variation (Yq— variant) or a true terminal deletion of the long arm of a Y chromosome (Yq—), as the fathers were not studied apart from one child reported by Walzer and Gerald.¹² Therefore, the incidence of Yq— (deletion) and Yq— (variant) is unknown.

Infertility or fertility, normal or short stature, normal intelligence or mental retardation, and varying dysmorphic features have been observed in Yq—. This child presented with different dysmorphic features, short stature, and mental retardation. In addition, he also had marked livedo reticularis and microcephaly. He was of normal birthweight and, therefore, does not come into the syndrome of microcephaly, snub nose, livedo reticularis, and low birthweight dwarfism.¹³ The dysmorphic features, apart from short stature, described in the reported patients with Yq— are not similar and thus not of a specific phenotype. Whether they are polygenic, spontaneous, or related to Yq— is unknown. A differentiation should be made between Yq— (deletion) and Yq— (variant) to determine whether clinical findings are specific.

The proband recently died at 9 years 6 months of age from massive confluent bronchopneumonia. An aganglionic segment of the distal colon was noted at necropsy.

PHILIP E PODRUCH, FU-SUN YEN,
NUHAD D DINNO, AND BERNARD WEISSKOPF
*Child Evaluation Center,
Department of Pediatrics,
University of Louisville,
School of Medicine,
Louisville, Kentucky, USA*

References

- Langmaid H, Laurence KM. Deletion of the long arms of the Y chromosome with normal male development and intelligence. *J Med Genet* 1974;**11**:208–11.
- Borgaonkar DS, McKusick VA, Herr HM, de los Cobos L, Yoder OC. Constancy of the length of the human Y chromosome. *Ann Genet (Paris)* 1969;**12**:262–4.
- Yunis E, Garcia-Conti FL, de Caballerro OMT, Giraldo A. Yq deletion, aspermia, and short stature. *Hum Genet* 1977;**39**:117–22.
- Meisner LF, Inhorn SL. Normal male development with Y chromosome long arm deletion (Yq—). *J Med Genet* 1972;**9**:373–7.
- Scherini A, Sangermani R, Elli P. Delezione delle braccia lunghe del cromosoma Y e malformazioni multiple. *Minerva Pediatr* 1979;**31**:729–31.
- Nakagome Y, Sasaki M, Matsui I, Kawazura M, Fukuyama Y. A mentally retarded boy with a minute Y chromosome. *J Pediatr* 1965;**67**:1163–7.
- Telfer M, Baker D, Rollin I. Probable long-arm deletion of Y chromosome in boy of short stature. *Lancet* 1973;**i**:608.
- Neilsen J, Sillesen I, Sorensen AM, Sorenson K. Follow-up until age 4–8 of 25 unselected children with sex chromosome abnormalities, compared with siblings and controls. *Birth Defects* 1979;**XV**(1):15–73.
- Hamerton J, Canning N, Ray M, Smith S. A cytogenetic survey of 14,069 newborn infants. 1. Incidence of chromosome abnormalities. *Clin Genet* 1975;**8**:223–43.
- Borgaonkar DS. Cytogenetic screening of community-dwelling males. In: Cohen *et al*, eds. *Genetic issues in public health and medicine*. Springfield, Illinois: Thomas, 1978:215–34.
- Kuleshov NP, Kulieva LM. Frequency of chromosome variants in human populations. *Genetika* 1979;**15**(3):745–51.
- Walzer S, Gerald PS. A chromosome survey of 13,751 male newborns. In: Hook EB, Porter IH, eds. *Population cytogenetics*. New York: Academic Press, 1977:45–61.
- Christian JC, Johnson VP, Biegel AA, Gresham EL, Rosenberg GJ. Sisters with low birth weight, dwarfism, congenital anomalies, and dysgammaglobulinemia. *Am J Dis Child* 1971;**122**:429–34.

Requests for reprints to Dr Philip E Podruch, Child Evaluation Center, 334 E Broadway, Louisville, Kentucky 40202, USA.

Gross congenital abnormality associated with an apparently balanced chromosomal translocation t(9;17)(q34;q11)

SUMMARY Gross mental and physical abnormality is described in an adult female who had some features similar to those of Ehlers-Danlos syndrome. There was no family history of the disorder. The patient also carried a balanced chromosomal translocation t(9;17)(q34;q11).

Surveys indicate that balanced chromosomal rearrangements are found in about 1·15% of newborn infants and that these rearrangements arise de novo in 0·02%.¹ Karyotypic imbalance is usually associated with mental retardation and multiple anomalies, whereas it is a general finding that persons with balanced chromosomal rearrangements are phenotypically normal.¹ Thus, almost all the newborn infants with balanced de novo rearrangements found by the surveys were phenotypically normal.¹ Nevertheless, some persons with balanced de novo chromosomal rearrangements have shown mental retardation or physical anomaly. Tharapel *et al*¹ reviewed 25 cases from the literature and described a further six cases. Most were ascertained because of their physical or mental anomaly and it is therefore not possible to reach a reliable estimate of their incidence. However, the absence of such

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Case reports

cases from the large newborn surveys indicates that they are rare. We report a further case who is of interest not only because of her balanced chromosomal translocation, but also because of the range and unusual nature of her congenital abnormalities.

