Greatest Clinicopathologic Cases S0013

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Learning Objectives

- “As is your pathology, so is your medicine,”
  - William Osler

- “The pathological changes are merely one side of a problem of which the other side is furnished by the clinical picture. Each throws light upon the other, and neither is complete by itself”
  - William Boyd, MD, Pathologist, 1885-1979
Learning Objectives

- Improve diagnosis by learning to correlate clinical and histopathologic findings
- Recognize the relationship between clinical features and histopathologic presentation
Disclosures

- Relevant Financial Relationships
  - None

- Off Label Usage
  - Yes
Case 1
Clinical Presentation

- 35 year old woman with rheumatoid arthritis
- On immunosuppression with prednisone and rituximab
- Recently hospitalized for 6 months of
  - Weight loss (40 lb)
  - Fatigue, weakness
  - Fever, night sweats
  - Myopathy
  - Headaches
  - Nausea
  - Pancreatitis
  - Bilateral sensorineural hearing loss
- PET/CT scan – Diffuse inflammation throughout the soft tissues and organs
- Laboratory evaluation:
  - $D\text{-dimer, CRP, ferritin, LFTs, RF, ANA}$
Case 1
Clinical Presentation

- Nontender, indurated skin-colored plaques on the proximal thighs without secondary skin changes
What is the most likely diagnosis based on the clinical presentation?

- A. Lymphoma
- B. Autoimmune disorder
- C. Paraneoplastic syndrome
- D. Infection
- E. Connective tissue disease
What is your next step?

- Incisional elliptical biopsy
Histopathologic Findings
What is the most likely diagnosis based on the clinical and histopathologic findings?

- A. Subcutaneous lymphoma
- B. Connective tissue disease panniculitis
- C. Sclerosing panniculitis
- D. Infectious panniculitis
- E. Erythema nodosum
Unremarkable: GMS, Fite, EBV-ISH
CD3, CD4, CD20, CD8, TIA-1, GranzymeB, TCR-BF1, TCR-Delta, Ki-67

CSF PCR: + Enterovirus
Requirements for Submitting Diagnostic Specimens/Cases to IDPB

A. U.S. health care professionals – first consult with your state health department regarding any sample submissions.

B. Send an email to Pathology@cdc.gov with:
   1. A brief clinical history
   2. A copy of the surgical pathology report or autopsy report (prelim reports are acceptable)
   3. A listing of available formalin-fixed specimen types (wet tissue, paraffin blocks, and/or slides)
   4. Relevant clinical, gross pathology, or microscopic pathology digital images, as available

C. After you receive approval by email to submit the case to IDPB:
   1. Electronically fill, save, and print both pages of the Specimen Submission Form CDC 50.34.
      a. The form must be filled electronically to generate 3 barcodes required for accessioning
      b. E-mail addresses of the Original and Intermediate submitters (if any) are mandatory fields
   2. Select Test Order Code CDC-10365 (Pathologic Evaluation of Tissues for Possible Infectious Etiologies)
   3. Click on links below for specific syndrome based tissue collection instructions:
      - Pathologic Evaluation of CNS Infections
      - Pathologic Evaluation of Influenza Virus Infections
      - Pathologic Evaluation of Myocarditis
      - Pathologic Evaluation of Suspect Pneumonia Infections
      - Pathologic Evaluation of Rash- and Eschar-Associated Illness
      - Pathologic Evaluation of Hepatitis
      - Pathologic Evaluation of Sudden Unexplained Infant Death with Pathologic or Clinical Suspicion of Infection
      - Pathologic Evaluation of Unexplained Illness Due to Possibly Infectious Etiology
      - Pathologic Evaluation of Suspect Mycobacterial Infections

