Electronic letter

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DEFECT 11 syndrome associated with agenesis of the corpus callosum

EDITOR—A total of 15 cases of DEFECT 11 syndrome (MIM 601224) have been reported to date.[1–8] It is a rare contiguous gene syndrome caused by a deletion in the 11p13-p11 region.[6] The main clinical manifestations of the syndrome include multiple exostoses (EXT), enlarged parietal foramina (foramina parietalia permagna, FPP), craniofacial dysostosis, and mental retardation. Various minor features have been described, such as small penis, seizures, hypotonia, obesity, simian creases, epicanthus, and telecanthus.[6] Recently, we encountered a Japanese patient who had EXT, FPP, and other associated findings of DEFECT 11 syndrome. An unusual finding seen in our patient was agenesis of the corpus callosum (ACC, MIM 217990).

The patient is the third child of a non-consanguineous marriage. Both parents are healthy and other family members have no medical problem. He was born at 32 weeks of gestation because of maternal pre-eclampsia. At birth, he weighed 1095 g and had hypospadias and bilateral undescended testes. The Apgar score was not recorded. At 5 months, he was operated on for left inguinal hernia. The first epileptic seizure was noted at 3 years of age. Developmental milestones were delayed. He had head control at 2 years, sat alone at 4 years, and crawled at 5 years.

On physical examination at 15 years, severe psychomotor retardation was obvious. He could neither speak nor stand. He had oxycephaly, a protruded tongue (fig 1), fat fingers, a small penis, bilateral undescended testes, and hypospadias. Neurological examination showed generalised hypotonia and bladder and anal disturbances. Electroencephalogram showed irregular polyspikes at the left parietal lobe. Routine blood examination showed no abnormalities. Radiological findings showed multiple exostoses, particularly in the shoulder, hand, and leg bones (fig 2A) and bilateral parietal foramina in the skull (fig 2B). Brain MRI showed hypoplasia of the medial aspect of the occipital lobes and complete ACC (fig 3). All of these clinical findings were compatible with a diagnosis of DEFECT 11 syndrome except for ACC which has not previously been described in patients with this syndrome.

Karyotype analysis (fig 4) on the patient's peripheral blood cells (SRL, Tokyo, Japan) showed (1) an interstitial deletion that involved 11p12, (2) an insertional translocation of band 11p13-p14.2 into 11p14.3, and (3) a paracentric inversion between p13-q11; thus, his karyotype was designated 46,XY,der(11)(pter-p14.3::p14.2-p13::p14.3-p14.2::p13-p13::q11-cen-p11.11::p11.2-p13::q11-qter). His parents had normal karyotypes.

To identify the deleted area of chromosome 11, genomic DNA from the patient and his parents was analysed by PCR amplification of polymorphic microsatellite markers located in the pericentric region of chromosome 11.[6 8] Primer sequences for Genethon markers were obtained from the Genome Data Base (http://www.genethon.fr).

PCR analysis on the patient's genomic DNA confirmed a de novo deletion of the maternal allele that involved D11S903, D11S1361, D11S1344, and D11S1326 and the presence of two alleles for markers D11S905 and D11S916. Therefore, the distal deletion breakpoint was located between D11S905 and D11S903. To the proximal side, the deleted region extended to D11S1326, which is located at the most proximal side on the short arm of chromosome 11. Since the centromere has to be present in the rearranged chromosome, the proximal deletion breakpoint must be located close to the centromere of 11p (fig 5). Thus, the deletion of our patient involved a portion of chromosome 11 quite close to those reported previously.[1–8]

