Klinefelter's syndrome associated with systemic sclerosis

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Summary

A case of systemic sclerosis is reported in a 41-year-old male with Klinefelter's syndrome. The significance of this association to the aetiology and pathogenesis of systemic sclerosis is discussed.

Introduction

The association of Klinefelter's syndrome (chromosomal complement 47, XXY) with systemic lupus erythematosus is well recognized (Masi and Kaslow, 1978). Tsung and Heckman (1974) report the occurrence of localized scleroderma, Raynaud's phenomenon, Sjögrens syndrome, Osler-Weber-Rendu disease and malignant lymphoma in a 47, XXY male. The case discussed here describes the association of Klinefelter's syndrome and systemic sclerosis.

Case report

A 41-year-old male, who had Raynaud's phenomenon for 12 years, presented with a one year history of skin thickening with discoloration and tightness of his hands, face, chest and thighs. He had also noticed increasing exertional dyspnoea, weakness and stiffness of his arms and neck, and had lost weight. His marriage was infertile.

He exhibited the classical features of scleroderma with extensive areas of thickened, tight, shiny and tethered skin. Pigmentation, depigmentation and telangiectasia were also present. He had microstomia and clawed hands. In addition, his body habitus was typical of Klinefelter's syndrome (height 179.6 cm: arm span 192.6 cm). He was obese, had infantile gonads, gynaecomastia and decreased body hair with a female escutcheon. Auscultation of the lungs revealed fine basal end-inspiratory crackles. There was mild neck flexor and shoulder girdle weakness.

His haemoglobin was 11.2 g/dl with normal

erythrocyte indices and a normal differential white cell count. The erythrocyte sedimentation rate was 41 mm in the first hour (Westergren). The serum urea, 12 channel biochemical profile, creatinine clearance and tests of thyroid, liver and small bowel function were within normal limits.

Immunological evaluation revealed an IgG anti-nuclear factor (1/300 titre) with a speckled pattern. Immunoglobulin levels and serum protein electrophoresis were normal, as were the C₃, C₄, CH₅₀ and Factor B components of complement. An assay for CIq binding was in the normal range. Tests for sheep red cell agglutination, latex fixation and antibodies to deoxyribonucleic acid, extractable nuclear antigen, smooth muscle, mitochondria and reticulon were negative. Cryoglobulins, cold agglutinins and lupus erythematosus cells were not detected. A Wassermann reaction and VDRL test were negative.

Profuse exfoliation of atypical alveolar macrophages was found on cytological examination of the sputum and pulmonary function tests showed a restrictive ventilatory impairment.

Radiological investigations revealed a normal thoracic inlet, plate atelectasis in the left lower lung zone and juxta-articular osteoporosis at the metacarpophalangeal joints. A gastrointestinal tract barium series was normal apart from disclosing a wide-necked diverticulum on the medial aspect of the ascending colon.

Buccal smear examination revealed sex chromatin in 9% of cells and Klinefelter's syndrome was confirmed by karyotype analysis with chromosome banding showing a 47, XXY pattern.

Discussion

This is the first report of systemic sclerosis developing in a patient with Klinefelter's syndrome, although scleroderma without post-mortem evidence of systemic sclerosis in a patient with Klinefelter's syndrome and a malignant lymphoma has been described (Tsung and Heckman, 1974). Although the

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possibility that this association is fortuitous cannot be excluded, both systemic sclerosis (annual incidence of 2.7 new cases per million population (Medsger and Masi, 1971)) and Klinefelter's syndrome (annual incidence of 0.93 per 1,000 live male births (Hook and Hamerton, 1977)) are sufficiently uncommon for this to be unlikely. The female preponderance of 3:1 in systemic sclerosis (Kurland *et al.*, 1969) suggests sex-related host factors in the increased susceptibility of females or, conversely, protection of males. Such factors may explain an association of systemic sclerosis and an XXY chromosome genotype.

It is of interest that a female preponderance and association with Klinefelter's syndrome occurs in systemic lupus erythematosus (Masi and Kaslow, 1978). Possible explanations include somatic mutation on X chromosomes, increased fetal wastage of genetically normal males predisposed to systemic lupus erythematosus (or systemic sclerosis), infectious agent susceptibility or altered immune responsiveness related to genetic or hormonal status, and direct hormonal effects on the tissues. In addition to the mandatory chromosomal abnormality in Klinefelter's syndrome there are a host of hormonal and biochemical abnormalities (Paulsen *et al.*, 1968).

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