Case report

The patient, a female born in 1946, was admitted to a mental home at the age of 5 years because of severe mental retardation and apparent Down's syndrome. She was noted to be "an obese very pale child with extensive bruises on the limbs and scars on the skin of the legs". She did not speak or feed herself and required full nursing care.

The patient was microcephalic with a prominent forehead and hypogenesis of the middle third of the face (fig 1), a short broad nose, a straight fish-mouth, and a large broad tongue with no median groove. She had a short neck and wide chest with abnormally widely spaced nipples. There was bilateral dislocation of the hips with rudimentary femoral heads present. The soles of the feet were convex distally (rockerbottom) and there were overlapping fingers and toes. Gross hypotonia of the skeletal muscles resulted in her being unable to stand without full support and in extreme hypermobility of the limb joints. She moved along the floor in a prone position resembling the movement of a seal on land.

Epilepsy was noted from the time of her admission and had been controlled by phenytoin. This drug and thioridazine were withdrawn 5 years before her death because of myelofibrosis of her bone

marrow at that time. No epilepsy occurred after their withdrawal. She died at the age of 34 years of bronchopneumonia. At necropsy, the brain was found to be small (1100 g) and there was a degree of parietal lobe atrophy.

The patient's mother was aged 26 and her father 36 when she was born. There were four children of the marriage. Her mother remarried after the death of the father and produced a further six children. These children showed no abnormality similar to the patient. A cytogenetic study of the family was not permitted.

The patient exhibited three notable features throughout her lifetime: anaemia and thrombocytopenia, a peculiar fragility of the skin, and an apparent inability to experience pain, at least that arising from trauma to the skin. These features will be discussed further.

Manifestations of anaemia and thrombocytopenia were present on her admission at the age of 5. During her subsequent 28 years she was never without bruises and pallor. The bruises usually appeared without any known trauma and were sometimes very extensive. She also had occasional epistaxis. Successive blood examinations throughout her adult life always showed anaemia, the degree varying from Hb 8 to 10.2 g/dl, PCV 0.27 to 0.33. The leucocyte count was below normal with a relative neutropenia; platelets were never above 68 000/mm³ and often only about 40 000/mm³. Folate, B₁₂, and iron supplies were repeatedly found to be adequate. A bone marrow aspirate taken in 1973 showed marrow hypoplasia and withdrawal of anticonvulsant and antipsychotic drugs produced no improvement. Splenomegaly and hepatomegaly were noted for the first time in November 1978, and progressed slowly up to the time of her death in 1980. A leukaemic change was suspected to be taking place, but was not supported by examinations of peripheral blood and bone marrow. At necropsy the spleen was grossly enlarged (weight 1100 g) as were lymph nodes in relation to the iliac vessels, the aorta, and splenic vessels. Microscopy showed that both spleen and nodes were the site of extramedullary haemopoiesis and also contained iron deposits. The bone marrow showed patchy myelofibrosis. Liver enlargement was the result of extensive fatty infiltration.

Throughout her 28 years in hospital the patient developed deep ragged splits in the skin at irregular intervals of a few weeks. The splits occurred mainly on the limbs but also on the trunk and varied in length from about 1 to 10 cm. They involved the whole thickness of the skin and extended into the subcutaneous tissue. Healing took several weeks even when the skin was sutured. Wide thin scars

FIG 1 The patient showing facial and general features.

FIG 2 *Dermatoglyphs of the patient's hands.*

resulted and ultimately occupied about one third of the total surface of the legs. These spontaneous skin ruptures had been occurring from before the age of 5 judging from the scars on the child's legs at the time of her admission. Necropsy of the skin exhibited a fibrotic dermis and very prominent vasculature with perivascular inflammatory infiltrate.

The patient did not react to pain-producing skin stimuli. It was repeatedly noticed by observers that the patient, though well able to make her displeasure known, never showed any sign of discomfort from her spontaneous skin splits and made no attempt to protect them from pressure or impact. Although

timid in other respects, she showed no evidence of discomfort from needle punctures, painful dental procedures, and bone marrow puncture or trephine. Postmortem microscopy of different segments of skin showed a paucity or absence of nervous tissue in the dermis.

DERMATOGLYPHS

Finger patterns were large and complex (fig 2). The cores of the loops and whorls were vertically orientated and the ridge count was increased (!58+). The palms had an A line which descended vertically, and on the left palm the *a* triradius was slightly deflected toward the radial border. The *d* triradii were deflected away from the ulnar border.

