Atypical chronology of manifestations and heterogeneous phenotypes in an autoimmune polyglandular syndrome (APS) type 1 kindred

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ABSTRACT
Autoimmune polyglandular syndrome (APS) type 1 is a rare autosomal recessive disorder caused by mutations in AIRE, the autoimmune regulator gene. We report a patient with Addison’s disease as the initial manifestation of APS1 and multiple siblings with variable presentations of the syndrome.

CASE
• 73-year-old male admitted for urinary retention; endocrinology was consulted for hypocalcemia
• Addison’s disease had been diagnosed at age 15 years, hypoparathyroidism when the patient was in his late 50’s, and onychomycosis in his mid-60’s
• Multiple siblings had experienced variable presentations of the same pathologies (Figure 1)

Figure 1. Family History

The patient is the oldest of 12 children. A sister died of hypocalcemia at age 10 years, a brother has classical APS1, and another sister has hypoparathyroidism and onychomycosis/nail dystrophy. Two other siblings have isolated onychomycosis/nail dystrophy for a total of six children with ectodermal dystrophy.

Table 1. Key admission laboratories

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dL)</td>
<td>7.8</td>
<td>8.8-10.0</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.9</td>
<td>3.4-4.9</td>
</tr>
<tr>
<td>Intact PTH (pM)</td>
<td>&lt; 0.4</td>
<td>0.9-7.7</td>
</tr>
</tbody>
</table>

Figure 2. “Twenty-nail dystrophy”

Panel A: Left hand demonstrating dystrophy of all nails, arthritis, and mild hypopigmentation. Panel B: Left foot showing representative lower extremity nail dystrophy.

DISCUSSION
• The patient and his family are an unusual APS1 kindred.
• Addison’s disease occurred at a typical age in the patient’s case, but other manifestations of APS1 occurred very late and out of order with the classical phenotype.
• The finding of petrified auricles is rare, though it has been reported in other cases of Addison’s disease.
• This case illustrates that APS1 may be quite different than the historically reported presentation of childhood mucocutaneous candidiasis and hypoparathyroidism followed by adolescent onset adrenal insufficiency.

REFERENCES
• Betterle C1, Greggio NA, Volpato M. Autoimmune polyglandular syndrome type I. J Clin Endocrinol Metab. 1998 Apr;83(4):1049-55.
• Nicholas S Mastronikolis, et al, Bilateral ossification of the auricles: an unusual entity and review of the literature, Head & Face Medicine 2009, 5:17

Figure 2. "Twenty-nail dystrophy"

Panel A: Plain film of the right hand showing changes of erosive osteoarthritis including central erosions, subchondral sclerosis, joint space narrowing, large osteophytes, and partial ankylosis. Panel B: Plain film of the skull demonstrating extensive auricular ossification (arrow).

Figure 3. Radiographic findings

Figure 4. Candida esophagitis

Panel A: Plain film of the right hand showing changes of erosive osteoarthritis including central erosions, subchondral sclerosis, joint space narrowing, large osteophytes, and partial ankylosis. Panel B: Plain film of the skull demonstrating extensive auricular ossification (arrow).

Endoscopic image showing white plaques indicative of esophageal candidiasis (arrows).