Pyostomatitis Vegetans And Orofacial Granulomatosis: A Case Report And Review Of The Literature

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Citation

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Abstract

Pyostomatitis vegetans (PV) is a rare, chronic inflammatory condition characterized by pustules, erosions and vegetations of the skin. Oral lesions of PV appear similar to dermatologic lesions and may present on the gingiva, as well as the labial or buccal mucosa. PV has a strong association with gastrointestinal disease and is considered a marker for inflammatory bowel disease. We describe a case of a 9 year old female who demonstrated PV lesions on the oral mucosa accompanied by orofacial granulomatosis.

INTRODUCTION

Pyostomatitis vegetans (PV) is a rare, benign chronic disease characterized by miliary pustules, erosions and vegetating dermatosis of the skin and oral mucosa [1, 2, 3]. These asymmetrical lesions typically affect the axillary folds and groin, and to a lesser extent involve the face and the scalp. [2, 4, 5] Oral mucosal lesions can involve the labial attached gingiva, as well as the labial and buccal mucosa. Oral lesions are distinct and appear as multiple pustules with an erythematous base that coalesce and undergo necrosis to form a typical “snail tracks” appearance.[5, 6] PV has a strong association with gastrointestinal disease and is considered a marker for inflammatory bowel disease (IBD). [3, 5, 6, 7, 8, 9]

In 1898, Hallopeau reported on five patients that presented with unusual pustular dermatosis the he called pyodermite vegetante. [8] Oral lesions that manifested throughout the mucosa were reported in two of these cases. McCarthy coined the term pyostomatitis vegetans, which he believed was a variant of the pyodermite vegetante, when he described three cases that displayed comparable oral lesions on initial presentation. [10] Since McCarthy's report in 1949, approximately 41 cases have been published in the literature.

The association of PV to other mucosal diseases which may present with intraepithelial abscesses and acantholysis including pyodermite vegetante (PDV), pemphigus vegetans and pemphigus vulgaris, is controversial. [10, 11] Pemphigus vulgaris consists of poorly healing, non-vegetating, and rapidly rupturing bullae, that progress to ulcers on the oral mucosa and skin. Unlike PV, pemphigus vulgaris is a potentially fatal, well characterized autoimmune mucocutaneous disease with the presence of auto antibodies and where diagnosis is confirmed by both positive direct and indirect immunofluorescence. Pemphigus vegetans, considered a variant of pemphigus vulgaris, [12] is characterized by a less severe course and the two are differentiated by the presence of vegetations along the ruptured bullae margins. It has also been associated with intraepithelial abscesses. The occurrence of bullae, acantholysis, and a possible fatal outcome [12] depict common features evident in both conditions and distinguish them from PV.

Clinically, PDV and PV feature localized pustules but lack rupturing bullae. Histologically, peripheral eosinophilia and miliary abscesses are distinct features of PDV and PV, although pemphigus vegetans may also display eosinophilia. Immunofluorescence studies have also been key in distinguishing between PV and pemphigus vulgaris. Both pemphigus vegetans and pemphigus vulgaris reveal strong intercellular deposits of IgG and C3 with direct immunofluorescence staining, and show positive circulating antibodies with indirect immunofluorescence .4 However, the pattern of immunofluorescence staining in PDV and PV ranges from negative to weak for both direct and indirect techniques. The atypical immunofluorescence in some PV cases may be the result of a secondary response to epithelial damage as opposed to pemphigus, where antibodies represent the primary response .[11, 13] Moreover, a weak

response to immunofluorescence from a diagnostic viewpoint does not exclude a diagnosis of PDV or PV especially when typical and histologic findings are present.

With a given diagnosis of PV, other reactive cutaneous and oral lesions may be evident in association with IBD such as erythema nodosum, pyoderma gangrenosum and aphthous stomatitis.[14,15,16] The first two occur only on the skin and the latter is characterized by a dense neutrophil infiltrate. The IBD can be sometimes diagnosed as Crohn's disease. Crohn's disease is a granulomatous disorder than can present with oral lesions.[17,18,19]

We present a case of a young girl with pyostomatitits vegetans, who later developed unspecified orofacial granulomatous disease, which has not been diagnosed as Crohn's disease.