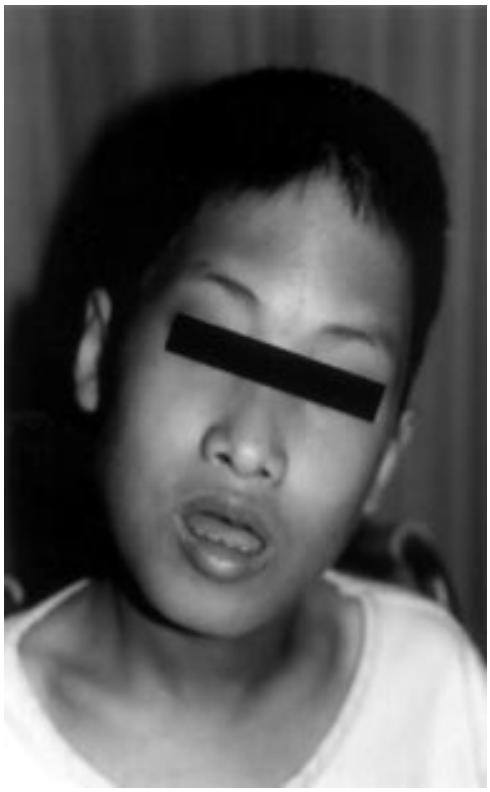

Figure 1 The patient at the age of 15 years.

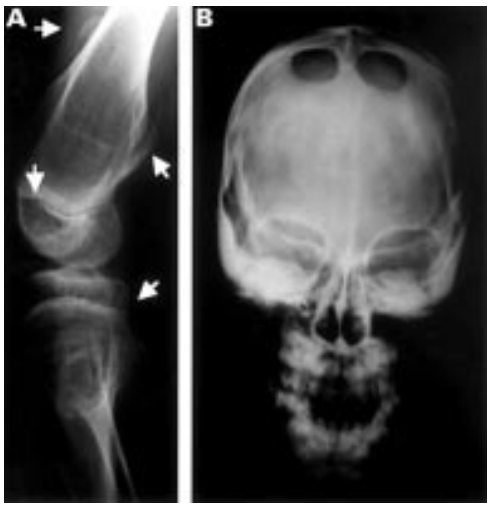

Figure 2 Radiographical findings in the bones. (A) X rays of the knee showing multiple exostoses (arrows). (B) Cranial x ray showing bilateral parieto-occipital foramina.

Both clinical and genetic findings indicated that our patient was a typical case of DEFECT 11 syndrome except

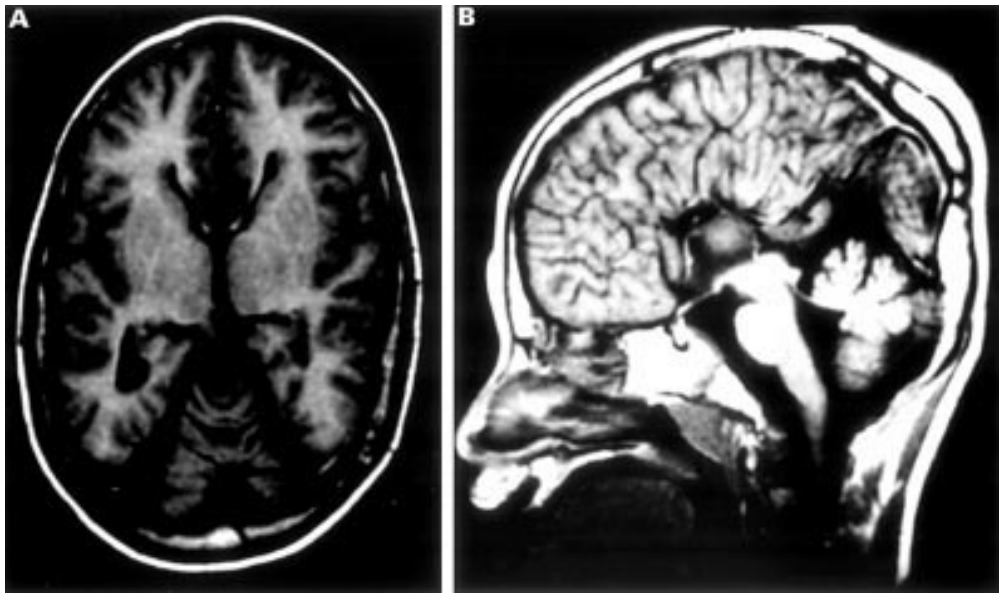

Figure 3 MRI findings. (A) An axial section showing hypoplasia of the medial side of the occipital lobes. (B) A sagittal section showing complete ACC.

