The Daily Dose: Study Tips for Exam and Board Preparation

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The Daily Dose: Bone Pathology

Recently, a colleague sent me information on a case for my opinion. Although the case appears rather complex, the details of the case made me think most about the broad spectrum of fibro-osseous lesions, osteomyelitides, osteonecrosis (secondary to either radiation, chemotherapy or immune suppression) and metabolic bone disease. What I'd like to do in this discussion is communicate as much of a simplified algorithm as possible and (at the risk of insulting the intelligence of the audience, which is not my intention) talk about how I teach this to the AEGD-1 residents, because I think the methodology may be useful and applicable to the BBOP audience and those individuals preparing for exams.

The case (short summary):

21 yo F with celiac disease, widespread joint pain (thought to be secondary to the celiac disease) and severe acne (treated with monthly cortisone injections of the lower anterior face since age 14-16) evaluated for a painful lesion of the anterior mandible suspicious for osteomyelitis
MRI was performed, favoring osteomyelitis; an iCAT (cone beam CT) demonstrated periosteal thickening
Biopsy was performed and expert opinion was sought, with a diagnosis that favored a fibro-osseous lesion; osteomyelitis was not favored
The patient was treated with a course of IV antibiotics, without resolution

I saw selected images and my impression was that this was a fibro-osseous lesion in agreement with my colleague's impression (what saw were variably complex bone trabeculae, without osteocementum or reversal lines, without brush borders, without round/ovoid cementicles or psammomatoid formations, with some osteoblast rimming, a fibrous background stroma with mild to moderate cellularity, without an obvious inflammatory component and without cellular or nuclear atypia

The discussion led to the following questions; I may not answer all of them since (a) I did not see the entire case, (b) I am not an expert in any of this by any means and (c) I will likely be wrong since I didn't think much about SAPHO [in my defense, I don't think I've ever seen a case]:

- Could this be secondary to the steroid injections, celiac disease, or be a component of SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis)
- Is s osteomyelitis?
- Is it a fibro-osseous lesion?

What I'd rather do is try to paint a big picture analysis of bone disorders and give you things to think about and begin with my list (as I relay to the AEGD-1 residents) whenever a bone disorder or disease is encountered:

- fibro-osseous lesions (including dense bone island, cemento-osseous dysplasia, osteoblastoma/ cementoblastoma/osteoid osteoma, ossifying fibroma)
- fibrous dysplasia
- Paget's disease
- osteomyelitis (either primary or secondary)
- osteoradionecrosis and osteochemonecrosis (I prefer to divide this way and then determine whether it's secondary to immune suppression, bisphosphonate, osteoclast inhibitor, etc.)

- metabolic disease (with the most focus on the effects of parathyroid, renal and GI disease on calcium absorption and metabolism that may lead to either multinuclear osteoclast-like giant cell lesions of the jaws or radiographic mimickers of fibro-osseous lesions or osteomyelitides)
- metastatic disease (especially breast and prostate cancer, reported to radiographically mimic bone deposition disorders and disease)

The most important next steps I take (and I tell the residents to take) are:

- examine the clinical history
- examine the radiographs for ALL bone disorders; in most cases I favor having at *least* periapical radiographs of the teeth involved (to evaluate the PDL and oeriodontium), a panoramic radiograph and if there's either clinical expansion or uncertainty about the presence or extent of the lesion then I suggest the smallest field cone beam CT possible that will show the maxilla and mandible and allow for cross-sectional imaging)
- look at the radiographic edge and lesional characteristics; dense bone islands are typically uniformly radiopaque with abrupt edges but may enlarge with time and may in up to 12% of cases result in root resorption, while other fibro-osseous lesions are often mixed radiodensity and often have radiolucent 'halos' or rims, while fbrous dysplasia and Paget's Disease are more often indistinct with either the 'ground glass' or 'cotton wool' appearance that blends into surrounding bone, while osteomyelitides and osteoradionecrosis/osteochemonecrosis are often 'dirtier' and indistinct
- vitality test any teeth that may be involved (to exclude pulpal disease)
- ask about pain (which would in my mind favor either osteoblastoma/cementoblastoma/osteoid osteoma, some cases of ossifying fibroma, some cases of fibrous dysplasia and Paget's Disease, or all the osteomyelitides/osteonecrosis or metabolic diseases and in my mind favor against dense bone island and cemento-osseous dysplasia)
- ask about clinical expansion (which in my mind would favor osteoblastoma/cementoblastoma, ossifying fibroma, or fibrous dysplasia and Paget's Disease)
- if you suspect or determine a diagnosis of fibrous dysplasia, consider referral for endocrine evaluation (fibrous dysplasia may be a component of McCune Albright Disease)

Experience and the guidance of my mentors has led me to believe that many of the lesions may be clarified simply by reviewing the radiographic images and history and that fewer lesions require biopsy than we may think. However, if biopsy is performed, here's what I've learned and adopted that has helped me come to (I hope reasonable) conclusions:

- most of the lesions overlap in their histologic features and are non-helpful without radiographs
- the presence or absence of osteoblastic rimming is relatively non-helpful
- osteocementum, reversal lines (usually violet or purple), cementicles or psammomatoid formations and a hemorrhagic or vascular stroma may favor cemento-osseous dysplasia
- brush borders, psammomatoid formations and a more fibrous stroma may favor ossifying fibroma
- stromal retraction has been reported as a feature in fibrous dysplasia
- cellularity, atypia and mitotic activity lead me to think about osteoblastoma/cementoblastoma, (low grade) osteosarcoma and metastatic disease especially when hidden in a very cellular or fibrous stroma
- the presence of multinucleated giant cells make me strongly consider parathyroid, renal or GI malabsorption diseases (aberrant calcium metabolism that may result in osteoclast activity or lesions)

I will freely admit to this audience that I have a slightly lower threshold for ordering immunohistochemical stains in selected cases, particularly those where I am even minimally suspicious of any of the following:

- a hidden nerve, nerve sheath or myofibroblastic proliferation (IHC: S100, desmin, SMA or SMMHC and perhaps B-catenin to exclude fibromatosis)
- a hidden epithelial tumor or metastatic disease (IHC: start with pancytokeratin and CK7 and CK20)

I haven't performed this yet, but there has been some recent examination of MDM2/CDK4 immunohistochemistry to help distinguish osteosarcoma from fibro-osseous lesions (suggest: Dujardin F et.al. *Modern Pathology* (2011) 24:624-637)

The point that I want to drive home is not unnecessary use of IHC or a drive to increase health care costs, but simply to relay that sometimes there are other lesions hidden in the histology, and a few simple stains can help draw out either spindle cell lesions or metastatic epithelial lesions.

REFERENCES:

The list of references I have is ridiculously long, but I will say that when bone pathology is a consideration, I do tend to go to the following:

- McCarthy EF, Frassica FJ. Pathology of Bone and Joint Disorders 2ed
- Unni K, Inwards C, Bridge J, Kindblom L, Wold L, AFIPAtlas of Tumor Pathology Series 4: Tumors of the Bone and Joints
- Neville B, Damm D, Allen C, Chi A. Oral and Maxillofacial Pathology 4ed.

The way I have my literature organized (at least in bone pathology) is as follows (and perhaps a topic for its own separate discussion and clarification of all the subheadings):

chondrogenic neoplasms
CPP-dihydrate deposition
fibro-osseous lesions
idiopathic root resorption
NICO (neuralgia inducing cavitational osteonecrosis) osteonecrosis
osteosarcoma
reactive
TMJ neoplasms