CASE REPORT

A 9 year old girl presented to the Oral Medicine practice at the Hospital of the University of Pennsylvania with a complaint of oral ulcers and sores in her mouth. The sores had been present approximately for 6 months prior to consultation. She reported that they began shortly after orthodontic braces were placed on her upper teeth. At that time she recalled a sore which her mother described as an ulcer, approximately 6 mm in diameter, and appearing as “crater-like” in the roof of her mouth. The patient reports that the ulcer slowly resolved over a period of multiple weeks. At that time she was seen by multiple practitioners, including a family practitioner, a pediatric otorhinolaryngologist, a general dentist, and a periodontist. A biopsy of the tissue was obtained, reporting granulation tissue with masses of neutrophils. Additionally, the specimen was thought to have a remanant of a purulent exudate. The lesion was inflammatory in nature as there was no evidence at that time of a malignancy.

The patient was treated with multiple palliative agents as well as various antibiotics. Additionally, the patient was prescribed an anti-inflammatory oral paste used to treat major aphthous ulcers. A routine blood test taken at the time of the biopsy noted a mildly elevated sedimentation rate at 22 as well as a normal total white blood count; however, she was noted to have an elevated eosinophilic count of 11%. The patient persisted with lesions for another 2 months then consulted our service.

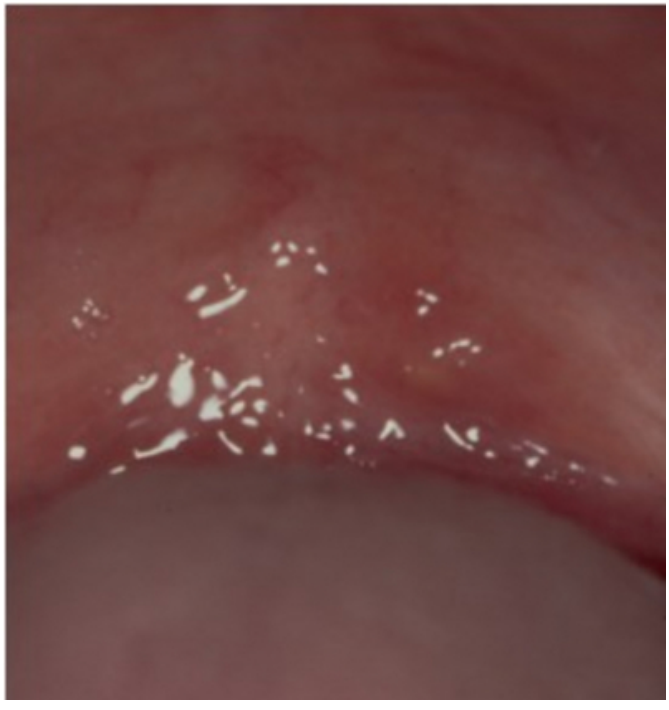
On presentation, she denied any significant past medical problems. She reported that she had a tonsillectomy, at age 5. Her family history was not significant for autoimmune or inflammatory disease, and her social history was not significant. Her detailed review of systems was not significant for nausea, vomiting, diarrhea or melena. She had no eye or skin lesions. Additionally, she did not have any significant odynophagia or dysphagia; however, when the oral lesions were present, and she had oral pain.

Her medications upon presentation were penicillin prescribed to help treat one of her oral ulcers. She had no known drug allergies.

Upon clinical evaluation the patient had a 1-2 cm firm movable right buccal lymph node as well as “shotty” submandibular and anterior cervical lymphadenopathy, bilaterally. In addition, the patient had multiple intact pustules in her soft palate (figure 1). Her dentition was intact and there were no other oral mucosal lesions. She had no thyromegaly and her salivary glands were free flowing. The skin of her face was normal, and her eyes were without injection.

Figure 1

Figure 1. Clinical appearance at time of presentation. Note intact pustules in the soft palate.



