Clinical Problem Solving

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Case One
Chief Complaint(s)

- Joint pains and fevers
How will you take your history?
History of Present Illness

• 41 year old male presenting with polyarthralgias and fever over the past two weeks
• Joint pains with associated swelling in all fingers, bilateral ankles, and bilateral wrists
• Fevers to 102 daily
• Also with a rash initially but it has come and gone
• Has been working on an oil rig off the coast of Equitorial Guinea for the past 4 weeks
Thoughts?
Past History

- No medical problems
- No surgeries
- Mother with colorectal cancer
- Denies alcohol, drugs, tobacco
- Does report that one of his coworkers developed a febrile illness with joint pains as well
- No drug allergies
Home Medications

• Reported taking his malaria prophylaxis
Review of Systems

- +fevers/chills
- No rhinorrhea, sore throat, congestion
- No chest pain
- No SOB
- No nausea, vomiting, diarrhea; +black stool
- +polyarthralgias; no myalgias
- +rash
- No loss of sensation, numbness, tingling
What are you looking for on exam?
Physical Examination

- VS: T 98.6, P 98, RR 22, BP 104/72
- Gen: Young AAM lying in bed who appears toxic
- CV: II/VI SEM
- Lymph: No LAD
- MSK: +swelling to all PIP in both hands; +swelling to bilateral wrists and ankles
- Skin: +BLE maculopapular rash
- Psych: AAOx4
What labs would you like?
<table>
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<th>Test</th>
<th>Value</th>
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<tr>
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</tr>
<tr>
<td>Alk Phos</td>
<td>3.4</td>
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</table>

- **AST**: 111
- **ALT**: 25
- **TP**: 7.3
- **Alb**: 2.0
- **T Bili**: 1.3
- **Alk Phos**: 182

- **S**: 92%
- **L**: 2%
- **M**: 4%
- **E**: 1%
- **Myelo**: 1%

- **MCV**: 75.4
- **MCV**: 285
- **NRBC**: 14
- **MDR**: 6.9
- **MDR**: 41.2
- **MDR**: 22.0
- **MDR**: 2.0
- **MDR**: 1.1
Ancillary Laboratory Data

- VBG 7.41/41/27; lactate 2.2
- CRP 48.6
- ESR 70
- CK 218
- RF 21, anti CCP negative
- ANA negative
- Hepatitis panel negative
- HIV negative
- UA negative
Ancillary Laboratory Data (continued)

- Iron 146, TIBC 223, Iron Saturation 65%
- Ferritin >100,000
- Haptoglobin 263
- LDH 1945
- TC 70, HDL 19, LDL 21, TG 149
Imaging

- CXR with no acute infiltrate
Plan

• Admitted with diagnosis of severe sepsis and started on meropenem and vancomycin; procalcitonin ordered
• Empirically treated for malaria with quinine and doxycycline; giemsa stain ordered
• Soluble IL-2 receptor ordered
What will our consultants say?
Consults, a plenty

- **Rheumatology**
  - Felt clinical picture to be more c/w hemorrhagic fever from a viral illness contracted in Africa

- **Hematology**
  - Bone marrow biopsy performed which showed viral inclusions in RBC precursors, no hemophagocytosis

- **Infectious disease**
  - No malaria parasites seen, but therapy begun before smear prepared
  - Outside of Ebola endemic area
  - Check serologies for parvovirus, dengue, and chikungunya
Hospital Stay, Continued

- Patient persistently febrile (upwards of 104°F) and persistent synovitis
- Procalcitonin returned 4.43
- EBV negative, parvo IgG elevated but IgM normal
- On hospital day 4, discontinued quinine, continued doxy/meropenem/vanc, started methylprednisolone 60mg BID
- On hospital day 5, marked symptom improvement with steroids; stopped meropenem and vancomycin
Hospital Stay, Continued

- On hospital day 7, IL-2 receptor came back elevated at 4270
- Abdominal ultrasound and NK cell activity ordered
- Abdominal ultrasound revealed mild splenomegaly
- Continued treatment with doxycycline and methylprednisolone
Hospital Stay, Continued

- On hospital day 10, NK cell activity returned low
- Patient continued to have good days and bad days regarding fever and pain
- On hospital day 14, patient started on dexamethasone/etoposide for treatment of HLH
Follow-up

- Received therapy for 4 months, then relapsed and started dexamethasone/etoposide again
- Subsequently started cyclosporine
- At 18 months out, patient’s ferritin level is 400
- Hematology has recommended BMT to prevent recurrence, however patient currently refuses
Hemophagocytic Lymphohistiocytosis

- Comprises two conditions that may be difficult to distinguish from one another
  - Primary form – autosomal recessive; fatal disease with a median survival <2 months if untreated; presents during infancy or early childhood
  - Secondary form – may develop as a response to a strong immunological activation; has been described in association with viral infections and malignancies

Hemophagocytic Lymphohistiocytosis

- Most typical findings are fever, hepatosplenomegaly and cytopenias
- Other common findings include hypertriglyceridemia, coagulopathy, elevated ferritin and transaminases, and neurological symptoms
- Less common findings include lymphadenopathy, skin rash, jaundice, and edema

Hemophagocytic Lymphohistiocytosis

- Differential diagnoses include:
  - Malignancy (leukemia, lymphoma, solid tumors)
  - Infections (viral, bacterial, or parasitic)
    - Also, viral infections (especially EBV) can trigger HLH
  - Rheumatoid disorders

