"Doctor! What happened to my leg?"

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Igor, 57, a visitor from the Ukraine, presents with bone pain in different parts of his body. His left leg has a deformity.

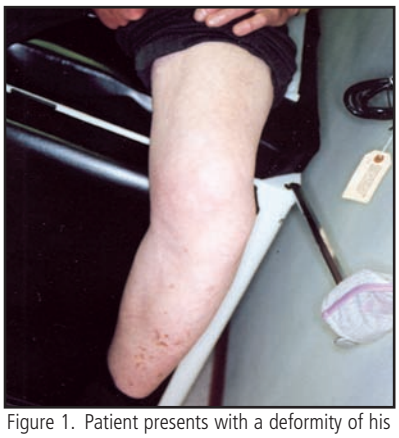

Figure 1. Patient presents with a deformity of his left leg.

Igor's statistics

- Igor appears healthy
- He is working as a taxi driver
- His left leg deformity has ben progressing over the last eight months (Figure 1)

Igor's medical history

- Igor is positive for hypertension
- He has a history of gout
- He is taking atenolol for blood pressure and occasionally ibuprofen for joints and left-leg pain
- He has smoked 1-1/2 packs of cigarettes per day for the last 25 years
- His father had Type 2 diabetes and passed away at age 78 from a heart attack. His mother is still alive
- His brother, 55, has had recurrent problems with gout
- Igor has three healthy children

Clinical investigations

- X-rays are taken of Igor's left knee and left calf (Figures 3 and 4)

Figure 3.

What's your diagnosis?

a) Severe osteoarthritis
b) Osteosarcoma
c) Paget's disease
d) Chondrosarcoma

Answer:

Paget's disease (Osteitis deformans)

About Paget's disease

Paget's disease is a disorder of unknown etiology in which there is a thickening and deformity of one or several bones. The rates of formation and resorption of bone appear to be uncoordinated.

Approximately 70% to 90% of patients with Paget's disease are asymptomatic; however, a minority of patients experience a variety of symptoms, including bone pain (the most common symptom), secondary osteoarthritis (when Paget's disease occurs around a joint), bony deformity (most commonly bowing of an extremity), excessive warmth (from hypervascularity) and neurologic complications (caused by the compression of neural tissues). The condition may be monostotic (17%), but is more frequently multifocal, with a predilection for the axial skeleton, long bones and the skull. The skeletal sites primarily affected are the pelvis, lumbar spine, femur, thoracic spine, sacrum, skull, tibia, and humerus. The hands and feet are very rarely involved; however, any bone may be affected. After onset, the disease does not spread from bone to bone, but it may become progressively worse at preexisting sites.

Complications from Paget's disease depend on the site affected and the activity of the disease. When Paget's disease occurs around a joint, secondary osteoarthritis may ensue. When the skull is involved, the patient may develop deafness, vertigo, tinnitus, dental malocclusion, basilar invagination, vertebral insufficiency and cranial nerve involvement.

Vertebral involvement from Paget's disease may be associated with serious complications, including nerve root compressions and *cauda equina* syndrome. Fractures, the most common complication of Paget's disease, may occur and have potentially devastating consequences. Rarely, pagetic bone may undergo a sarcomatous transformation.

Pathophysiology

The phases of Paget's disease are as follows:

1. Paget's disease begins with the **lytic phase**, an increase in bone resorption with an abnormality in the osteoclasts found at the site of bony involvement. These osteoclasts are more numerous and have many more nuclei (up to 100) than normal osteoclasts (5 to 10 nuclei). This results in a bone turnover rate of up to 20 times more rapid than normal.
2. This significant increase in bone resorption leads to the **mixed phase**. There are rapid increases in bone formation with numerous osteoblasts, which are increased in number but remain morphologically normal. The new bone that is made is abnormal; the newly formed collagen fibres are deposited in a haphazard fashion rather than linearly (as with normal bone formation).
3. In the final phase, known as the **sclerotic phase**, bone formation dominates and the bone that is formed has a disorganized pattern (woven bone) and is weaker compared to normal adult bone. This woven bone pattern allows the bone marrow to be infiltrated by excessive fibrous connective tissue and blood vessels, leading to a hypervascular bone state. Eventually, the hypercellularity may diminish, leaving a pagetic bone, which is known as burned-out Paget's disease.

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How is the diagnosis of Paget's disease made?

The proper way to establish a Paget's diagnosis is by X-rays, bone scanning and testing the blood for alkaline phosphatase. Only when an elevation of the alkaline phosphatase is observed can we start making a diagnosis. The alkaline phosphatase is a chemical enzyme produced by bone cells and is over-produced by Pagetic bone. Therefore, the blood level of alkaline phosphatase is a reflection of the extent of the disease and its degree of activity. The repeated measurement of alkaline phosphatase from time to time can be used to determine if the condition is stable or not. It is especially helpful in finding and recognizing the patient's response to the treatment with a variety of anti-Pagetic medication.

Treatment of Paget's disease

Treatment involves an expert endocrinologist, consultation with a neurosurgeon, neurologist, orthopedic surgeon, and otolarangologists, at times, are advisable.

These physicians treat the patient with two types of medications:

1. Calcitonin, which is a synthetic salmon calcitonin, and sometimes synthetic human calcitonin, which is referred to as cibacalcin. These are typically given by injection, although recently inhalation of the medication has been advised, as well as with other newly investigated methods.
2. The bisphosphonates, a new class of drugs that inhibits abnormal bone cell activity, are the second type of medication. Etidronate disadium is administered by a tablet. It is recommended to be taken on an empty stomach at least 30 minutes before eating. No other medication or antacid should be given for two hours before or after this medication. Treatment with this medication should not exceed more than six months, but repeat courses have been done.

There is a group of medications called Pamidronate disodium that can be given intravenously and can have prolonged effects after a short course of treatment.

Correction of Paget's deformities by surgery is not usually recommended. Nevertheless, when pressure on the nerves is involved, a neurosurgical approach by decompression of the cochlear nerve (the nerve involved in hearing) or optic nerve (the nerve involved in vision) intracranially, has been approached.

Treatment of Pagetic bone fracture by fixation or surgery also may need to be done as the case develops. Total joint replacement of the hips and knees should be reserved for the most severe cases of arthritis and Paget's disease when other methods of treatment fail. The procedure of osteotomy for surgical cutting and realignment of Pagetic bone and deformity may help weight-bearing joints, especially the knee. Medical therapy prior to the surgery should be carried out to decrease the bleeding and other complications that usually follow the Pagetic patient. Dx