SHORT REPORTS

Unusual chromosomal variant in Klinefelter's syndrome

Unusual variants of common conditions can be informative about the origins of abnormalities associated with those conditions. Classical cases of Klinefelter's syndrome have a combination of hypogonadism, azoospermia, small testes, tall stature, gynecomastia, and diminished intelligence. This syndrome is usually associated with the karyotype 47 XXY. We therefore describe a patient with Klinefelter's syndrome in whom one of the X chromosomes is an isochromosome for the long arm, karyotype 47 XXqiY. The patient was of normal stature, had normal male habitus, and was of average intelligence. The patient's chromosome complement thus provided unique information about the influence on development of the individual arms of the X chromosome.

Case report

A 36-year-old service engineer was referred to an endocrine clinic because of infertility after four years of marriage. Azoospermia had been documented on two occasions. The patient had been partially impotent for the previous six months. He had grown a beard while in the Merchant Navy and since leaving the Service had shaved daily. In the past he was said to have suffered from Reiter's syndrome.

His height was 164.5 cm. He was of average intelligence, judged by his occupation and his response to investigative procedures. He had a normal male habitus, with normal male distribution of facial and body hair. There was no gynecomastia. The testes were firm and small, volume 2 ml each. We also obtained the heights of his family: father 165 cm, mother 152 cm, and sisters 162 cm and 150 cm.

Investigations showed a low serum testosterone concentration of 5.9 nmol/l (laboratory normal range 8.5-27.5), and raised gonadotropin concentrations: luteinising hormone 33.0 U/l (normal range 1-7), and follicle stimulating hormone 28.0 U/l (normal range 1-6). These findings indicated intrinsic gonadal failure. A skull x-ray film was normal. A culture of peripheral blood lymphocytes yielded cells of the karyotype 47 XXqiY, one of the X chromosomes being an isochromosome long arm (see figure). The mother and both sisters have normal karyotypes, 46XX.

The sex chromosomes from two cells of a lymphocyte culture from the patient. (Trypsin-giemsa banding. $\times 2000$.)

Comment

Chromosomally the patient differs from the normal male (46XY) in having an extra chromosome made up of two long arms of an X chromosome, (Xqi), and differs from the standard case of Klinefelter's syndrome (47 XXY) in having no extra short arm (Xp) material and having two long arms of X (Xq) extra instead of the usual one Xq extra.

Evidently excess of p arm material is not necessary to produce atrophy of the seminiferous tubules, sterility, and testosterone deficiency. Nevertheless, the complete androgenisation of facial and body hair is a small indication that excess of p arm material contributes to the speed at which testicular atrophy occurs in people with an XXY configuration, although normal facial and body hair are occasionally seen in these patients. Klinefelter's syndrome is usually associated with diminished intelligence but many cases are seen with normal intelligence. In these respects our patient is therefore only a little unusual.

The stature of our patient is quite exceptional for Klinefelter's syndrome, being almost exactly that expected of a normal son of his parents, whereas persons with Klinefelter's syndrome are usually tall. We have compared his height with 42 cases, who were not inmates of mental deficiency hospitals and were aged between 18 and 60 years, reported by Court Brown *et al.*¹ Their mean height was 178.4 cm.

(SD 6.277) and our patient is shorter than all of them. On the other hand, six personal (JEG) cases of Klinefelter's syndrome with the karyotype 46 XX had heights of 160, 155, 173, 150, 175, and 170 cm, and our patient fits neatly into their mean of 164 cm.

The stature of our patient would support the idea that there are genes on the short arm of X (Xp), and on Y, but not on the long arms of X (Xq), that act in a simple additive way to increase stature. Thus persons with 45X, 46XXqi, and 46XXp⁻ (deletion of short arm) configurations are all short; those with 46XX, 46XXq⁻, 46XY, and now 47XXqiY, are normal in height for their sex; and 47XXX, 47XXY, 47XYY are tall for their sex. The final stature in each case is also dependent on the rest of the genetical background and environment.

We have not found another published report of the karyotype 47XXqiY.

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¹ Court Brown, W M, *et al*, *Medical Research Council Special Report Series No 305*. London, HMSO, 1964.

