

Unsuspected Klinefelter syndrome mosaicism presenting as osteoporosis: a case report

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Abstract

Hypogonadism secondary to genetic disorders like Klinefelter syndrome has been described as a cause of male osteoporosis, but the diagnosis is frequently missed or delayed because the clinical features are often subtle or at times normal. We report the case of a 25 year old male mosaicism Klinefelter syndrome lacking typical clinical features such as tall stature, gynecomastia or low intelligence, whose sole presentation was low back ache due to diffuse osteoporosis involving the vertebra and pelvic bones. Bone loss is a minor characteristic of KS, while it is a distinctive feature of idiopathic hypogonadotrophic hypogonadism. There are only a few reported cases of Klinefelter mosaicism in which the sole presenting symptom complex was osteoporosis. The diagnosis is often missed or delayed because of the low index of suspicion that many health care professionals have toward genetic diagnoses in adults.

Key words: Klinefelter syndrome, osteoporosis, mosaicism.

Introduction

Osteoporosis in young males always warrants investigation to find out the underlying cause. Hypogonadism secondary to genetic disorders like Klinefelter syndrome has been described as a cause of male osteoporosis but the diagnosis is frequently missed or delayed because the clinical features are often subtle. This is especially true of mosaic Klinefelter syndrome in which the phenotypic expression can be entirely normal. Isolated osteoporosis as the sole presentation of mosaic variant of Klinefelter syndrome has been described in only a few case reports in literature. The diagnosis can be missed completely if a high index of suspicion is not maintained by the treating physician.

Case report

A 25 year old male, mechanic by profession, presented to our hospital with low backache, bone pain, myalgia, and easy fatigability of 4 years duration. These symptoms were of insidious onset, gradually progressive and now were severe enough to interfere with his work.

He did not give any history of fever, joint pains, oral ulcers or skin rash suggestive of connective tissue disorder. There was no history of impotence, loss of libido, or loss of facial or pubic hair. No history suggestive of poor performance at school or work. He was born of a consanguineous marriage and there was no history of a similar illness in the family.

Physical examination revealed a young male of average build and nourishment with a body weight of 60 kg and a height of 177 cm. His secondary sexual characters were well developed, with normal facial, axillary, and pubic hairs. External genitalia were normal with normal sized testis by palpation. There was no gynecomastia. His clinical examination revealed no other significant findings. Baseline investigation showed – Hb 14.2 gram/dl, total count 7500/cm, differential – Poly 68 Lymphocyte 32, Platelet 4,39000, peripheral smear was normal. Blood urea 15mg/dl, blood sugar 92 mg/dl, Sodium 135 mmol/l, Pottassium 4.8 mmol/l, Serum calcium 8.5 mg/dl, Phosphorous 4.3 mg/dl, uric acid 6.8 mg/dl. His liver function tests were normal with alkaline phosphatase 154 IU/ml.

X rays of the lumbar spine and hip joints showed diffuse osteoporosis as evidenced by osteopenia and increased trabecular markings. Computed tomogram of the spine and pelvis revealed similar findings with diffuse osteoporosis of the lower lumbar vertebra and pelvic bones (Figure 1).

A diagnosis of secondary osteoporosis in the youth was made and a careful search was undertaken to identify the predisposing factors.

Serum parathormone assay and vitamin D levels were normal ruling out hyperparathyroidism and osteomalacia. His 24 hour urinary calcium excretion was 126 mg/day which was not raised (normal 150-

300) ruling out renal loss of calcium. His thyroid profile was normal and serum cortisol was 64 ng/ml (normal 50-200) ruling out hyperthyroidism and Cushing syndrome as possible causes of osteoporosis.

Connective tissue disorder work up including ANA, LE cell, CRP, RA factors were negative. His ESR was 16 mm at 1 hour and his ultrasound abdomen including the scrotum was normal with the normal testicular size.

Although there were no clinical features of hypogonadism in this patient, a full hormone profile was done as no other apparent cause for his symptoms could be found. His hormone analysis (Table I) revealed a low testosterone with normal FSH and LH. Subsequently, a karyotyping was done which revealed a chromosomal pattern of 46 XY/47 XXY (4:1) diagnostic of Klinefelter syndrome mosaicism (Figure 2). Thus, a final diagnosis of male osteoporosis secondary to mosaic Klinefelter syndrome was made.

The patient was started on testosterone injection 50 mg intramuscularly every two weeks along with alendronate 70 mg per week PO and calcium/vitamin D3 supplements. After 6 months of the therapy, the patient showed marked symptomatic improvement with reduction in bone pain and fatigue. Repeat x rays and CT scan showed similar osteoporotic changes as before which was expected in a case of Klinefelter syndrome. He was asked to continue the same drugs and is under regular follow up.

Table I. Hormone profile

Hormones	Values	Normal range (in males)
Testosterone	159 ng/dl	300-1000 ng/dl
FSH	3 miu/ml	1-15 miu/ml
LH	10 miu/ml	7-24 miu/ml
Cortisol	64 ng/ml	50-200 ng/ml
Parathormone	27-30 pg/ml	12-72 pg/ml

Discussion

Hypogonadism often secondary to genetic disorders like Klinefelter syndrome has been well described as a cause of male osteoporosis [1]. The incidence of osteoporosis in Klinefelter syndrome is about 25% [2], with most of the patients showing the classic phenotype of primary testicular failure like gynecomastia, small testes, sparse body hair, tall-



Figure 1.

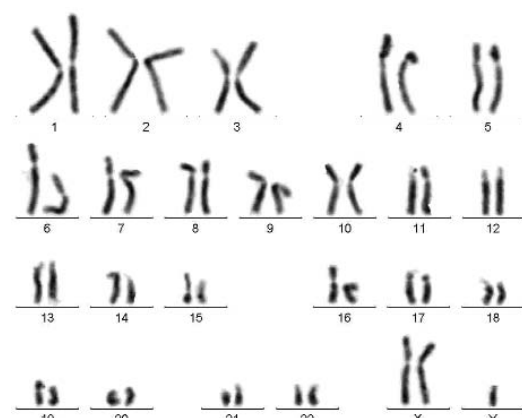


Figure 2.

ness, and infertility [4, 5]. But this classic presentation may be lacking in some patients, especially the mosaic variants who can have an entirely normal phenotype. We could come across only one case report of Klinefelter mosaicism in which the sole presentation was osteoporosis [5]. Moreover, bone loss is a minor characteristic of KS, while it is a distinctive feature of idiopathic hypogonadotropic hypogonadism [6]. Our patient presented with osteoporosis alone with no clinical features of Klinefelter syndrome. So hypogonadism was not suspected initially as the cause for his symptoms and he was investigated along other lines which all came normal. The possibility of subclinical hypogonadism was reconsidered in him and the subsequent hormone assay showed a subnormal testosterone level. Further karyotyping revealed a klinefelter mosaic clinching the diagnosis. The fact that our patient was a mosaic would explain the absence of the typical phenotype in our patient.

We highlight this case because he had no clinical features of hypogonadism and the diagnosis was unsuspected before the hormonal analysis. The diagnosis of Klinefelter syndrome is often missed or delayed because of the low index of suspicion that many health care professionals have toward genetic diagnoses in adults. This case is a reminder to the physicians to be on the look out for subclinical hypogonadism as a risk factor for male osteoporosis even in a clinically normal appearing patient.

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