

# Pyodermatitis-Pyostomatitis Vegetans: A Cutaneous Clue for Crohn's Disease

**Keywords:** Pyodermatitis-pyostomatitis vegetans; Crohn's disease; Inflammatory bowel disease

## Abstract

Pyodermatitis-pyostomatitis vegetans is a neutrophilic dermatosis that is classically associated with inflammatory bowel disease. It is rare with less than 40 cases reported in the literature within the last 10 years. We discuss the case of a 30-year-old male who presented with pyodermatitis-pyostomatitis vegetans and previously undiagnosed Crohn's disease. We aim to emphasize the importance of prompt recognition of pyodermatitis-pyostomatitis vegetans order to commence a thorough investigation of underlying inflammatory bowel disease, and initiate appropriate therapy. Because no standardized treatment regimens have been established, we also describe the variability in treatment responses seen with pyodermatitis-pyostomatitis vegetans with a review of the literature.

## Abbreviations

Pyodermatitis-pyostomatitis vegetans (PPV); Inflammatory bowel disease (IBD); Non-steroidal anti-inflammatory (NSAID); Direct immunofluorescence (DIF); Gastrointestinal (GI); Ulcerative colitis (UC)

## Introduction

Pyodermatitis-pyostomatitis vegetans (PPV) is a neutrophilic dermatosis characteristically associated with underlying inflammatory bowel syndrome (IBD) [1]. The first reported case of PPV was in 1898 by Francois Hallopeau [2], and only 37 cases of PPV were reported in the literature between 1979 and 2011 [3]. Diagnosis can be challenging due to its resemblance to autoimmune blistering disorders such as pemphigus vegetans, and infectious etiologies such as *Staphylococcus aureus* and blastomycosis. Recognizing the signs and symptoms of PPV is critical in order to prompt further work up for IBD and begin appropriate management, especially considering that responses to treatments can be variable among patients and often require trial and error to maintain remission. Here, we report a case of PPV that highlights the importance of prompt diagnosis, especially in cases where underlying IBD has yet to be uncovered. We also perform a literature review of treatment responses in patients with PPV.

## Case Presentation

A 30-year-old Caucasian male with fever, hypotension, and tachycardia was admitted for one-week history of abdominal pain, diarrhea, rash, and concern for sepsis. Past medical history revealed another recent admission for melena, diarrhea, and abdominal pain which he had self-managed with 1 gram of ibuprofen per day. At that time, EGD and colonoscopy revealed edematous and ulcerated tissue with mucopurulent material. Biopsy revealed ulceration and granulation tissue, which was diagnosed as non-steroidal anti-inflammatory drug (NSAID)-induced colitis. NSAIDs were discontinued, however diarrhea and melena had since persisted.



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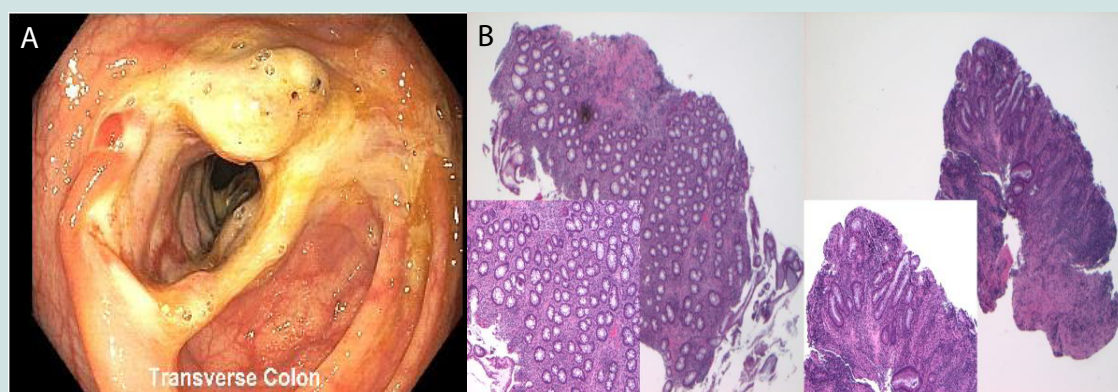
Additional past medical history included intravenous drug abuse managed with buprenorphine and naloxone, and recent unintentional 35-pound weight loss.



**Figure 1:** Pyodermatitis vegetans lesions and histopathology. **A.** Multiple erosions and crusts were observed on the face. **B.** On the extensor surfaces were multiple erythematous papules and plaques with pustules studding the borders and verrucous crust in the center of the lesions. **C.** Hematoxylin and eosin at x 2, inset at x10; Punch biopsy from left arm showed an ulcerated lesion with underlying neutrophilic abscesses and a neutrophilic interstitial infiltrate. PAS, GMS, AFB Fite stains were all negative for microorganism. Direct immunofluorescence was negative. Bacterial and fungal tissue cultures were all negative for growth.

