An unbalanced (6q;13q) translocation in a male with clinical features of Ehlers-Danlos type II syndrome

P R SCARBROUGH*, J DAW‡, A J CARROLL*, AND S C FINLEY*†

*Laboratory of Medical Genetics, †Department of Pediatrics, and ‡Department of Psychiatry, University of Alabama in Birmingham, Birmingham, Alabama, USA.

SUMMARY Ehlers-Danlos syndrome has been divided into several different types according to the variety and severity of clinical manifestations, and may follow autosomal dominant, autosomal recessive, or X linked patterns of inheritance.¹ Only rarely have chromosome anomalies been seen in patients manifesting phenotypic features of the syndrome and most are considered insignificant.² However, one case report³ involved a balanced t(9;17)(q34;q11) in a female with the clinical features of Ehlers-Danlos type I and IV syndromes and, as noted by McKusick: "It is possible, furthermore, that certain very rare syndromes that are transmitted in a Mendelian manner are the result of small chromosome aberrations, such as deletion or inversion, affecting the action of several genes".⁴ We present a 14 year old male with features of Ehlers-Danlos type II syndrome and an unbalanced (6q;13q) translocation.

Case report

The patient, a 14 year old white male, was admitted to the Adolescent Psychiatry Service of a University Hospital for evaluation of increasingly aggressive behaviour. Before admission the patient had been suspended from school for verbal and physical aggression toward peers and teachers. Juvenile court authorities had become involved when the patient physically attacked his mother. The court requested evaluation to determine the most appropriate treatment and placement for the patient.

The patient was a 3.4 kg term infant. His mother was described as nervous and depressed during pregnancy. Labour was induced. The mother reported that the infant's cord was wrapped around his neck but stated there were no complications. The patient was reported to be a jerky, fretful infant. He sat alone at approximately 9 months and walked at 14 months. He was described as uncoordinated

with many falls and bruises. The patient wore orthopaedic prescribed shoes because "his feet turned in". Other developmental milestones were normal except for nocturnal enuresis. The patient began kindergarten at the age of 5 and was dismissed because of immaturity and disruptiveness. He was evaluated by a child psychiatrist who felt he was hyperactive and recommended a trial of Ritalin (methyl phenidate). The parents did not follow through with the recommendation for medication. The patient started first grade at the age of 7 and has had a history of poor academic performance and behaviour problems throughout his school career.

The patient was admitted to hospital at the age of 7 for concussion following a motor vehicle accident. Five days after admission he was discharged with no neurological deficit. He had no other admissions to hospital. The patient was on no medication at the time of admission.

The patient's biological parents were married for approximately 10 years and divorced when the patient was 8. The patient lived with his father and older sib for 3 years and then was placed in a residential treatment facility until discharged to his mother 4 months before this admission. Both parents have remarried and the older sib is currently residing in a residential treatment facility.

Family history is significant for the sib, an aunt, and a cousin having received psychiatric treatment. The patient's mother is described as double jointed.

Examination at the time of admission revealed a cooperative white male in no apparent distress. Vital signs were normal. His height was 157 cm (25th centile) and weight 44.5 kg (25th centile). Significant findings included hyperextensibility of the joints (fig 1), particularly the wrists, ankles, and temporomandibular joints. Fingers and toes were elongated. There were several well healed parchment-like scars over both shins. Skin texture was somewhat velvety. Eye examination was positive for intermittent exotropia, hyperopia, and mild amblyopia. Neurological examination was positive for mild frontal bossing of the skull, bilateral hyperreflexia, a mild right hemiparesis, and an unusual gait. Hearing was normal bilaterally. Laboratory studies revealed normal electrolytes, liver function, and CBC.

FIG 1 *Hyperextensibility of joints in the proband.*

An EEG revealed abnormal bursts of generalised spike and wave activity and some bioccipital sharp and slow wave complexes. A Phillips CT brain scan was performed and revealed mild third ventricular and moderately severe lateral ventricular enlargement. Dysplasia was thought to be more probable than hydrocephalus. Neurology consultants felt both abnormalities could be residual effects of anoxia at birth although congenital malformation of the ventricular system is a possibility.

The patient's phenotypic features, including hyperextensibility of the joints in the hands and feet, velvety skin, mild propensity for bruising, and scar formation, were consistent with a diagnosis of

Ehlers-Danlos type II syndrome. Cytogenetic studies were performed because of the history of aggressive behaviour.

CYTOGENETIC STUDIES

Chromosome preparations were obtained from short term phytohaemagglutinin stimulated lymphocytes. Cells were analysed using GTG banding and revealed the presence of 45 chromosomes and an unbalanced translocation between a chromosome 6 and 13. Breakpoints were assigned to 6q27 and 13q11. The karyotype was designated as 45,XY,-6,-13,+der(6),t(6;13)(q27;q11) (fig 2a, b). The proband was monosomic for 13pter→13q11 and a small part of 6q27. Results of cytogenetic studies on the father's peripheral lymphocytes were normal. Other relatives were unavailable for cytogenetic study.

