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CASE REPORT

Giant Cell Tumour of the Tibia with Xeroderma Pigmentosum

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ABSTRACT

Xeroderma pigmentosum is known to be associated with cutaneous malignancies due to the defects in the DNA repair mechanism.An association with giant cell tumour of the bone is not reported.A review of literature of these rare lesions is presented and analysed to see if this is an association or is a chance coincidence.

Key words: Giant cell tumour, Xeroderma pigmentosum, malignancy

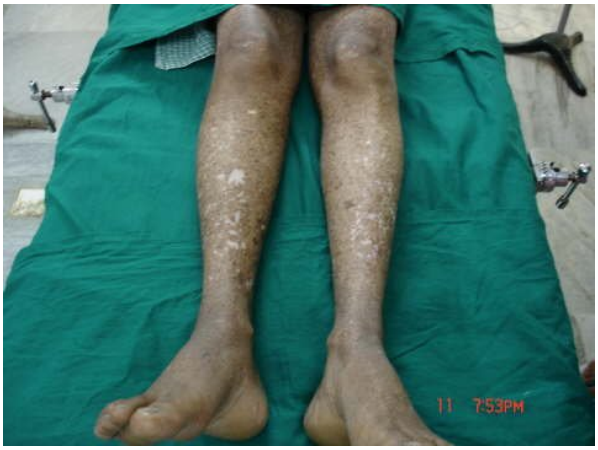
Introduction

Xeroderma pigmentosum (an autosomal recessive skin disorder) is characterized by photosensitivity, pigmentary changes and premature skin aging.Since the ability to repair damaged DNA is defective ,there is an association with several skin tumours. Giant cell tumour of the bone is commonly seen round the knee joint as a lytic lesion and responds well to surgical excision. An association of these two lesions is previously unreported.

Case Report

A 30-year-old lady with proven xeroderma pigmentosum [Table/Fig 1] presented with complaints of dull aching pain in the left knee for four weeks duration. A clinical examination showed effusion of the knee joint,with difficulty in weight bearing but the X-ray (Left leg –AP and lateral view) taken at that time was normal.The patient returned six weeks later with inability to bear weight and a swelling around the knee joint. X-ray of the left tibia taken showed a lytic lesion involving the posterior tibial condyle with erosion of the posterior cortex [Table/Fig 2]. MRI showed a well-encapsulated lytic lesion with intact articular surface. Fine needle aspiration showed giant cells, suggestive of osteoclastoma-the giant cell tumour. The lesion was treated by exploration and curettage [Table/Fig 3] followed by a bone graft from the iliac crest 5 weeks later. The patient is well and is now allowed partial weight bearing with a hinged knee brace. The final histopathology was suggestive of giant cell tumour of the bone.

Table/Fig 1: Extensive freckling and the pigmentation seen in Xeroderma pigmentosum



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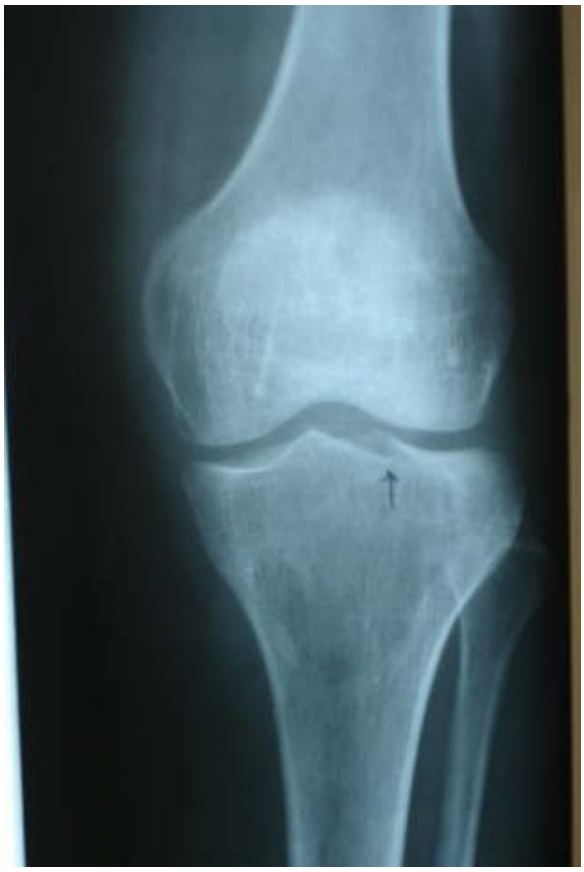
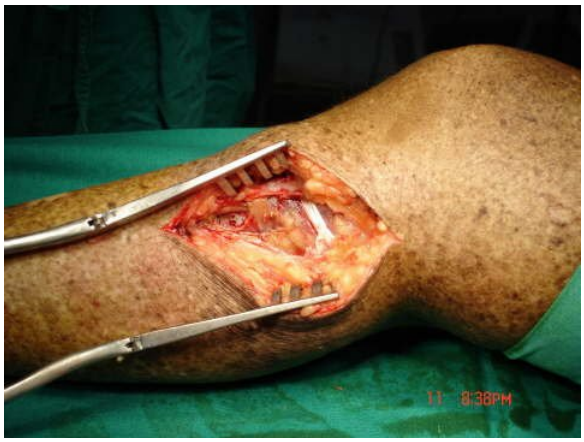
Table/Fig 2: The X-ray shows a lytic lesion with the well preserved rim of cortex on the tibia