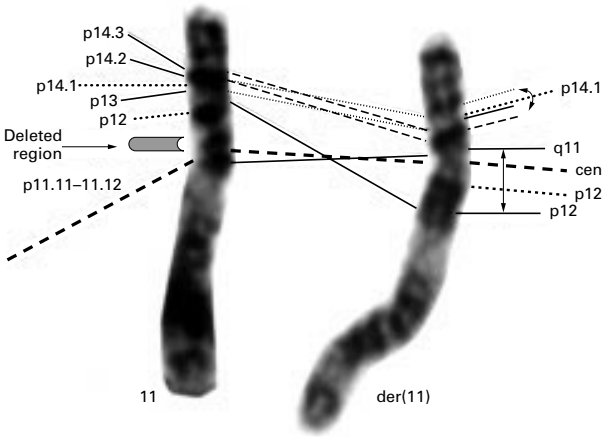

Figure 4 Chromosomal analysis obtained from phytohaemagglutinin blood cultures using trypsin (GTG) banding. See text for details.

for ACC which has never been described in previous cases. Although the presence of a coincidental genetic lesion in other loci could not be excluded, the findings in our patient suggest the presence of gene(s) responsible for ACC in the proximal portion of the short arm of chromosome 11 or in other dissected sections at chromosomes 11p14.3, 14.2, 13, and q11.

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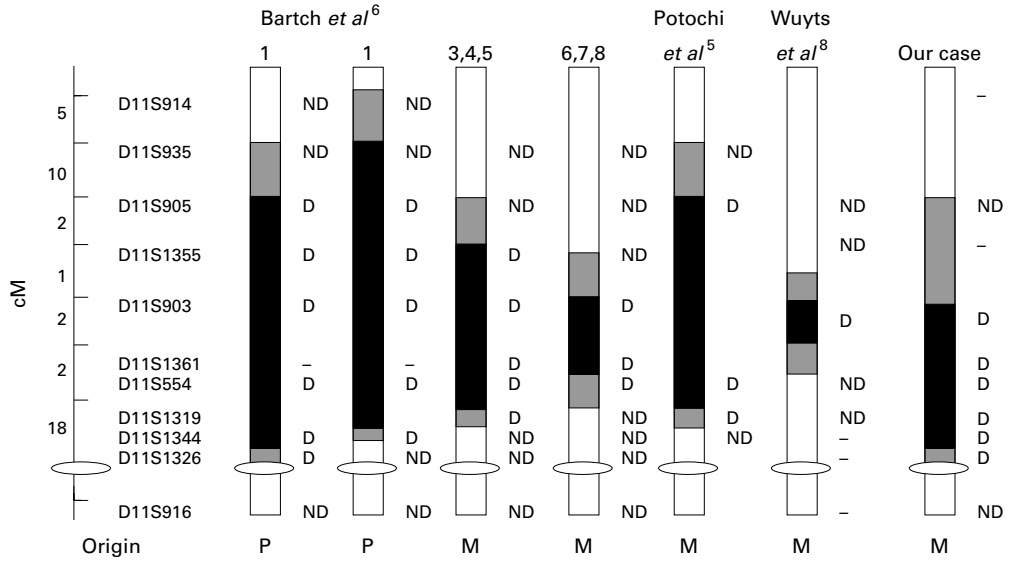

Figure 5 Detection of centromeric chromosomal markers by genomic PCR. According to Bartsch et al,[6] the determination of the deletion breakpoints was solely based on the presence or absence of the parental alleles. P: paternal origin, M: maternal origin, D: deleted, ND: not deleted, -: not informative or not mentioned.

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