At time of presentation our differential diagnosis included pyostomatitis vegetans, as well as recurrent aphthous stomatitis. A complete blood count was taken which revealed a normal hematologic exam except for an increase

in the percentage of eosinophils at 8.5% (normal: 2.4%). Serum chemistry and liver function tests were normal. Given the association of aphthous stomatitis and hematologic deficiencies, vitamin B12, folate, iron as well as ferritin levels were drawn and noted to be normal. An antinuclear antibody titer was noted to be positive at 1:320 (normal: 1:160) and the pattern was diffuse, while it was centromere negative. Her erythrocyte sedimentation rate (ESR) was normal at 21mm (normal range: 0-25mm).

It was at this time that further sectioning was requested on the initial specimen as well as additional staining including stains for fungal elements and PAS staining. A deeper section revealed that the patient had non-caseating granulomatous inflammation.

PAS stains for fungus and for acid fast bacteria were negative. Foreign material was not observed.

The patient was given a presumptive diagnosis of pyostomatitis vegetans associated with orofacial granulomatosis. An MRI of her neck was ordered, and the masses in her buccal space, submandibular and neck area were in fact, reported to be reactive lymphadenopathy.

Given the positive biopsy of granulomatous inflammation, an antineutrophil cytoplasmic antibody screening test (ANCA) and an angiotensin converting enzyme (ACE) level was ordered. An assay to rule out chronic granulomatous disease of childhood (Dichlorofluoroscein – DCF assay) was also performed The ACE level and DCF assay were reported normal. The ANCA was positive with a perinuclear pattern (p-ANCA) and hence supported a diagnosis of ulcerative colitis (UC). An UC specificity test (Prometheus Lab's Proprietary UC Specificity Test- San Diego, CA) revealed that the p-ANCA pattern was eliminated when treated with deoxyribonuclease (Dnase) suggesting a high probability (>70%) of UC. [20,21,22,23,24]

The patient was referred to the gastroenterology service, where a colonoscopy was performed. The colonoscopy revealed no significant findings. Multiple sections of tissue were sampled from various areas in the patient's large bowel. The lymph node on the patient's face was increasing in size and now pointing to the skin surface. An open biopsy of the tissue also revealed granulomatous inflammation. Special stains including acid fast, AFB, PAS, Spiner and GMS were all interpreted as negative. A detailed GI evaluation was concomitantly pursued including an upper GI series with a small bowel follow through. There was no evidence of small bowel folding or thickening which might be suggestive of Crohn's disease. There were, however, small nodules in the terminal ileum suggestive of extensive lymphoid hyperplasia. This finding raised the possibility of early inflammatory bowel changes.

At this time the patient is being monitored for the development of IBD or Crohn's disease in association with her pyostomatitis vegetans.

DISCUSSION

Pyostomatitis vegetans is a rare, chronic inflammatory condition that is thought to be the oral mucosal counterpart of PDV, which affects the dermis. It can manifest in all age groups with a male to female ratio of approximately 2:3. Cutaneous lesions are asymmetrical, crusted, erythematous papulopustules that extend peripherally and coalesce to form large vegetating plaques. [3,4,25] These lesions commonly manifest in the axillary folds, groin and scalp areas, and to a lesser extend involve the face, trunk and distal extremities. Skin lesions may appear concurrently with oral lesions. Oral lesions are characterized by multiple white to yellow pustules, with an erythematous and thickened mucosa that often ruptures, resulting in ulceration and erosions. The oral mucosa may have a granular morphology but vegetating pustules undergo degeneration, ulceration and suppuration, leading to a folded, fissured “snail track” appearance. The labial attached gingiva, buccal and labial mucosa, hard and soft palate, vestibule and tonsillar regions re most frequent affected. 9 The floor of the mouth and tongue are usually spared the filliform and fungiform lingual papillae may be atrophic. [26] Patients usually only experience mild tenderness or discomfort despite extensive involvement of the oral tissues.

