Case Presentation

• A previously healthy 48 year-old-male patient presented with a 2nd toe lesion

• Clinical impression: Mucus Cyst
Differential Diagnosis?

1. Hidradenoma

Hidradenoma
- Also known as eccrine acrospiroma
- Usually affects elderly with slight female predominance
- Most commonly on the head and neck
- Solitary, slowly growing measuring 1 - 2 cm

Histopathologic Features of Hidradenoma
Differential Diagnosis

1. Hidradenoma
2. Hidradenocarcinoma (Malignant hidradenoma)
Hidradenocarcinoma

- Also known as malignant acrospiroma
- A rare neoplasm (<100 cases documented in the literature)
- Has a high potential of metastasis (lymph nodes, lung, bone) and in some series high mortality rates

Histopathologic Features of Hidradenocarcinoma

The following architectural and cytological features were graded as either present or absent:

- Loss of circumscription
- Infiltrative growth pattern
- Deep extension
- Necrosis
- Perineural invasion or vascular invasion
- Nuclear pleomorphism
- ≥4 mitoses per 10 high-power fields

≥3 features → Malignant hidradenoma
1-2 features → Atypical hidradenoma
None of the features → Benign hidradenoma

- Relatively circumscribed dermal tumor
- Areas of hyalinization
- Polygonal and clear cells
Differential Diagnosis

1. Hidradenoma (eccrine acrospiroma)
2. Hidradenocarcinoma (Malignant hidradenoma)
3. Aggressive Digital Papillary Adenocarcinoma

Aggressive Digital Papillary Adenocarcinoma

- A rare sweat gland neoplasm
- Most commonly affects male patients in the 4th-5th decade
- Usually solitary

Histopathologic Features of Aggressive Digital Papillary Adenocarcinoma

- Affects acral sites (mostly distal portion of the finger) and occasionally periungal sites
- Other reported sites include the soles, ankles and wrists
- Most lesions are around 2 cm in size
Final Diagnosis
Aggressive Digital Papillary Adenocarcinoma
1979: First Description
• Dr. Elson B. Helwig first presented this entity at the AAD conference
• 22 cases (13 recurred and two metastasized)
• Referred to this entity as “Aggressive Digital Papillary Adenoma”

1987: Classifying the Entity
• Kao et al. published a series of 57 cases that were divided into Aggressive Digital Papillary Adenomas and Adenocarcinomas
• “Adenocarcinoma” showed at least one of the following features: poor glandular differentiation, necrosis, atypia and pleomorphism, >3 mitotic figures per single high power field, lymphovascular invasion and bone invasion

1987: Classifying the Entity
• Recurrence: 45% patients with adenoma and 47% with adenocarcinoma
• Metastases: 41% patients with adenocarcinoma developed metastases (3 died of metastatic disease)

2000: Revisiting the Diagnosis
• Duke et al. after having further follow-up on three of the previous patients from the AFIP records that were primarily diagnosed as “adenoma” and subsequently developed metastasis; prompted a review and re-evaluation of the histologic criteria

2000: Revisiting the Diagnosis
• 30 cases originally diagnosed as aggressive digital papillary adenoma: 9 cases recurred and 3 cases metastasized
• 13 cases originally diagnosed as adenocarcinomas: 3 recurred and 3 metastasized

2000: Revisiting the Diagnosis
• They concluded that none of the originally proposed histologic parameters were predictive of recurrence or metastatic potential
• Proposed that all of these neoplasms to be designated as “Aggressive Digital Papillary Adenocarcinoma” without a benign counterpart
Hidradenoma versus Aggressive Digital Papillary Adenocarcinoma

Eccrine acrosiroma
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Acrosiroma located on the palms and soles and especially on the digits must be distinguished from aggressive digital papillary adenoma. In 1979, I presented 22 examples of aggressive digital papillary adenoma of which 21 occurred on the digits and one on the sole (17).