Table/Fig 3: Curettage of the lytic lesion around the knee



Discussion

Xeroderma pigmentosum

Xeroderma pigmentosum (XP) was first described in 1874 by Hebra and Kaposi. In 1882, Kaposi coined the term xeroderma pigmentosum for the condition, referring to its characteristic dry, pigmented skin. These manifestations are due to a cellular hypersensitivity to ultraviolet (UV) radiation resulting from a defect in DNA repair.

It occurs equally in all races and in both sexes [1].

The disease is characterized by normal skin at birth. The lesions appear from 6 months of age and typically show erythaema, freckling and dry skin with areas of pigmentation [Table/Fig 1]. The second stage is characterized by poikiloderma.The third stage is heralded by the appearance of numerous malignancies, including squamous cell carcinomas, malignant melanoma, basal cell carcinoma, and fibrosarcoma.[1] [Table/Fig 4] outlines the various stages of XP). These malignancies may occur as early as age 4-5 years and are more prevalent in sun-exposed areas [2]. Photosensitivity, ocular problems and neurological problems are seen in patients with XP [1],[2]. De Sanctis-Cacchione syndrome refers to the combination of XP and neurologic abnormalities (including mental retardation and cerebellar ataxia), hypogonadism, and dwarfism [1].

Table/Fig 4: The various stages of XP

Stage 1	Stage II	Stage III- malignancies
Erythaema	Poikiloderma	Squamous cell carcinoma
Freckling	Skin atrophy	Basal cell carcinoma
Dry skin	Telangiectasia	Malignant melanoma
Pigmentation	Mottled hypo/ hyperpigmentation	Soft tissue sarcomas

Pathophysiology

The basic defect in XP, is in the nucleotide excision repair (NER), which leads to deficient repair of DNA damaged by UV radiation. This extensively studied process consists of the removal and the replacement of damaged DNA with new DNA. Two types of NER exist- global genome (GG-NER) and transcription coupled (TC-NER). Seven XP repair genes, XPA through XPG, have been identified. These genes play key roles in GG-NER and TC-NER.

Following detection of DNA damage, the damaged DNA is removed. Various defects in cell-mediated immunity have been reported in XP. These defects include impaired cutaneous responses to recall antigens, decreased circulating T-helper cells-to-suppressor cells ratio, impaired lymphocyte proliferative responses to mitogen, impaired production of interferon in lymphocytes, and reduced natural killer cell activity [3]. These are probably the mechanisms that predispose to malignancies [4].

The giant cell tumor of bone (GCT) is a local osteolytic tumor with variable degrees of aggressiveness. The lesion most frequently occurs in the epiphysis of long tubular bones of the knee region, grows eccentrically and predominantly affecting young adults after closure of the growth plate. It represents 15% of benign and 3% of all bone tumours and is common in India and China [5].