D. Mailing/Contact Info:
   1. Ship to Dr. Sherif Zaki, CDC, IDPB, 1600 Clifton Rd NE, MS: H18-SB, Atlanta, GA 30329-4027
   2. Mail in suitable packaging for delivery Monday-Friday, excluding Federal holidays
   3. Send tracking number to Pathology@cdc.gov
   4. Tel: 404-639-3132, Fax: 404-639-3043; Email: Pathology@cdc.gov
<table>
<thead>
<tr>
<th>VIRUS</th>
<th>SEROTYPES</th>
<th>CLINICAL DISEASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polioviruses</td>
<td>3 types</td>
<td>Asymptomatic infection, viral meningitis, paralytic disease, poliomyelitis</td>
</tr>
<tr>
<td>Coxsackie A viruses</td>
<td>23 types (A1-A22, A24)</td>
<td>Viral meningitis plus, rash, ARD, myocarditis, orchitis</td>
</tr>
<tr>
<td>Coxsackie B viruses</td>
<td>6 types (B1-B6)</td>
<td>Viral meningitis, but no orchitis</td>
</tr>
<tr>
<td>Echoviruses</td>
<td>32 types</td>
<td>Viral meningitis, with orchitis</td>
</tr>
<tr>
<td>Other Enteroviruses</td>
<td>4 types(68-71)</td>
<td>Viral meningitis</td>
</tr>
</tbody>
</table>
Coxsackievirus A9

- **Disseminated opportunistic Enterovirus infection** in the setting of B cell depletion caused diffuse inflammation of solid organs, muscles, and soft tissues, tying together her constellation of symptoms

- **Treatment**
  - IVIG 1 gm/kg q month X 6; weaning of prednisone
Inflammatory infiltrate in the subcutaneous fat

- Inflammatory disorder of the skin
  - Primary panniculitis
  - Secondary panniculitis
- Infection – Bacterial, Deep Fungal, Mycobacterial
- Neoplasm
- Crystal Deposition Disease associated with Panniculitis
Infectious Panniculitis

- Mostly seen in *immunocompromised* patients
- Bacterial, mycobacterial & fungal organisms involved
- Acute & granulomatous lobular inflammation
- Don’t forget *viral panniculitis*
Case 2: Clinical Presentation

- 69 year old woman
- Stage IVB EML4-ALK fused lung adenocarcinoma
- Multiple, nontender, firm, subcutaneous nodules on the cutaneous and mucosal lip, right arm, left buttock, left thigh and left shin present for 1 month
- On lorlatinib, an ALK inhibitor, for 3 months
- Previously developed a drug reaction to alectinib, an ALK inhibitor
Case 2 Clinical Presentation
Generalized morbilliform eruption that developed 3 days after starting alecitinib
Based on the clinical presentation, the most likely diagnosis is?

- A. Cutaneous metastasis
- B. Infection
- C. Panniculitis
- D. Drug reaction
- E. Vasculitis
Histopathologic Findings
What is the best diagnosis based on the clinical and histopathologic findings?

- A. Sarcoidosis
- B. Drug reaction
- C. Metastasis
- D. Infection
- E. Lymphoma
Sarcoidal granuloma

- Sarcoidosis
- Granulomatous rosacea
- Foreign body granuloma – tattoo, beryllium, silica, zirconium
- Infection (late syphilis, deep fungal, tuberculoid leprosy, post-zoster scars)
- Cutaneous Crohn disease
- Sarcoidal-type granuloma annulare
- Orofacial granulomatosis
- Lymphoma
- **Drugs** (TNF-alpha inhibitors, checkpoint inhibitors, and ALK inhibitors)
Adverse Reactions associated with ALK Inhibitors

- Sarcoidosis-like drug reaction involving the skin has not been previously reported
  - A case of pulmonary “sarcoidosis-like” drug reaction
  - Acute allergic reactions and cutaneous drug reactions

- Identification of drug reactions to targeted therapy can avoid long term sequelae and misinterpretation of the clinical findings as progression of disease or underlying infection
Thank you!

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Summary

- Correlation of clinical information with histopathologic findings is crucial in arriving at an accurate diagnosis in inflammatory, infectious and neoplastic skin diseases.
- Formulate a diagnostic approach and appropriate DDx.
- Avoid pitfalls.
- Apply this knowledge to provide optimum care & improve patient outcomes.