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Placement of central feeding catheters

Long-term intravenous feeding in infants and children often requires the use of central veins. These may be approached percutaneously^{1 2} or by cutdown. The inferior vena cava, however, has been avoided owing to the risk of thrombosis and embolism.³ The advent of fine Silastic catheters has greatly diminished these risks.^{4 5}

Method and results

Adequate sedation is essential for the procedure, which is carried out with full aseptic technique, preferably in the operating theatre. The distance from the groin to the sternum is measured. After skin preparation and infiltration with local anaesthetic an incision is made 1.5 to 2 cm below the medial end of the inguinal ligament. The long saphenous vein is then exposed by blunt dissection and transfixed with a fine needle. Cutting along the needle with a scalpel avoids inadvertent division of the vein (figure). A Silastic catheter 0.6 mm outside diameter (Dow Corning Corporation, Medical Products Division, Midland, Michigan) is then threaded in the required distance. It is unnecessary to ligate the lower end of the vein or to anchor the catheter within the vein. After further infiltration with local anaesthetic a 19G lumbar puncture needle is inserted in the anterior surface of the thigh 1 to 2 cm above the patella and advanced subcutaneously to the groin wound. The proximal end of the catheter is threaded through in retrograde fashion

Opening the vein.

and the needle is withdrawn. The catheter is connected to a 23G butterfly needle and an x-ray picture is taken after injecting Hypaque (sodium diatrizoate) 45%. The catheter tip should lie in the termination of the inferior vena cava or low in the right atrium. Since it is simple to withdraw the catheter an adequate length should be inserted in the first instance. The incision is then closed. The catheter is anchored to the skin at its point of entry by spraying with Dow Corning Medical Adhesive B. The butterfly needle and the catheter are then taped securely to the thigh.

Ten catheters were inserted in nine children aged from 2 weeks to 2 years and 3 months. They remained in place for 3-42 days. They were removed either on completion of intravenous feeding or because of septicaemia. The one removed at three days was inadvertently disconnected shortly after insertion and septicaemia resulted. No other catheter was removed in under 14 days. There were no complications related to the insertion or to the position of the catheter. There was no infection at the site of entry of the catheter. Septicaemia occurred in three children and in each case was due to disconnection at the needle-catheter junction. Three children, of whom two were previously septicaemic, died of unrelated causes several weeks after the catheters had been removed. Necropsy showed no evidence of thrombosis in the inferior vena cava.

Comment

This technique may be used when no suitable peripheral veins are available for cannulation.² Subclavian vein catheterisation is an accepted alternative but carries its own hazards.¹ There may also be cases when the head and neck veins cannot be used. Nursing care is easy since no splintage is required and the children may be easily changed and dressed. The incidence of septicaemia is disturbing but it seemed to be due solely to needle-catheter disconnection. Methods of safeguarding this junction are being investigated. Lastly, the technique described is simpler than the operative approach to the internal jugular vein and never requires general anaesthesia.

¹ Groff, D B, and Ahmed, N, *Journal of Pediatric Surgery*, 1974, **9**, 171.

² Shaw, J C L, *Pediatric Clinics of North America*, 1973, **20** (2), 333.

³ Bansmer, G, Keith, D, and Tesluk, H, *Journal of the American Medical Association*, 1958, **167**, 1606.

⁴ Boros, S J, et al, *Pediatrics*, 1975, **56** (6), 981.

⁵ Irving, I M, et al, *Journal of Pediatric Surgery*, 1971, **6**, 724.

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Microcrystalline calcium hydroxyapatite compound in corticosteroid-treated rheumatoid patients: a controlled study

Osteoporosis is common in rheumatoid arthritis (RA), particularly when treated with corticosteroids. It may lead to fractures, especially in the spine. The management of osteoporosis is unsatisfactory, so methods are sought to prevent its development. In postmenopausal women calcium supplements partly prevent bone loss. Loss of bone mineral, however, is not the same as loss of calcium, since mineralisation also depends on magnesium, phosphate, fluoride, and other substances. We have conducted a controlled trial using a microcrystalline hydroxyapatite compound (MCHC) given as Ossopan. MCHC is prepared from young bovine bones by grinding and sieving after removing the fatty constituents, leaving the minerals in their natural ratios as well as residues of matrix, proteins, and glycosaminoglycans.