Discussion

Ehlers-Danlos syndrome presents with a wide spectrum of clinical manifestations which creates the basis of the nine subgroups. A common feature seen in all types, however, is an apparent abnormality of connective tissue secondary to aberrant collagen synthesis. Specific enzyme deficiencies have been elucidated for types V, VI, and VII.⁵ It follows that several different gene loci must be involved to provide these varied clinical and biochemical abnormalities. In the case of our patient, genes located in the area of the breakpoints 6q27 or 13q11 may be responsible for the features of Ehlers-Danlos type II syndrome. Further studies, including identification of a specific enzyme defect for this syndrome, should help define the significance of the phenotypic features present in this patient and the presence of an unbalanced translocation resulting in relatively well defined small chromosomal deletions.

The technical assistance of Vinnia Anderson and Barbara Thornton and the secretarial assistance of Shirley Gann and Barbara Rodgers are gratefully acknowledged. This study was partially supported by Grant No MJC-000905-20-0, Department of Health and Human Services.

FIG 2 (a) *Partial karyotype of the proband with normal chromosomes 6 and 13 and derived chromosome 6.* (b) *Diagrammatic illustration of the chromosome rearrangement t(6;13)(q27;q11). Breakpoints are indicated by arrows.*

References

- ¹ Bergsma D, ed. *Birth defects atlas and compendium*. 2nd ed. The National Foundation-March of Dimes. Baltimore: Williams and Wilkins, 1979.
- ² Beighton P, Price A, Lord J, Dickson E. Variants of the Ehlers-Danlos syndrome: clinical, biochemical, haematological and chromosomal features of 100 patients. *Ann Rheum Dis* 1969;**28**:228-42.
- ³ Dockery HE, Neale HC, Fitzgerald PH. Gross congenital abnormality associated with an apparently balanced chromosomal translocation t(9;17)(q34;q11). *J Med Genet* 1982;**19**:380-3.
- ⁴ McKusick VA. *Human genetics*. New Jersey: Prentice Hall, 1964.
- ⁵ Stanbury JB, Wyngaarden JB, Fredrickson DS, Goldstein JL, Brown MS, eds. *The metabolic basis of inherited disease*. 5th ed, chap 63. New York: McGraw-Hill, 1983:1434-7.

Correspondence and requests for reprints to Dr P R Scarbrough, Laboratory of Medical Genetics, University of Alabama in Birmingham, University Station, Birmingham, Alabama 35294, USA.

Mosaic hexasomy 21 *

A KETUPANYA†, B F CRANDALL‡, K BLANCHARD†, AND D W ROGERS§

Departments of Obstetrics and Gynecology† and Pediatrics and Psychiatry‡, UCLA; and §Pathology Department, Santa Monica Hospital, Los Angeles, California, USA.

SUMMARY Cases in which there are more than three copies of a sex chromosome, and rarely of an autosome, have been reported, but to our knowledge hexasomy has never been described except in tissue undergoing neoplastic change. This report describes a female infant with multiple malformations in whom we found a mosaic hexasomy 21. This was first detected in amniotic fluid cells and subsequently in skin fibroblasts.

Case report

Spontaneous delivery of this female infant occurred at about 36 weeks' gestation. Birth weight was about 4000 g and the head circumference was 34 cm. Respirations were gasping and irregular and there was acrocyanosis with dusky discolouration of the lips. The anterior fontanelle was large and cranial sutures, including the metopic, were widely open. Despite its circumference, the head appeared small in comparison to the body. There was marked hypertelorism with short upward slanting palpebral fissures. The globes were small and the corneae cloudy. There was a right sided cleft of the lip, complete cleft of the palate, and marked nasal hypoplasia. The ears were low set and rotated, and the lobes were fleshy. The neck was short with redundant soft tissue folds posteriorly.

*This research was supported in part by HD 5615, Developmental Biology in Mental Retardation, and HD 04612, Mental Retardation Research Center grant.

Received for publication 15 September 1983.

Accepted for publication 3 October 1983.

The chest was narrow with hypoplastic nipples. The heart was normal on auscultation. The sternum was of normal length. External genitalia were normal female and the anus was anteriorly placed. The spine appeared normal.

The upper limbs were hypotonic and abnormalities were confined to the hands. Both thumbs were triphalangeal and the fingers were tapered with hypoplastic nails. There was camptodactyly of fingers 4 and 5 on the right and clinodactyly of the right second and left fourth fingers. There were simian lines bilaterally. Dermatoglyphs were unremarkable.

The lower limbs were hypotonic with prominent heels and a midplantar vertical crease bilaterally.

The baby died shortly after birth. Necropsy confirmed the physical observations. The heart was normal on gross examination and the brain on gross and microscopical study. X-ray examination failed to reveal any skeletal abnormalities and confirmed the clinical impression of borderline microcephaly.

The mother and father were both aged 36 and in good health. There had been two previous pregnancies, one ending in an early spontaneous abortion and the second with a normal female whose development has been entirely normal. There was no other relevant family history.

The pregnancy had been unremarkable except for an influenza-like illness early in gestation which lasted about one week. An amniocentesis was requested because of maternal age and was performed at about 16 weeks' gestation.