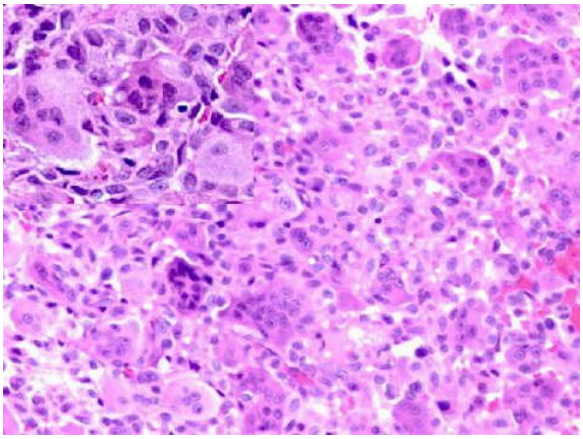
The symptoms are non-specific, local swelling, warmth and pain. The X-ray shows a well-defined lytic lesion involving epiphysis and thinning the cortical bone [5],[6].

Camapanacci has graded GCT as Grade I-III.Grade I has a well marginated border of a thin rim of mature bone and the cortex is intact or slightly thinned but not deformed. Grade II has well defined margins but no radio-opaque rim-the combined cortex and rim of reactive bone is thin and moderately expanded but still present. Grade III has fuzzy borders, suggesting a rapid and permeative growth and is not limited by an apparent shell of reactive bone [8].

CT is useful to differentiate GCT from other lesions like aneurysmal bone cysts, chondroblastoma, chondromyxoid fibroma, giant cell reparative granuloma and non-ossifying fibroma [6],[7].

The characteristic histological appearance of GCT displays a high number of osteoclast-like multinucleated giant cells [Table/Fig 5], which resulted in the classification "osteoclastoma" or "giant cell tumor". These multinucleated cells are derived from stromal cells, either by fusion of mononuclear cells, or less probably by amitotic division or nuclear segmentation of stromal cells without corresponding cytoplasmic division. Apart from the multinucleated giant cells, there are two mononuclear cell types in the GCT. The first one has a round morphology and resembles a monocyte. The second cell type is the spindle-shaped, fibroblast-like stromal cell.

Table/Fig 5: Cluster of osteoclast like giant cells with the left top inset showing the high power view of the giant cell



Pathophysiology of GCT

Cell culture experiments with GCT cells revealed the stromal cell to be the proliferating component of the GCT. The other two cell types, the monocyte and the multinucleated giant cell, were lost after a few cell culture passages [9]. Furthermore, latest results from GCT reveal that the stromal cells secrete a variety of cytokines (macrophage colony stimulating factor, interferon gamma, tumour necrosis factor alpha) and differentiation factors, including MCP1, ODF and M-CSF. These molecules are monocyte chemoattractants and are essential for osteoclast differentiation, suggesting that the stromal cell stimulates blood monocyte immigration into tumor tissue and enhances their fusion into osteoclast-like, multinucleated giant cells. The multinucleated giant cell itself demonstrates properties of a normal osteoclast that is able to resorb bone leading to extended osteolysis. This new model of GCT genesis supports the hypothesis that the stromal cell is the neoplastic component whilst the monocytes and the multinucleated giant cells are just a reactive component of this tumor [9].

Management of GCT

Surgical treatment consists of curettage and bone grafting [10]. Various adjuncts that remove tumours cells that remain after curettage because of their thermal effects (liquid

nitrogen,methymethacrylate) or chemical (phenol, hydrogen peroxide, alcohol)have been used [11–13]. Good results have been published recently with the use of high-pressure pulsatile lavage and a high-speed dental burr. En bloc resection is advocated in Grade III tumours [9]. Radiotherapy with (supervoltage therapy or linear accelerator) in the dose of 40-60Gy is useful for local oncological control [14]. Pulmonary metastases, local recurrence and malignant transformation are known to occur with GCT [15].

The mechanism that triggers malignancies in patients with XP is not clear, but uncontrolled cell proliferation is the final pathway in tumorigenesis. Is defective DNA repair a pathway in giant cell tumour formation? Further studies are needed to say whether this is causation or just a chance association.

Conclusions

While there are reports of skin tumours and soft tissue sarcomas reported in patients with xeroderma pigmentosum,this is the first known report of giant cell tumour of the bone with XP.

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