Diverse cutaneous manifestations of Erdheim-Chester disease in a woman with a history of Langerhans cell histiocytosis

Julia Pettersen Neckman, MD,[a] Joyce Kim, MD,[b] Mahan Mathur, MD,[c] Peggy Myung, MD,[a] and Michael Girardi, MD[a]
New Haven, Connecticut

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INTRODUCTION

Erdheim-Chester disease (ECD) is a rare, systemic, non–Langerhans cell histiocytosis (non-LCH). Diagnosis is based on a combination of specific radiologic, histologic, and clinical findings. Although there have been hundreds of prior reports of ECD, very few cases have described the spectrum of potential cutaneous manifestations.[1-4] Most of these cases describe ECD skin findings as xanthelasmalike lesions surrounding the periorbital area,[1,2] whereas 2 patients were reported to have a red-brown papular eruption affecting the chest and lower extremities.[3,4] We discuss a case of a 45-year-old woman with an extensive childhood history of LCH who then presented more than 20 years later with a new eruption of polymorphous skin lesions distributed over the face, trunk, arms, and legs. These lesions were clinically varied yet histologically all consistent with xanthogranulomas. Upon further workup, the patient was found to have specific radiographic findings pathognomonic for ECD and a *BRAF* V600E mutation, which has been reported in both LCH and ECD. Our case is unique, in that this patient was affected by both diseases within her lifetime. Identification of the *BRAF* V600E mutation suggests the possibility of a common origin between LCH and ECD.

Abbreviations used:

ECD:	Erdheim-Chester disease
LCH:	Langerhans cell histiocytosis
PET-CT:	Positron emission tomography–computerized tomography

CASE REPORT

A 45-year-old woman presented with complaints of a new widespread eruption across her face, arms, and legs. The patient described an occasionally pruritic, nonpainful, papular rash that would erupt sporadically without a known trigger and resolve to leave hyperpigmented macules. A review of systems was noncontributory, including no episodes of fever, chills, night sweats, or weight loss. The patient's medical history was significant for childhood LCH that manifested as eosinophilic granuloma of the cranium, treated at age 3 with surgery, radiation, and vincristine. She also had recurrent disease treated with prednisone and methotrexate between the ages of 9 and 24. The patient had no other chronic medical problems, no allergies, and no relevant family history and was not taking any medications. On physical examination, erythema was noted on her face, arms, chest, and back. Upon closer inspection, the erythema was composed of numerous, pinpoint, pink-to-red papules (Fig 1). In addition, examination found yellow papules coalescing into thin plaques along her bilateral temples and periorbital regions (Fig 1) and scattered 2- to 4-mm red brown papules across her arms and legs. Biopsies performed on the arm, leg, and face, found foamy cells and multinucleated cells in the dermis without 2-toned cytoplasm. Immunohistochemistry found positive CD68 and negative CD1a and S-100 staining, consistent with non-LCH histiocytosis (Fig 2). The patient was subsequently referred to the hematology department

From the Departments of Dermatology,[a] Internal Medicine,[b] and Radiology,[c] Yale School of Medicine.
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Correspondence to: Michael Girardi, MD, Department of Dermatology at Yale School of Medicine, PO Box 208059, 333 Cedar St, New Haven, CT 06520-8059. E-mail: michael.girardi@yale.edu.

