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

T Sollecito, E Stoopler, S Rangarajan, A Pinto

Citation

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. These asymmetrical lesions typically affect the axillary folds and groin, and to a lesser extent involve the face and the scalp. 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. PV has a strong association with gastrointestinal disease and is considered a marker for inflammatory bowel disease (IBD).

In 1898, Hallopeau reported on five patients that presented with unusual pustular dermatosis he called pyodermitie vegetante. 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 pyodermitie vegetante, when he described three cases that displayed comparable oral lesions on initial presentation. 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 pyodermitie vegetante (PDV), pemphigus vegetans and pemphigus vulgaris, is controversial. 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, 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 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 migratory 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. 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. 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. 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.

We present a case of a young girl with pyostomatitis 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, 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.
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. An assay for infectious etiology has persistently yielded negative results, as bacterial, viral and fungal culturing consistently reported in 90% of the cases.

Peripheral eosinophilia can aid in diagnosis and has been reported in 90% of the cases. Peripheral 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 inflammatory infiltrates containing numerous eosinophils in the earlier stages and subsequently an increasing lymphohytic 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
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 8 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
sulfamethoxypyridazaine that can be used for their steroid
sparing effect. Sulfamethoxypyridazine has the advantage
of being both effective and less apt to produce the side
effects, namely erythema multiforme and hemolytic anemia.
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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.

CORRESPONDENCE TO

Thomas P. Sollecito D.M.D. Department of Oral Medicine
University of Pennsylvania School of Dental Medicine 240
South 40th Street Philadelphia PA 19104 Phone:
215.898.2048 Fax: 215.573.7853 Email:
tps@pobox.upenn.edu

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Author Information

Thomas P. Sollecito, D.M.D.
Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine

Eric T. Stoopler, D.M.D.
Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine

Shrikanth Rangarajan, D.M.D.
Former dental student and research assistant, University of Pennsylvania School of Dental Medicine

Andre Pinto, D.M.D.
Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine