Clinical Pathologic Conference Case 2: Langerhans Cell Histiocytosis

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Clinical Presentation

A 74-year-old female was seen and evaluated for a complaint of oral soreness. The clinical exam was significant for the presence of multiple erythematous, ulcerated, boggy lesions of the palate and gingiva (Figs. 1–3) that had persisted for over a month's duration. Evaluation of a panoramic radiograph revealed no remarkable findings (Fig. 4).

The patient reported being ill 2 months prior to the onset of the oral lesions and developed lesions under her breast and in the groin that were subsequently diagnosed by a dermatologist as a yeast infection. She was diagnosed with multiple sclerosis 25 years ago but was not significantly impaired. Her list of medications and supplements included lanaflex, borage oil, dantrolene sodium, and multivitamins.

Differential Diagnosis

The differential diagnosis for multiple erythematous, ulcerated, boggy lesions of the palate and gingiva could be quite large. However, working on the assumption that her complaint of feeling “ill” and her skin lesions were related the differential diagnosis would then include several systemic conditions, including lymphoma (mycosis fungoides), disseminated fungal infection, Langerhans cell histiocytosis, and sarcoidosis.

Mycosis fungoides is a form of cutaneous T-cell lymphoma. In its early stage it presents as rash-like patches that can mimic other conditions such as eczema [1]. It is not unreasonable to consider that perhaps this patient's skin lesions had been misdiagnosed as a fungal infection and were actually the early stage of mycosis fungoides. Although involvement of the oral cavity is very rare, there have been case reports of mycosis fungoides presenting as erythematous, indurated plaques and ulcerated tumors [1]. This patient's oral lesions could therefore be compatible with a diagnosis of mycosis fungoides.

Disseminated fungal infection, such as histoplasmosis, was also a consideration. Oral lesions occurring in patients with generalized, disseminated histoplasmosis consist of ulcerations as well as lesions that mimic lymphomas [2]. Skin lesions caused by a disseminated fungal infection can have a variety of clinical presentations including macules and patches. Both the oral and skin lesions could, therefore, be compatible with the presentation in this patient. In addition, the patient's age, history of multiple sclerosis, and reports of feeling “ill” could indicate a weakened immune system thereby making her susceptible to a disseminated fungal infection.

Langerhans cell histiocytosis (LCH) is a rare form of histiocytosis that results in a clonal proliferation of Langerhans cells. Mucosal lesions of LCH can present as ulcerations with surrounding erythema [3]. Although very rare, mucosal lesions occurring in the absence of osseous lesions have been reported. LCH involves the skin in 40 percent of cases. As with the previously mentioned entities, the skin lesions can present in varied forms, including scaly papules.

Sarcoidosis is an acquired systemic granulomatosis that rarely involves the oral mucosa. Although the most common site of oral involvement is salivary glands, soft tissue

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Fig. 1–3 Clinical presentation of multifocal erythematous, ulcerated, boggy lesions of the palate and gingiva

Fig. 4 Panoramic radiograph demonstrating no remarkable findings

lesions have been reported. The clinical presentation can vary and includes well-circumscribed brownish red or purple swellings, papules, and submucosal nodules with superficial ulceration and erythematous gingival hyperplasia [4]. The skin lesions in sarcoidosis can exhibit such varied presentations that cutaneous sarcoidosis is considered one of the “great imitators” in dermatology. Again, it is possible to consider that her skin lesions could have been misdiagnosed.

Results

An incisional biopsy was performed and routine H&E stained histologic sections revealed sheets of histiocytes with interspersed areas rich in eosinophils. The histiocytes were pale-staining and had indented or irregular nuclei and indistinct cytoplasmic borders (Figs. 5, 6). Immunohistochemical stains showed that these lesional cells were positive for CD68 and CD1a, in a membranous pattern (Fig. 7). Based on clinical, radiographic, and histologic findings the final diagnosis was rendered as Langerhans Cell Histiocytosis, multifocal soft tissue presentation.

Discussion

Langerhans cell histiocytosis (LCH) is typically understood as a spectrum of clinicopathologic disorders involving a proliferation of mononuclear histiocytes accompanied by eosinophils and other inflammatory cells. Studies have shown the lesional histiocytes to be of a monoclonal nature, supporting the idea that it is a neoplastic process [5].

Monostotic or polyostotic lesions of bone are termed “eosinophilic granuloma”, and are the most common

Fig. 5 H&E stained photomicrograph (40x objective) showing sheets of pale-staining histiocytes, some demonstrating indented nuclei

Fig. 6 H&E stained photomicrograph (40x objective) showing pale-staining histiocytes with interspersed eosinophils

Fig. 7 CD1a stain (40x objective) demonstrating positive membrane staining of lesional histiocytes

presentation of the disease. The chronic disseminated form involves bone, skin, and viscera, and predominantly affects children. The acute disseminated form occurs most often in infants and may display cutaneous, visceral, and bone marrow involvement. Despite these classic forms of the disease, many authors have cited the overlapping clinical features and noted that many cases defy a discrete category [6].

What makes this case particularly unusual is the combination of its multifocal nature and the limited involvement to soft tissue. It is worth mentioning that the skin lesions related in the patient history were never biopsied, so these could potentially represent involvement of LCH within another organ system.

Two cases of a similar clinical nature were reported in 2001 [7]. An additional case involving multifocal pelvic lesions with obstructive uropathy was reported in 2010 [8]. It is extremely rare to have multifocal disease lacking bony involvement. There is evidence to suggest that the patient's advanced age and apparent lack of visceral involvement portends a more favorable prognosis [9]. Overall, most studies of the LCH spectrum focus on the pediatric population. Whitaker et al. noted that only 1–4% of multifocal LCH cases affect adults [6]. Of those, greater than 99% have bony involvement. Thus, it is exceedingly rare for multifocal LCH to present in an adult without bony involvement.

This patient was treated with topical steroids to help manage the lesions. She was also referred for bone scan and additional immunologic testing to rule out bony or visceral involvement. Several studies have shown that lesional injection of kenolog has been helpful in resolving soft tissue lesions [7]. Older studies cite radiation therapy, although the associated long-term risk for developing other malignancies is an obvious concern of this treatment modality.

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