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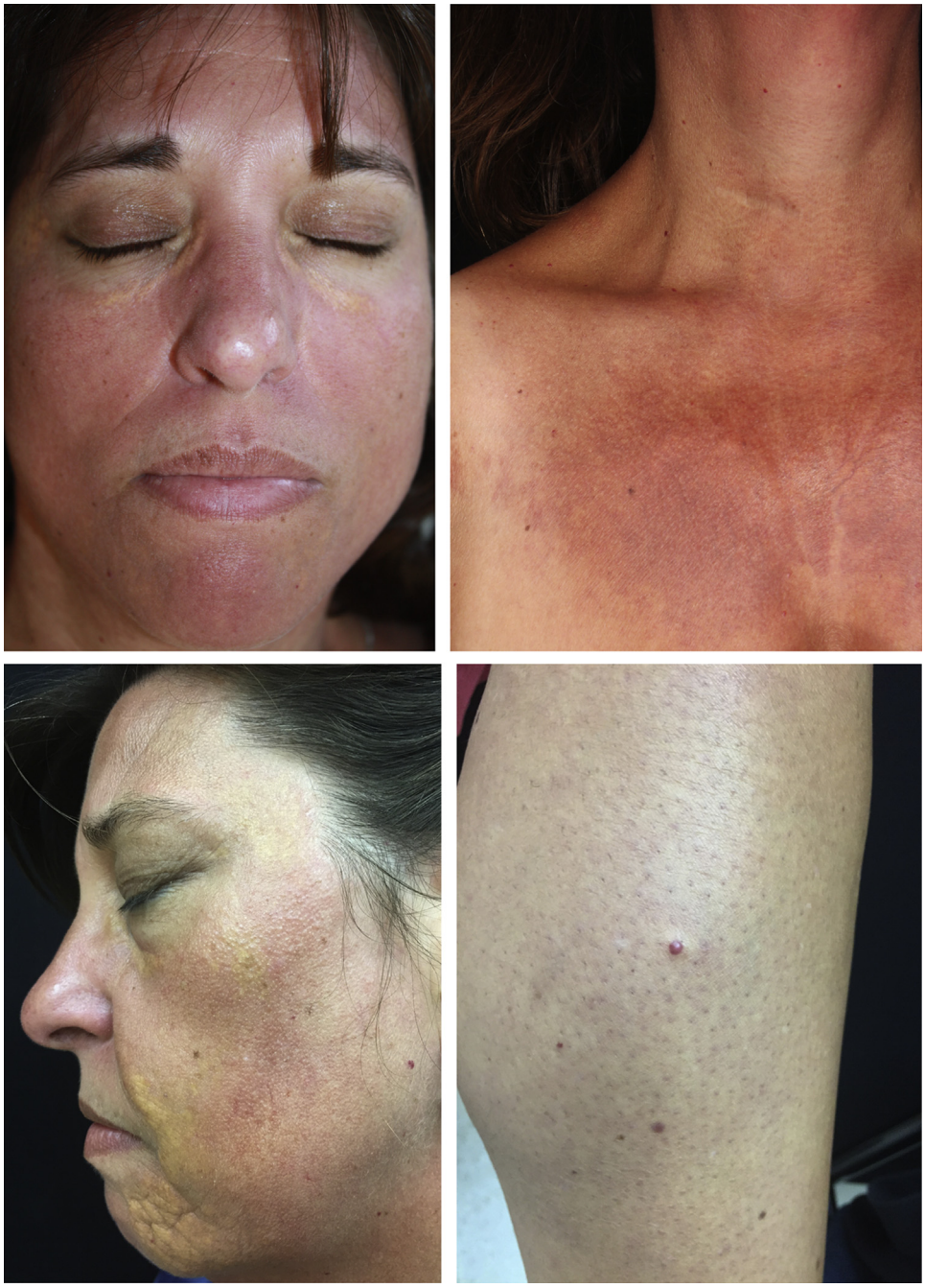

Fig 1. Clinical photographs of ECD.

for further evaluation of an underlying hematologic malignancy given the xanthogranulomas on histology, but findings from a thorough workup (a complete blood count, comprehensive metabolic panel, lactate dehydrogenase, peripheral blood flow cytometry, serum protein electrophoresis, serum immunofixation electrophoresis, β-2 microglobulin, quantitative immunoglobulins, and serum free light chains) were normal. A positron emission tomography—computerized tomography (PET-CT) scan was performed to evaluate for multiorgan involvement. The PET-CT scan was significant for multifocal 18F flurodeoxyglucose avid sclerotic changes in the sternum, sacrum, and bilateral symmetric uptake in the femoral and tibial bones, and the diagnosis of ECD was made based on these pathognomonic radiologic findings (Fig 3). Given recent findings of the high prevalence of *BRAF* V600E mutation in ECD patients and potential therapeutic implications,[5,6] the tissue was tested for this mutation and found to be *BRAF* V600E positive. The patient was then enrolled in an open-label, phase II clinical trial