Increased prevalence of myeloid neoplasms in patients with Erdheim-Chester disease

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Background

• Several case reports of concomitant/secondary hematological neoplasms with LCH
  • Acute myeloid leukemia
  • Non-hodgkin lymphoma
  • Histiocytic sarcoma

• Case report of ECD following JAK2 V617F essential thrombocytosis

Lurlo A et al. Medicine (Baltimore). 2016 May;95(20):e3697
Background

- Recent study showed high prevalence of myeloid neoplasms in ECD and mixed histiocytosis:
  - 10.1% in the entire cohort (n=189)
  - 7.8% in ECD cohort
  - 25% in mixed histiocytosis cohort

- Common myeloid neoplasms
  - Myeloproliferative neoplasm (MPN)
  - Myelodysplastic syndrome (MDS)
  - MDS/MPN overlap (including CMML)

Methods

• Retrospective study of ECD patients diagnosed from 1998 to 2016 at Mayo Clinic
• The diagnosis was made using clinical criteria in conjunction with histopathologic findings
• Pathology slides were independently reviewed at our institution

## Results

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ECD patients (1998-2016)</td>
<td>72</td>
</tr>
<tr>
<td>Mixed histiocytosis</td>
<td>1</td>
</tr>
<tr>
<td>Median age</td>
<td>55 years (range, 34-80)</td>
</tr>
<tr>
<td>Bone marrow biopsies</td>
<td>22 (30%)</td>
</tr>
<tr>
<td>Indications for bone marrow biopsy</td>
<td></td>
</tr>
<tr>
<td>Abnormal peripheral blood count</td>
<td>15</td>
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<tr>
<td>Aid diagnosis of ECD</td>
<td>6</td>
</tr>
<tr>
<td>Rule out metastatic prostate cancer</td>
<td>1</td>
</tr>
<tr>
<td>Myeloid neoplasm</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Diagnoses</td>
<td></td>
</tr>
<tr>
<td>CMML</td>
<td>2</td>
</tr>
<tr>
<td>MPN, NOS</td>
<td>1</td>
</tr>
<tr>
<td>ECD involving the marrow</td>
<td>6 (27%)</td>
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Case 1

- A 75y/o M with known MDS-single lineage dysplasia in 2009
- Not on treatment for the MDS
- December 2013: presented with chronic fatigue, unintentional weight loss of 9 pounds, abdominal pain, progressive ataxia
Case 1 continued

• Lacrimal gland pathology consistent with ECD, *BRAF-V600E*

• Monocytosis $2.2 \times 10^9/L$

• Bone marrow: CMML-0 and ECD

• Treatment:
  • Steroid, Anakinra (1 month Rx): Progressive disease
  • Vemurafenib (6 months Rx): intolerance—fatigue
  • Dabrafenib (4 months Rx): partial response but intolerance

• October 2016: hospitalization for multi-organ failure, pancytopenia $\rightarrow$ death
Case 2

- A 59y/o F with skin lesions
- Skin biopsy Nov 2009: Xanthogranuloma, ECD diagnosis, *BRAF V600E* negative by IHC
- Monocytosis 1.15 x 10^9/L, splenomegaly
- Bone marrow: CMML-1
- Treatment: Hydroxyurea in April 2013 for CMML
- Death within 3 months of initiation of hydroxyurea (July 2013)
Skin biopsy
Skin biopsy
CD163
BRAF V600E
–ve IHC
Bone marrow c/w CMML
Bone marrow BE/CLE
Case 3

- A 51 y/o M with JAK2 V617F essential thrombocytosis in 1995
- Treatment with hydroxyurea
- ECD diagnosis (peri-renal tissue) in Sep 2012, BRAF-WT
Case 3 continued

• Bone marrow 10/2012: MPN, not otherwise specified, JAK2 V617F

• Peri-renal biopsy positive for JAK2 V617F (suboptimal sample)

• Treatment and follow-up
  • Interferon alfa: Progressive disease Sept 2013
  • Subsequent follow-up at an outside facility

• Passed away in June 2016 (exact cause unknown)
Perirenal biopsy
BRAF V600E -
JAK2 V617F +
Bone marrow
MPN, NOS,
JAK2 V617F +
Bone marrow
CD163
Results

• 72 patients followed for 256 years
• 3 (4%) developed myeloid neoplasms
• 1.2 myeloid neoplasms per 100-patient years
Conclusions

• Myeloid neoplasms present in 4% of ECD, higher than expected in general population
• CMML most common myeloid neoplasm.
• All these patients with notable abnormality on their peripheral blood counts.
• May consider bone marrow biopsy in ECD patients with peripheral blood count abnormalities
Thank you

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