WEEK 4

ASSIGNMENT, OBJECTIVES, AND CASE STUDY

TOPIC OF THE WEEK: GENETICS

REQUIRED READING:

Cotran, Kumar, Robbins: PATHOLOGIC BASIS OF DISEASE, 6th Edition,
Genetic Disorders (Chapter 6 pp. 139-187) (Some of this material has been covered by courses in Human Genetics and will serve as a review.)

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REQUIRED STUDY FOR SMALL GROUPS

CASE BASED STUDY Small Group Sessions

ASSIGNMENTS:
- Laboratory Medicine Case Book Chapter 13 OR
- Laboratory Medicine Case Set CD ROM Chapter 17
- Printed Case 1 (attached)

OBJECTIVES:
1. Case Book, Chapter 13 OR Case Set Chapter 17
   - Familial hypercholesterolemia with hyperlipemic xanthosis
   - Coronary artery atherosclerosis
   - Variant (Prinzmetal’s) angina
   - Tests for lipid/lipoproteinmetabolism (understanding, interpretation, diagnostic use):
     - Ravel: Clinical Laboratory Medicine, pp. 357-363;
     - Raskova, Shea, Skvara, and Mikhail: Laboratory Medicine Case Book, pp. 145-146
   - Tests for cardiac injury (understanding, interpretation, diagnostic use):
2. Printed Case (Attached)
- Pathogenesis and histopathology of diagnosed problems
- Evaluation of genetic disorders (understanding, interpretation, diagnostic use):
  Ravel: Clinical Laboratory Medicine. p. 592; lysosomal storage disorders, pp. 595-596 & 677-678
- Acid phosphatase as a test (understanding, interpretation, diagnostic use):
  Ravel: Clinical Laboratory Medicine, pp. 564-565
- Angiotensin converting enzyme as a test (understanding, interpretation, diagnostic use)
  Ravel: Clinical Laboratory Medicine, p. 641

**PATHTALK Small Group Sessions**
**ASSIGNMENTS:**
- *Projection slides* on carousels in the Media Library, labeled by weekly topic and subject
- Slide Manual (pp.20-24, Genetics)
- Journal Club Article (see your Course Book)

**OBJECTIVES:**
- Correlations of histopathology, gross pathology, and laboratory findings
- Review of pathophysiology

**ADDITIONAL MATERIAL (Optional, unless indicated otherwise)**

- SELF- STUDY MATERIAL, MATERIAL FOR SELF EVALUATION and VISUAL AND AUDIOVISUAL MATERIAL

See your Course Book (page 4) for a complete listing.
Clinical summary: The patient is a 64 year-old female who presents with sudden onset of severe right-sided hip pain. She has also complained for years of a sensation of abdominal fullness and intermittent bouts of multifocal bone pain accompanied by a mild fever. Multiple moderately enlarged lymph nodes can be palpated. Relevant history includes the facts that the patient is Jewish and grandparents on both sides were immigrants from Russia. Physical exam reveals a markedly enlarged spleen and liver.

Laboratory

Hemoglobin = 11.5
Platelets = 85
WBC = 2.7
Elevated serum acid phosphatase.
Mildly to moderate elevated liver enzymes.
By mistake, the ordering physician checked the box for angiotensin converting enzyme levels, and was serendipitously surprised when the test showed an elevated result.

At this point, what might the differential diagnosis include?

Imaging studies showed multiple bony abnormalities including features suggestive of avascular necrosis of the right femoral head. In addition, marked hepatosplenomegaly was seen. At this point the patient underwent right total hip replacement, and the femoral head and proximal femur were sent to pathology. After an inordinately long wait, the pathology report confirmed that avascular necrosis was present. It also noted an expansion of the femoral medullary space, and partial replacement of the hematopoietic marrow, by sheets of large cells with a low nuclear-cytoplasmic ratio and cytoplasmic inclusions resembling crumpled...
Questions

1. What does the differential diagnosis now include? What test(s) should be ordered to distinguish the correct diagnosis? What is the underlying defect? How common is it?

2. How do the patient’s lab values correlate with the physical and radiologic findings? What are the different kinds of acid phosphatase, and in what circumstances can they be elevated?

3. Is there a direct, clear-cut genetic basis for this disease? If so, what is it?

4. Clearly the patient has a form of the disease with an adult onset. Are there other forms?

5. What are the other diseases in the same family as this one? Do they have clear-cut underlying genetic defects?

6. Is the patient’s ethnic background significant? Are there any genetic diseases that correlate with ethnic background?

When the pathologist saw that the marrow had been partly replaced by abnormal cells, why wasn’t he worried about a neoplastic process? What is the significance of a low nuclear-cytoplasmic ratio?