13.1q13.3) de novo.ish dir dup(19)(q13.1q13.3) (wcp19+).
An unusual dup(19q) presented by Quack et al \(^4\) described a supernumerary ring chromosome in an overweight boy with dysmorphic facies and mental retardation. On physical examination, he had macrocephaly, hypertelorism, downward slanting palpebral fissures, and a bluish ring around the eyes. He also had a prominent nose and an unusually shaped ear. FISH studies showed the ring to be derived from the long arm of chromosome 19, r(19)(q11.05q13.2). The mother showed the same extra r(19) chromosome. Her phenotype is mild, possibly because of the genetic content and the size of the trisomy 19q, and may result in a less severe phenotype associated with more proximal duplication. It appears that the patient has essentially pure duplication. The phenotype of both mother and child is similar to the case reported by Cotter et al \(^2\). The patient presented with a pure de novo direct duplication. The mechanism for the formation of duplications is not known. In theory, duplications are thought to result from an insertion or translocation involving the other homologue, or unequal crossing over or sister chromatid exchange at meiosis.\(^5\) Our patient presented with a pure de novo direct duplication. The phenotype is mild, possibly because of the genetic content and the size of the trisomy 19q, and may result in a less severe phenotype associated with more proximal duplication. It appears that the patient has essentially pure trisomy 19(q13.1-q13.3). Ideally, to provide further characterisation of the breakpoints, locus specific probes could be used. This may delineate more clearly a critical region associated with the milder phenotype. However, there was insufficient specimen to carry this out and the parents have declined to have any further blood tests.

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