Clinicopathologic Correlation Cases

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Disclosures

• None
• Off-label usage of medications will be discussed
Case 1:
Clinical

• 72-year old woman with a 25-year history of itching, burning rash
• Rash triggered by heat
• History of fibromyalgia
• History of subjective sense of “foggy-headedness” and sweats, attributed to menopause
Poll

- Although more information is required for a definitive diagnosis, what is the most likely diagnosis?
  - Chronic urticaria
  - Inflammasome disorder
  - Recurrent erythema multiforme
  - Urticarial bullous pemphigoid
  - Urticarial vasculitis
Poll

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Additional patient information

- SPEP: Monoclonal gammopathy (IgG-k)
- Radiographs: Osteosclerosis about the knees
Schnitzler syndrome

- Auto-inflammatory condition characterized by urticarial skin eruption, fever, bone pain, and monoclonal gammopathy
Pathogenesis

• Autoinflammatory disorder (IL-1β-mediated; neutrophil-dominated)
• Involves the development of neutrophil extracellular traps (NETs), mediated by NLRP3 inflammasome

Bonnekoh et al., Frontiers in Immunology, 2019
Clinical features

- Fever (85%)
- Arthralgias (70%)
- Leukocytosis (70%)
- Elevated ESR (70%)
- Bone pain (50%)
- Lymphadenopathy (40%)
- Organomegaly (5%)

Sokumbi et al., J Am Acad Dermatol, 2012
Clinical features

• Monoclonal gammopathy:

  - IgM-kappa: 80%
  - IgG-lambda: 10%
  - IgG-kappa: 5%
  - IgM-kappa and lambda: 5%

Sokumbi et al., J Am Acad Dermatol, 2012
Histopathologic features

- Neutrophilic perivascular and interstitial inflammation (57%)
- Predominantly mononuclear cell perivascular inflammation (29%)
- Eosinophils (50%)
- No leukocytoclastic vasculitis

Sokumbi et al., J Am Acad Dermatol, 2012
Time to diagnosis

• 2-13 years (average: 7.6 years)
Relevance of accurate diagnosis

- Recognition of associated monoclonal gammopathy (100%) or hematologic malignancy (45%)
Relevance of accurate diagnosis

- Treatment options include IL-1 blockade via anakinra (95% response*)

Schnitzler syndrome
Case 2:
Clinical

• 59-year-old woman with several-month history of growing lesion on dorsal nose
• Skin biopsy — “Irritated SK vs. other”
Poll

• Based on clinical and histopathologic features, what is the most likely diagnosis?
  • Inflamed malignant melanoma *in situ*, lentigo maligna type
  • Leukemia cutis
  • Lichenoid keratosis
  • Lupus
  • Rosacea
Atypical plasmacytoid dendritic cell infiltrate

• Recommended correlation with bone marrow biopsy
Patient course

- Patient endorsed unintentional weight loss (15#), fatigue, tremor, and lymphadenopathy
- Bone marrow biopsy:
  - Acute myeloid leukemia, M5b
  - Positive FLT3 internal tandem duplication mutation
Poll

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  • Lichenoid keratosis
  • Lupus
  • Rosacea
Blastic plasmacytoid dendritic cell neoplasm, heralding AML

• Median survival:
  • Traditional chemotherapy: 6 months
  • Hematopoietic cell transplantation: 23 months
  • New biologic agent (CD123 cytotoxin – tagraxofusp): 8 months

Borchiellini et al. JEADV, 2012
Pagano et al. Haematologica, 2013
Patient course

• Successful allogeneic hematopoietic cell transplantation
• Doing well and in remission 5 years later!
Clinical clues for BPDCN?

- Spontaneous hemorrhagic, bruise-like lesion with constitutional symptoms
Histopathologic clues?

- Unusually dense infiltrate
- Enlarged cells with fine chromatin
- CD4 > CD3
- Immunophenotype:
  - CD4+, CD56+, CD123+, TCL1+, MPO-
Histopathologic clues for BPDCN?

A: [Image of histologic section]
B: [Image of histologic section]
C: CD4
D: CD56
E: CD123
F: MPO

Incidental diagnosis of blastic plasmacytoid dendritic cell neoplasm in skin excision for basal cell carcinoma

Jayson Medena, Shane R. Starr, May P. Chan
First published 10 August 2018 | https://doi.org/10.1111/jcp.13338
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