Cutaneous Digital Papillary Adenocarcinoma
A Clinicopathologic Study of 31 Cases of a Rare Neoplasm
With New Observations

Although hidradenomas can occur at almost any site, involvement of acral sites particularly on digits is exceptional. Given the degree of overlap between hidradenoma and ADPA, it is possible that these tumors represent part of a spectrum. Three cases in our series were initially diagnosed as hidradenoma.

(Ann J Surg Pathol 2012;36:1883-1891)

Take Home Messages
- Recognize the different histopathologic variants of Aggressive Digital Papillary Adenocarcinoma

Take Home Messages
- Despite the nomenclature, papillary projections can be very focal or even absent
- Location, location, location

Next Case
Case Presentation

- 53-year-old female with a "xanthelasma" on her right lower eyelid
- Past medical history significant for micropapillary thyroid carcinoma

Differential Diagnosis?
Differential Diagnosis

1. Xanthelasma/Xanthoma

Xanthomas

- Common yellowish macule, papule, or plaque, often multiple
- Often associated with hyperlipidemia
- Multiple variants have been described with different forms of hyperlipidemia

Histopathologic Features of Xanthoma

- Sheet of foamy histiocytes in the superficial dermis
- Usually shows a background of fibrosis
- Sheets of foamy cells with scattered lymphocytes
Lipid profile is within normal limits

**Further Clinical Information**

**Differential Diagnosis**

1. Xanthelasma/Xanthoma
2. Juvenile xanthogranuloma

**Juvenile Xanthogranuloma (JXG)**

- Usually a solitary lesion
- It can appear as an erythematous, brown, or yellowish lesion
- Range in size from 1 – 10 cm in diameter

**Histopathologic Features of Juvenile Xanthogranuloma**

- Nodular and well-defined dermal proliferation
Clinical Follow-up

• Three years after the initial presentation, the patient presented with flank pain and low grade fevers

• Imaging studies showed extensive fibrosis/infiltrative process involving the retroperitoneum inducing bilateral hydronephrosis
Are these two different processes?

Molecular Studies

• Both eyelid and retroperitoneal specimens were found to harbor BRAF V600E mutation (c.1799T>A)

Which histiocytic disorders harbor the BRAF V600E mutations?

- Rosai-Dorfman disease (23 cases)
- Juvenile xanthogranuloma (12 cases)
- Histiocytic sarcoma (3 cases)
- Xanthoma disseminatum (2 cases)
- Interdigitating dendritic cell sarcoma (1 case)
- Necrobiotic xanthogranuloma (1 case)

BRAF V600E mutations were detected in:
- 13 of 24 (54%) Erdheim-Chester Disease
- 11 of 29 (38%) Langerhans Cell Histiocytosis
- Not detected in any of the other histiocytoses:

Radiographically

• The patient does have multiple sclerotic bone lesions in her spine and ilium

What other radiologic information would you like to obtain?
Final Diagnosis

Erdheim-Chester Disease

- First described in 1930 by Erdheim and Chester
- Reported two patients that had diffuse sclerotic lesions involving diaphyseal and metaphyseal parts of the major long bones and the presence of lipid-laden histiocytes

Clinical Presentation

- Greater than 80% of patients present after age 40 years
- Male-to-female ratio of approximately 3:1
- The most frequent symptom at presentation is bone pain, with diabetes insipidus and neurologic symptoms

Clinical Presentation

- Commonly involved extra-skeletal sites include:
  - Skin
  - Cardiovascular system (including aorta)
  - Central nervous system
  - Retroperitoneum (kidneys and ureters)
  - Lungs

Xanthelasma Like Lesion histologically compared with classic xanthelasma shows:
- More frequently involvement of the reticular dermis
- More multinucleated or Touton cells
- Less extensive fibrosis
Take Home Messages

- Cutaneous manifestations can be the first presenting symptom in Erdheim-Chester Disease
- The most frequent cutaneous manifestation is xanthelasma-like lesions (XLL)
- XLL histologically show reticular dermis involvement, more Touton giant cells and less fibrosis in comparison to xanthelasma

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