CYTOGENETICS

Peripheral blood lymphocytes cultured with PHA and Giemsa banded showed a translocation of the long arm of chromosome 17 to the long arm of a chromosome 9 (fig 3). This appeared to be a simple balanced translocation. Any reciprocal exchange must have involved minor amounts of chromosome material which were not visible. C banding showed that the centromeric region of the remaining fragment of chromosome 17 was intact and that there was no constitutive heterochromatin from chromosome 17 near the point of translocation on chromosome 9. The translocation breakpoints appeared to

FIG 3 *Giemsa banded metaphase cell from the patient, 46,XX,t(9;17)(q34;q11).*

be 9q34 and 17q11. This translocation was found in all 55 metaphase cells examined from cultures of two separate blood samples. Attempts to get bone marrow aspirate for cytogenetic studies were not successful, and skin biopsies failed to grow in culture.

Discussion

Balanced chromosomal interchanges are usually associated with a normal phenotype, but there is a small number of cases which have an abnormal phenotype. These cases may represent the chance association of chromosomal change and unrelated developmental abnormality. On the other hand, the degree and complexity of congenital physical abnormality shown by many of these patients, and certainly by the present patient, are such as might be expected to result from major genetic imbalance. It is also recognised that apparently balanced interchanges may carry significant cytogenetic imbalance at the submicroscopical level, possibly resulting from earlier recombinational events, or genetic imbalance may result from the separation of functionally related genetic elements as in a position effect. It is therefore possible that our patient's physical abnormality resulted from the cytogenetic changes.

Among the gross congenital abnormalities shown by our patient, some were similar to the abnormal features characterising forms of Ehlers-Danlos syndrome.^{2,3} The spontaneous skin splitting and hyperextensibility of the joints were suggestive of Ehlers-Danlos syndrome type I, although skin fragility and splitting in Ehlers-Danlos syndrome is usually seen over bony prominences and not necessarily on the trunk. Her tendency to bruising was suggestive of Ehlers-Danlos syndrome type IV. Some other features of the patient could have been secondary to these basic features. Thus, her haematological complications might have been secondary to the loss of blood, and her inability to feel pain might have been related to brain damage resulting from intracranial bleeding. On the other hand, the patient's microcephaly and facial and chest deformity were not characteristic of Ehlers-Danlos syndrome, and a number of her features might be explained by retardation or a form of sensory neuropathy.

Whereas our patient cannot be said to have Ehlers-Danlos syndrome, some of her abnormal features appear to have had an origin similar to features of that syndrome. Ehlers-Danlos syndrome covers a range of abnormality which is the basis of eight syndrome types.³ Defective connective tissue, which most probably results from a collagen abnormality, is basic to all types and specific defects in collagen synthesis have been identified for some

types. Ehlers-Danlos syndrome is also inherited in several forms, autosomal dominant, autosomal recessive, and sex linked.³ Clearly, several different gene loci are involved in the aetiology of the disorder. It is possible that the translocation in our patient may help to locate the position in the human chromosome complement of some of the genes that determine features of Ehlers-Danlos syndrome. Such genes might be located near chromosome 9q34 or chromosome 17q11, the breakpoints of the translocation. However, future independent studies will locate the position of genes that determine Ehlers-Danlos syndrome and such information may be relevant to an understanding of the present patient.

No significant association has been shown between Ehlers-Danlos syndrome and chromosomal abnormality, except for a case associated with enlargement of the short arm of a G group chromosome in an earlier study.⁴

The translocation (9;17)(q34;q11) carried by our patient is different from any of the balanced translocations found in the 31 phenotypically abnormal patients that were reviewed and described by Tharapel *et al.*¹ Indeed, this translocation does not appear to have been described before.⁵

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HEATHER E DOCKERY*, H C NEALE*, AND
P H FITZGERALD†

*Cytogenetics Unit, Nelson Hospital and
Ngawhatu Hospital, Nelson; and

†Cytogenetics Unit, Christchurch Hospital,
Christchurch, New Zealand

References

- 1 Tharapel AT, Summitt RL, Wilroy RS, Martens P. Apparently balanced *de novo* translocations in patients with abnormal phenotypes: report of 6 cases. *Clin Genet* 1977; **11**: 255-69.
- 2 Bergsma D, ed. *Birth defects atlas and compendium*. The National Foundation—March of Dimes. Baltimore: Williams and Wilkins, 1974.
- 3 McKusick VA. *Mendelian inheritance in man*. 5th ed. Baltimore: Johns Hopkins University Press, 1978.
- 4 Vormittag W, Kühböck J, Weninger M. Vergrößerung der Region des kurzen Armes eines kleinen akrozentrischen Chromosoms. *Humangenetik* 1972; **14**: 112-21.
- 5 Borgaonkar DS. *Chromosomal variation in man*. New York: Liss, 1977.

Requests for reprints to Dr P H Fitzgerald, Cytogenetics Unit, Christchurch Hospital, Christchurch, New Zealand.