Methods and results

Seventy-two corticosteroid-treated patients with rheumatoid arthritis aged 50 years or over with stable disease and without other systemic disease were divided into two groups matched for age, sex, and corticosteroid dosage. In addition one group received MCHC 6 g daily for 12 months. The patients were seen frequently, with detailed assessments initially and at 26 and 52 weeks. Eight withdrew (one for gastrointestinal intolerance, one who

disliked the powder, two who failed to attend, and four because of corticosteroid withdrawal) but the groups remained well-matched.

Over the year patients in both groups lost stem height (the crown-seat distance with the patient sitting in a standard chair), but significantly more did so in the control than in the MCHC group (table). Bone density was recorded by photon absorption densitometry at a standard site across the left radius and ulna well away from the wrist and elbow. The radial bone density decreased in both groups but significantly more so in the controls. When recalculated as a percentage of the initial bone density the loss among the controls remained higher, although the difference did not quite reach statistical significance. The ulna bone density decreased in both groups, minimally but not significantly more in the controls. Changes in the spinal radiographs during the year were small and similar in both groups. The patients' spinal symptoms were scored and changed in a similar fashion in both groups, but more controls noted that they worsened. The drug did not affect the activity of the arthritis. No patient developed hypercalcaemia, hypercalciuria, or other toxic effects. About 20% disliked the sweet taste of the powder.

Changes in indices of osteoporosis after one year

	Control group	MCHC-treated group	P value
Mean loss of stem height (cm $\pm$ SD)	1.16 $\pm$ 0.71	0.87 $\pm$ 0.58	0.01 < P < 0.05
Mean loss of radial bone density (BMC/W $\pm$ SD)* ..	0.056 $\pm$ 0.033	0.043 $\pm$ 0.029	P < 0.05
Mean loss of radial bone density (% of initial density $\pm$ SD)	5.29 $\pm$ 3.34	4.78 $\pm$ 3.55	NS†
Mean loss of ulna bone density (BMC/W $\pm$ SD) ..	0.033 $\pm$ 0.031	0.030 $\pm$ 0.026	NS
No of new vertebral crush fractures on radiographs ..	4	3	NS
Back symptoms:			
Better	6	8	
Same	15	20	NS
Worse	11	4	

*BMC/W = Bone mineral content/bone width.

†NS = Not significant.

Comment

MCHC has been reported to improve healing of fractures and to help back pain in postmenopausal osteoporosis.¹ Dent and his colleagues^{2,3} gave MCHC in hypophosphataemic osteomalacia and idiopathic juvenile osteoporosis with benefit. Dent (personal communication) regarded MCHC as preferable to other calcium supplements because it seemed better absorbed, since the calcium and phosphate are in optimal proportions and in a suitable microcrystalline form, and because of the other components. There is evidence that calcium is better absorbed from MCHC by mouth than from other calcium preparations⁴ and that calcium ions are more readily absorbed in the presence of amino-acids.⁵ But long-term comparisons of MCHC with, for example, calcium gluconate are required. The results of this trial suggest that MCHC has a significant prophylactic effect in preventing the development of osteoporosis in corticosteroid-treated rheumatoid patients. Perhaps the drug should be started concurrently with the corticosteroids rather than waiting until osteoporosis has developed.

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¹ Durance, R A, et al, *Clinical Trials Journal*, 1973, **10**, 67.

² Dent, C E, and Stamp, T C B, *Quarterly Journal of Medicine*, 1971, **40**, 303.

³ Brenton, D P, and Dent, C E, in *Inborn Errors of Calcium Metabolism*, ed H Bickel and J Stern, p 222. Lancaster, MTP Press, 1976.

⁴ Windsor, A C M, et al, *Age and Ageing*, 1973, **2**, 230.

⁵ McCance, R A, Widdowson, E M, and Lehmann, H, *Biochemical Journal*, 1942, **36**, 686.

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