THE TIP OF THE ICEBERG

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The patient is a 48 year-old female, who recently returned from a trip to Puerto Rico.

She presents to the ED with 48hrs of a worsening cough, pleuritic chest discomfort, and scant hemoptysis, concerning for TB.

Medical history includes a chronic skin condition treated with oral Dapsone for >10 yrs. Recent flaring was reported as she has self-discontinued her daily Dapsone. She also has a history of chronic anemia and MGUS (2012).
CT scan of the chest revealed bilateral pulmonary infiltrates with multiple cavitary lesions, raising the suspicion for infectious vs. malignant etiology.
Case

**CBC** - Chronic Anemia at baseline

**CRP and ESR** – Elevated

**ANA profile** – Negative

**Complements** – Normal

**ACE level** – Normal

**c-ANCA and p-ANCA** – Normal

**CCP** - Negative

**Infectious workup** – negative for HIV, AFB, hepatitis B and C, fungal antibody, cryptococcal antigen, blood cultures, anaerobic/aerobic cultures, quantiferon TB gold, and an unremarkable bronchoscopic lavage.
Case

A wedge resection of the lung revealed a perivascular neutrophilic infiltration suggestive of *leukocytoclastic vasculitis*. Although non-specific, it is a key finding consistent with the histology of her chronic skin condition, *Erythema elevatum diutinum (EED)*.

IgA kappa MGUS with small plasma cell population of 1% on flow cytometry and marrow biopsy (2012)

Repeat bone marrow sample demonstrated expansion of plasma cell population to 10-20%. She was referred to Hematology-Oncology and currently plans to start treatment (Revlimid, Velcade, Dex) and further investigate the extent of this smoldering myeloma.
Discussion

Erythema elevatum diutinum (EED) is a rare, chronic, skin disorder with a poorly understood pathogenesis, thought to be a variant of immune complex mediated leukocytoclastic vasculitis (Arthus reaction?). The lesions often consist of violaceous, red-brown, yellowish papules, plaques, or nodules that typically favor the extensor surfaces symmetrically.
Discussion

- It typically affects adults ages 30-60
- Prolonged course, characterized by fluctuating periods of exacerbation and stability
- Early lesions are soft on palpation and become firm and fibrotic when chronic
- Ulcerative lesions are rare but do occur in severe cases
- Typically asymptomatic but lesions can be pruritic or burning
Early-stage lesions demonstrate a dense perivascular infiltrate of neutrophils admixed with lymphocytes and histiocytes.
Late-stage lesions, typical show minimal inflammatory infiltrates and marked perivascular fibrous thickening.
Discussion

Review of the current literature describes numerous systemic conditions associated with EED without any definitive evidence of a causative relationship.

Infectious
- HIV and HHV-6 infections
- Recurrent Streptococcal infections
- Hepatitis C

Neoplastic
- Myelodysplastic syndrome
- Lymphoma
- Breast carcinoma
- Multiple myeloma
- IgA monoclonal gammopathy (Most Common)
- Hyperimmunoglobulinemia
Autoimmune/Inflammatory Conditions

- Antiphospholipid antibodies and cryoglobulinemia
- Ulcerative colitis, Crohn’s disease, and Celiac’s
- Hashimoto’s thyroiditis
- Relapsing polychondritis
- SLE and Rheumatoid arthritis
- Dermatomyositis
- Sjogren’s
- Pyoderma gangrenosum
- Granulomatous polyangiitis
- Several ANCA positive cases (Mostly IgA ANCA)
The diagnosis requires histologic confirmation with clinical correlation and a thorough search for underlying conditions.

The severity of the EED lesions may indicate increased underlying disease activity, as seen in our patient.

Several authors recommend that there should be lengthy follow-up and monitoring for patients with both EED and IgA paraproteinemia because of the risk of progression to IgA myeloma. Asymptomatic tumor proliferation and malignant transformation can occur in 20% of patients during long-term follow-up.

In one case report, EED lesion progression was associated with development of pulmonary infiltrates and accelerated fibrosis. There are however no documented cases of EED manifesting as vasculitic cavitary lung lesions.
While the majority of EED cases are responsive to oral Dapsone monotherapy (>80%), some may need aggressive treatment of the underlying infection, malignancy, or associated inflammatory condition. Corticosteroids and agents such as methotrexate, colchicine and cyclosporine have been used with reported success in refractory cases.
This case was prepared under the guidance of Dr. Kristin Ingraham and with a significant contribution from the LVHN Pathology Department.

- Patterson JW, Ph.D. G.A. Weedon’s Skin Pathology. The Vasculopathic reaction pattern, Churchill Livingstone; 2015.
- Chowdhury MMU, Inaloz HS, Motley RJ, Knight AG. Erythema elevatum diutinum and IgA paraproteinaemia. Int J Dermatol 2002; 41: 368–70.