Hemophagocytic Lymphohistiocytosis

- **Diagnosis requires > 5 of the following clinical features or laboratory findings**
  - Fever
  - Splenomegaly
  - Cytopenias affecting multiple lineages in peripheral blood
    - Hemoglobin <9
    - Platelets <100000
    - Neutrophils <1000
  - Hypertriglyceridemia or hypofibrinogenemia
  - Hemophagocytosis in bone marrow, spleen, or lymph nodes
  - Low or absent NK cell activity
  - Ferritin >500
  - Soluble IL2 receptor >2400

Hemophagocytic Lymphohistiocytosis

- **Treatment**
  - Etoposide and dexamethasone
  - May eventually need HSCT

Case Two
Chief Complaint(s)

- Flushing
How will you take your history?
History of Present Illness

- 55 year old male presents with episodic flushing
- Has been occurring over the last few weeks
- During the episode, he feels warm and then cool
- BP during the episode was 180/120; baseline BP of 120/80
- No associated chest pain, headache, fever, chills or night sweats
Thoughts?
Past History

• No past medical history
• Surgical history
  ▫ Rotator cuff repair, left
  ▫ Knee surgery, left
  ▫ Neck surgery
  ▫ Back surgery
• Family history non-contributory
• Social History
  ▫ Non-smoker, non-drinker, no illicit drugs
  ▫ Employed as a local church pastor
Home Medications

- Tylenol 500mg q6hr PRN
- Zyrtec-D 5/120mg one to two times daily PRN
- Xanax 0.5mg 1-2 times daily PRN anxiety
- Excedrin migraine 1 tab daily PRN headache
- Nexium 40mg QD
- Fluticasone 50mcg/spray two sprays per nostril daily
Review of Systems

- Good appetite; no weight changes
- No CP, palpitations
- No SOB, wheezing
- No diarrhea
- No dysuria, hematuria
- No heat/cold intolerance; no hair loss
- No TIA or stroke symptoms
- No rashes
What are you looking for on exam?
Physical Exam

- VS: T 98.8, P 91, BP 149/92
- Gen: White man sitting calmly on the exam table
- HEENT: no goiter
- CV: NR, RR, no m/r/g
- Pulm: CTAB without c/r/w
- Abd: Soft, NT, ND, BS+
- Skin: Warm, dry, no rashes
What now?
Plan

• Check basic labs
• Check serum metanephrines
## Basic Laboratory Data

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<tr>
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<th>Value</th>
<th>Reference</th>
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<tr>
<td>Free normetanephrine</td>
<td>0.57</td>
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</table>
Further evaluation

- TSH and fT4 ordered
  - TSH 5.73, fT4 0.959
- Testosterone ordered
  - 402.1
- Chromogranin A ordered
  - 568 (ref <93)
Further Evaluation

- Octreotide scan ordered
  - No focal increased uptake in the abdomen to suggest a neuroendocrine tumor
  - Faint focal increased uptake in the anterior neck and right thyroid bed with slightly elevated TSH; thyroid u/s recommended to evaluate for a thyroid nodule, medullary thyroid carcinoma, and/or MEN
Further Evaluation

- Thyroid ultrasound showed 1.5cm nodule which was aspirated
- In the interim, CT C/A/P was obtained
  - Two low attenuation liver lesions of uncertain significance
  - No other compelling evidence of carcinoid tumor
- Thyroid nodule aspiration returned as follicular lesion of unknown significance
Consultants

- Hepatobiliary Surgery
  - Clinical carcinoid syndrome
  - Pancreas MRI to r/o involvement
  - Colonoscopy
  - If no primary identified, recommend removing the visualized liver disease with intraoperative ultrasound of pancreas and manual exploration of the small bowel and appendix
Consultants

- GI
  - Performed colonoscopy with no evidence of carcinoid primary visualized
Further Evaluation

- 24-hour urine 5-HIAA elevated
- MR abdomen
  - Findings that may suggest the presence of a small carcinoid or islet cell tumor
  - Multiple hemangiomas in the liver
Continued course

• Given MR findings, patient scheduled for pancreatic enucleation vs resection and potential liver resection as well as exploration with intraoperative ultrasound

• Operative findings:
  ▫ 2 masses with vascular flow in the distal pancreas, which were included in the pancreatic resection
  ▫ Meckel’s diverticulum was found and resected
  ▫ The ultrasound did not show any lesions in the liver that were not seen on MRI
  ▫ Appendix was removed
Pathology report

- Pancreas
  - No diagnostic histopathologic alterations
  - No tumor identified
- Small bowel with Meckel diverticulum
  - Well-differentiated carcinoid tumor of the small bowel arising within a Meckel diverticulum (0.3 cm in the biggest dimension)
Flushed

• Sensation of warmth accompanied by transient erythema that most commonly occurs on the face
Most common causes

- Fever
- Hyperthermia
- Emotional blushing
- Menopause
- Rosacea

Differential diagnosis of flushing

<table>
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<tr>
<th>Autonomic-mediated</th>
<th>Vasodilator-mediated</th>
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<tr>
<td>Thermoregulatory flushing</td>
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<tr>
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<td>Food ingestion</td>
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<tr>
<td>Migraine</td>
<td>Androgen deficiency in men</td>
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