put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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Paget's disease of bone

the second most common bone disorder in elderly persons (after osteoporosis)

HISTORY OF PRESENTING ILLNESS:

MOST COMMONLY:
Isolated LFT abnormality:
Raised Alkaline Phosphatase
And otherwise asymptomatic…

GRADUALLY WORSENING PAIN AND DEFORMITY:
most affected are
- **Pelvis**
- **Spine**
- **Skull**
- **Femur**
- **Tibia**

FRACTURE may be the first presenting sign

The pain is typically bony pain, i.e dull and gnawing, worse @ night

EXAMINATION:
- **Obvious deformities**
- **Warmth + tenderness to palpation**
- **Examine the JOINTS for OA**
- **TEST HEARING!!**
- **Scope the fundus: Optic Nerve Atrophy?**

What kind of deformity?
- **BOWING of the tibia** → May cause secondary arthritis; walking on bowed tibias causes unnatural mechanical stresses on your joints
- **Worsening KYPHOSIS**
- **FRONTAL BOSSING**
- **HEAD ENLARGEMENT (!)**
- **FACIAL DEFORMITY**
- **LOSS OF TEETH**
- **CRANIAL NERVE ENTRAPMENT especially CN 8- thus, HEARING LOSS**

DIFFERENTIALS ACCORDING TO THE FACULTY
Metabolic bone disease
- osteoporosis +/- crush fractures, Paget's disease.

Primary malignancy of bone or marrow
- e.g. multiple myeloma, osteosarcoma

Extra-vertebral disease effecting bone,
- eg bony metastases from remote tumour.

Infection
- spinal osteomyelitis or epidural abscess.

Degenerative spinal disease
- facet joint OA, disc herniation, spinal canal stenosis,

Referred pain
- abdominal aortic aneurysm, carcinoma pancreas

DIAGNOSIS IS USUALLY MADE THOUGH CHARACTERISTIC X-RAY AND BIOCHEM

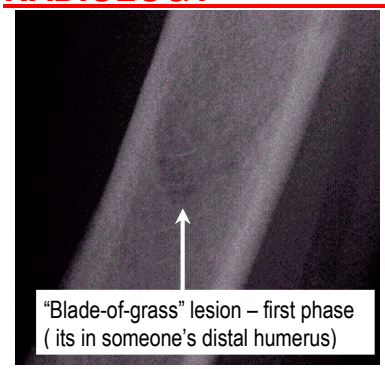
INVESTIGATIONS
- **Alkaline Phosphatase: Bone-specific AP is better; marker of bone formation**
- **Urinary Hydroxyproline levels, marker of bone resorption**

The degree of bone marker elevation reflects the extent and severity of the disease.
Serum total ALP remains the test of choice for assessing response to treatment

- **Calcium, Phosphorus**
- **Serum 25OH Vitamin D**

Should all be normal if this is really Paget disease!
Sometimes they CAN get hypercalcemic, but its uncommon

RADIOLOGY


"Blade-of-grass" lesion – first phase (its in someone's distal humerus)

CHARACTERISTIC FEATURES:
- **Blade of grass lesion** (advancing lytic front)
- **Cortical Thickening:** Vertebral cortical thickening of the superior and inferior end plates creates a "picture frame" vertebra
- **Bone bowing**
- **Fused sacroiliac joint**
- **Sclerotic changes (dense brittle bone)**
  - Diffuse radiodense enlargement of a vertebra is referred to as "ivory vertebra."

RADIONUCLIDE BONE SCAN for active disease

MANAGEMENT: must stop the osteoclasts!

BEWARE: Bisphosphonates arent very well absorbed PO. Its even worse- Calcium Supplements interfere with the absorption as well! SO: don't take them within 2 hrs of each other

CALCIUM SUPPLEMENTS + BISPHOSPHONATES: the "-dronates"; tiludronate, alendronate, and risedronate

FOSAMAX
Is Alendronate

PAMIDRONATE is the only one used intravenously. !! BE SURE TO GET ENOUGH Ca^{++}
synthetic analogues of pyrophosphate that bind to the hydroxyapatite found in bone. Fosamax (alendronate sodium) is a bisphosphonate that acts as a potent, specific inhibitor of osteoclast mediated bone resorption. Preferentially to sites of bone resorption, specifically under osteoclasts, and inhibits osteoclastic bone resorption with no direct effect on bone formation.

May result in hypocalcemia if bone formation proceeds at a ridiculous rate while bone resorption is inhibited.

ANALGESIA – NSAIDs + / - Opiates (try to stay out of the opiates)
Plus… SURGICAL MANAGEMENT of severe deformity + access devices eg canes, walkers…

Pathophysiology of Paget's Disease and its Complications

RISK FACTORS:
Genetics
- positive family history in 5 to 25% of patients
- disease 7 or 10 times more prevalent in first degree relatives
- genes implicated include a receptor activator for a nuclear factor (RANK) involved in osteoclast differentiation.
- Other genes as well, far too many to list

Overall, a heterogenous multigenic inheritance pattern

EXACT AETIOLOGY IS UNKNOWN:
? does a virus (measles) alter the DNA of those osteoclasts? Maybe another virus?

Over-recruitment of precursors by an increased level of IL-6

Hyper-responsiveness of the precursor (inactive) osteoclasts to active Vit D

Osteoclasts are hyper-responsive to the RANK ligand (genetic abnormality)
(RANK seems to mediate the effects of all other bone growth factors on the osteoclast)

OVER- Expression of the c-fos proto-oncogene in the osteoclast: (thus launching osteoclasts into relentless activity)

OVER-Expression of the anti-apoptotic bcl-2 gene: hence prolonged osteoclast survival

Increased NUMBER and ACTIVITY of
Pagetic osteoclasts
- **Large**
- Increased 10- to 100-fold in number,
- A greater number of nuclei (as many as 100 compared to the normal 3 to 5 nuclei)
- **THUS: sevenfold increase in resorptive surfaces; and so**
- **Erosion rate of 9 times the normal**

Thus, the CHARACTERISTIC FEATURES:
increased bone resorption + accelerated bone formation

Alkaline Phosphatase is released

initial osteolytic phase
- prominent bone resorption
- marked hypervascularization.
- warmth and swelling can be palpated

Radiographically, this looks like an advancing lytic wedge, or "blade of grass" lesion

The cells that come to replace the bone that is being destroyed are **FUNCTIONALLY NORMAL OSTEOBLASTS**

Second phase: Woven Bone Formation
replaces normal lamellar bone with haphazard (woven) bone. Not structurally sound, is it.
At the same time, fibrous connective tissue may replace normal bone marrow

Hypervascularity
Happens because woven bone is much more permeable to blood vessels

The final Sclerotic Phase,
bone resorption declines progressively
Remaining behind from this process:
hard, dense, less vascular pagetic or mosaic bone, which represents the so-called burned-out phase of Paget disease.

WITH MASSIVE SKELETON INVOLVEMENT: the diversion of blood into the great volume of hypervascular bone may cause HIGH OUTPUT HEART FAILURE; **PLUS so much calcium floating around causes AORTIC STENOSIS and diffuse VASCULAR CALCIFICATION**