Peripheral eosinophilia can aid in diagnosis and has been reported in 90% of the cases. [11] Eosinophilia can be higher than 20% on a differential white blood cell count. A search for infectious etiology has persistently yielded negative results, as bacterial, viral and fungal culturing consistently reveal normal oral flora.

Histological examination of the oral lesions demonstrate characteristic features of intraepithelial and/or subepithelial miliary abscesses containing numerous eosinophilia in the earlier stages and subsequently an increasing lymphocytic infiltrate with less eosinophilia as lesions mature. The underlying lamina propria is usually populated with a dense mixed inflammatory infiltrate containing eosinophils, neutrophils, lymphocytes and plasma cells. Acanthosis,

hyperkeratosis and areas of intraepithelial dissociation are evident but acantholysis is not a primary feature. [25]

Skin lesions of PDV can appear shortly after or prior to the occurrence of oral PV lesions. Moreover, the clinical progression of PDV and PV follows the activity of inflammatory bowel disease (IBD), namely ulcerative colitis and Crohn's disease, by months to years 3 and the severity of the oral lesions can mirror the activity of IBD. [18] Of the 41 cases described in the literature since McCarthy's publication, 32 cases have been associated with IBD, mainly ulcerative colitis. Although PV is a highly specific marker for IBD, their relationship is not absolute. [9] Gastrointestinal disorders sometimes present with very subtle symptoms and may remain undetected unless a thorough gastrointestinal examination is performed. Forman, in 1965, advocated that all patients diagnosed with PV should follow up with a complete gastrointestinal workup. Additionally, Philpot et al [6] reported a possible link between PV and hepatic disease. Approximately 21% of all PV cases have had some type of liver dysfunction and suspected PV cases should be evaluated for hepatic disorders. [6]

Ficarra et al [17] documented a case in which PV associated with oral CD was caused by malabsorption of zinc. They reported the only case of PV and oral Crohn's disease associated with zinc malabsorption that contributed to both the pathogenesis of PV and to the clinical findings. The clinical manifestations in this case regressed after the administration of zinc supplements.

Management of PV is often based on treating the underlying gastrointestinal disease via diet modifications, psychotherapy[9] and the administration of systemic agents such as antispasmodics, antibiotics, sulfalazine, corticosteroids, azathioprine and dapsone. Surgical treatment in severe cases IBD involves total colectomy and has resulted in permanent remission of symptoms. [5,6]

The oral lesions can be managed with local therapies utilizing antiseptic mouthwashes such as chlorhexidine or topical corticosteroids such as triamcinolone acetonide paste of betamethasone mouthwash. [17] However, topical steroid therapy has limited success and complete resolution of the lesions usually requires the administration of systemic steroids such as prednisolone. A regimen of moderate to high doses of corticosteroids is very efficient in resolving lesions and efforts to taper patients off such therapy often results in exacerbations. Dapsone has been effectively employed as a second line agent to control a relapse when steroid therapy has been halted or tapered down. Unfortunately, dapsone's utility is limited by its side effects, which include hemolytic anemia, hepatitis, agranulocytosis, and the possibility of a drug mediated allergic reaction. [5]

Strategic treatment initially consists of steroid therapy that is directed toward resolving and controlling lesions. Subsequently, a secondary agent is used that permits the gradual decrease of the steroids while maintaining resolution. Other second line agents include azathioprine and sulfamethoxypyridiazine that can be used for their steroid sparing effect. Sulfamethoxypyridiazine has the advantage of being both effective and less apt to produce the side effects, namely erythema multiforme and hemolytic anemia. [11]

In contrast, azathioprine is only minimally effective and is associated with the risk of bone marrow suppression and hepatotoxicity. [3] Moreover, the patients on second line therapy must be regularly monitored with the use of complete blood counts and liver function tests to detect any adverse side effects.

CONCLUSION

Pyostomatitis vegetans has been described in association with PDV. Few cases, however, have described only oral manifestations. The suggested relationship between PV and IBD has also been a subject of controversy. We present a case where PV accompanies orofacial granulomatosis and where only minimal inflammatory changes suggesting IBD have been detected.

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