Clinicopathologic Self-Assessment

S003 – AAD 2017

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No relevant conflicts
CASE 1
CASE 1

- 25 year-old African-American female
- Itchy, painful eruption over entire body for past 8 weeks
- Flu-like symptoms preceded eruption
  - Fever, arthralgia, myalgia, sore throat
Pathology
Question 1

What is the most likely diagnosis?

A) Sarcoidosis
B) Disseminated cryptococosis
C) Lepromatous leprosy
D) Granulomatous mycosis fungoides
E) Granulomatous secondary syphilis
Question 1

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B) Disseminated cryptococcosis
C) Lepromatous leprosy
D) Granulomatous mycosis fungoides
E) **Granulomatous secondary syphilis**
Question 2

Which special stain would be useful to confirm the diagnosis?

A) Ziehl-Neelsen stain
B) Fite stain
C) PAS stain
D) GMS stain
E) IHC using Anti – Treponema antibody
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Granulomatous Syphilis

- Prominent granulomatous inflammation relatively uncommon in secondary syphilis
  - Most common with tertiary syphilis
- When present, usually late stage secondary syphilis
  - Majority cases 16 weeks or longer in duration
  - Reported in acute cases also (10 days)
- Occasionally in HIV/AIDS patients: altered immunity results in unusual histology

*J Cutan Pathol 2014; 41: 370–379.*
Granulomatous Syphilis

- Histiocytes, lymphocytes and variable number of plasma cells (sparse to numerous)
- Granulomas epithelioid, palisading, tuberculoid, sarcoidal or interstitial granuloma annulare-like
  - +/- multinucleated giant cells
  - *Usually not as “tightly” sarcoidal as sarcoidosis*
- Arranged in a T-shape or candelabra-like pattern
- Extension along nerves, follicular and eccrine structures
- IHC with Anti-*Treponema pallidum* antibody stain of choice
  - Higher sensitivity (90%) and specificity than traditional silver impregnation techniques

Moral of the Story

• Think syphilis! Still the great imitator!
• Sometimes in order to be a good dermatopathologist, you have to...
CASE 2
Case 2

• 42 year old woman female with 6 year history of right thumbnail dystrophy
• Had been treated for onychomycosis for over 1 year
• Nail clipping 1 year previously was negative for hyphae
• 2015 - Nail clipping and culture
  • H&E and PAS negative
  • No visible growth on agar slant
Kerydin
(tavaborole) topical solution 5%

White vinegar soaks
Case History, cont.

- Follow up April 2016: some improvement but no good regrowth
- October 2016: patient reported that “nail fell off”
  - Small, skin-colored subungual papule noted
  - Shave biopsy performed
Question 1

What is the most likely diagnosis?

A) Melanoma
B) Squamous cell carcinoma
C) Onychomycosis
D) Lichen planus
E) Pemphigus vulgaris
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A) **Melanoma**
B) Squamous cell carcinoma
C) Onychomycosis
D) Lichen planus
E) Pemphigus vulgaris
Final diagnosis

- MALIGNANT MELANOMA, RIGHT THUMB NAIL BED
- Clarks level IV, 3.5mm thickness, ulcerated
- All margins involved
- Mitotic index: 2/mm$^2$
- Perineural involvement noted
Follow up

- PET scan negative for metastatic disease
- Amputation performed distal to PIP joint
- Lymph node dissection; no nodal metastasis
- Continued monitoring by dermatology, surgical oncology, and medical oncology
Amelanotic Subungual Melanoma: May Simulate Other Conditions
Question 2

What percentage of nail unit melanomas are amelanotic?

A) 2%
B) 5%
C) 10%
D) 15%
E) 25%
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Nail Unit Melanoma

- Only 1-2% of all melanomas in Caucasians; 15-25% in Asians and Blacks
- Fingers>>Toes; most commonly on thumb and hallux
- 25% amelanotic
- <2.5mm 88% 5 year survival
- >2.5mm 44% 5 year survival
Nail unit melanoma

- No clear-cut relationship with UV exposure
- Genetically more akin to MM arising in non-sunexposed skin
  - BRAF less prevalent
  - KIT is more common
  - NRAS in 4/16 nail unit melanomas
Challenges in diagnosing nail unit melanoma

• Clinically mimics other nail diseases
• May be present for many months prior to diagnosis
• Often asymptomatic; low motivation to seek medical advice
• Physicians reluctant to perform nail biopsies
  – Time consuming
  – Lack of familiarity with procedure
  – Lack of proper instrumentation
  – Insufficient sampling, sampling error
What can we do better?

- Maintain high clinical suspicion
- Lower threshold to biopsy nail abnormalities involving JUST ONE NAIL
- Obtain sufficient tissue given high risk of sampling error
- Educate patients, residents, fellows
- Only submit specimen to dermatopathologist with expertise and SEND PHOTO along with biopsy!
CASE 3
Case History

- 73 year old male with long standing lesion on the occipital scalp

- Clinical impression: rule out MALIGNANT MELANOMA
Diagnosis

- Malignant melanoma, > 2.1 mm in thickness, Clark’s level 4
- 3 mitoses/mm$^2$
- Non-ulcerated
- Patient referred to general surgery for wide excision
Which is the Most Likely Diagnosis?

A. Angiomatoid melanoma
B. Angiosarcoma
C. Nodular fasciitis
D. Malignant fibrous histiocytoma
E. None of the above
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A. Angiomatoid melanoma  
**B. Angiosarcoma**  
C. Nodular fasciitis  
D. Malignant fibrous histiocytoma  
E. None of the above
Clinical Course

• Re-excision revealed features characteristic of angiosarcoma
• Clinical pictures were reviewed and special stains performed
  - ERG & CD31 +
  - Melan-A & SOX-10 -
  - S-100 protein highlighted many cells, including a discontiguous nodule
• Final diagnosis: pigmented epithelioid angiosarcoma simulating melanoma
Question 1

Angiosarcoma most commonly affects all of the following sites except:

A) Face
B) Scalp
C) Areas of chronic lymphedema
D) Previously irradiated area
E) Palms and soles
Question 1

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Question 2

Angiosarcoma is associated with amplification and overexpression of:

A) MYC  
B) FLT4  
C) erbB-2  
D) A&B  
E) None of the above
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Teaching Points

- Soft tissue neoplasms are often multi-phasic histologically
  - Samples taken from one area may differ significantly from other areas
  - Superficial shaves and punches VERY prone to sampling error
  - Incision biopsy ideal
- Multiple variants of angiosarcoma described
  - Epithelioid may simulate epithelial neoplasms and melanoma
- Special stains may have aberrant patterns and can lead to erroneous diagnoses
- *Take and send clinical picture of any unusual neoplasm to increase accuracy of diagnosis!*
Beware of Imitators!!