**Table 1:** Pyodermatitis-pyostomatitis vegetans case reports since 2015.

Author	Demographics	Presentation	Treatment and Response
Gara et al. 2020 [2]	Male, 20s	PPV of lips, buccal, and nasal mucosa 6 years after Crohn's disease onset	Improvement with systemic corticosteroids with dose of 1 mg/kg/d
Gheisari et al. 2020 [3]	Female, 32	PPV of scalp, back, and lower abdomen after a 16-year history of well-controlled Crohn's disease on mesalamine and azathioprine 150 mg daily	Failed ciprofloxacin and cephalexin; cleared with clobetasol 0.05% lotion daily for scalp, clobetasol ointment twice daily for trunk, and dapsone 25 mg daily
Tharwat & Eltoraby 2020 [6]	Male, 32	PPV of face and oral mucosa associated with simultaneous autoimmune hepatitis	Cleared with prednisolone 1 mg/kg/d for 4 weeks
Li et al. 2020 [7]	Male, 25	PPV of oral mucosa, groin, and penis without history of IBD	Cleared with prednisone 25-40 mg daily; flared when tapered; cleared with sulfasalazine 500 mg daily reduced to 250 mg daily after 3 months
Alfurayh et al. 2019 [8]	Male, 35	PPV of trunk, axillae, inguinal folds, and lower limbs after a 13-year history of Crohn's status post colectomy for refractory disease	Cleared with clindamycin and rifampin 300 mg twice daily each; had recurrence 3 months later that cleared with prednisone 0.5 mg/kg/d followed by prednisone 10 mg daily
Bertlich et al. 2019 [9]	Female, 51	PPV of scalp, intertriginous areas, and chest plus a 5-year history of uncontrolled UC	Failed 2 months of azathioprine 150 mg daily, prednisolone 80 mg daily, and topical betamethasone cream; failed prednisolone 150 mg daily plus azathioprine 200 mg daily plus topical mometasone cream; cleared with infliximab 5mg/kg every 4 weeks plus prednisolone 30 mg daily tapered to 5 mg daily plus topical mometasone
Dodd et al. 2017 [4]	Female, 30s	PPV with history of Crohn's and primary sclerosing cholangitis	Failed azathioprine, budesonide, adalimumab; Crohns responded to infliximab 5 mg/kg every 6 weeks; skin lesions cleared with intralesional triamcinolone 10 mg/mL injection plus dapsone 100 mg daily
Kawahira et al. 2017 [10]	Male, 64	PPV with IBD excluded via colonoscopy	Cleared with 1 month of prednisolone 30 mg daily
Carvalho et al. 2016 [11]	Female, 79	PPV of vulva without history of IBD	Cleared with amoxicillin/clavulanic acid 875 mg/125 mg twice daily for 2 weeks plus prednisolone 0.5 mg/kg/d tapered over 1 month
Uzuncakmak et al. 2015 [12]	Male, 16	PPV with 4-year history of UC 7 months status post total colectomy and discontinuation of corticosteroids	Cleared with 1 month of methylprednisolone 40 mg daily plus topical mupirocin
Stingeni et al. 2015 [13]	Male, 17	PPV with active UC	Cleared with prednisone 1 mg/kg/d; GI symptoms returned after tapering but cleared with azathioprine 125 mg plus mesalamine 4800 mg daily
Kim et al. 2015 [1]	Male, 27	PPV with 2-year history of Crohn's disease treated with mesalamine and azathioprine	Cleared with prednisolone 20 mg daily, dapsone, and colchicine with low dose prednisolone plus dapsone required for maintenance



**Figure 2:** Inflammatory bowel disease. **A.** Colonoscopy revealed large ulcers found at the cecum, in the ascending colon, transverse colon, descending colon, and sigmoid colon. There was narrowing of the mucosa at several sites throughout the colon located near the ulcerations. **B.** Hematoxylin and eosin at x 4, insets at x10; On histology, there was focal active colitis with ulceration and granulation tissue. No granulomas were seen.

On admission, he was noted to have an elevated white blood cell count of 12,800 /UL with 87% polymorphonuclear lymphocytes. C-Reactive Protein was elevated at 189.5 mg/L (normal <8 mg/L). Due to concern for sepsis secondary due to bacterial endocarditis, vancomycin, cefepime, and metronidazole were started. Examination of the rash revealed crusted vegetative plaques with a rim of pustules localized to the face, arms, and legs (Figures 1A and 1B), and multiple

erosions on the hard palate. Dermatologic differential diagnosis included deep fungal infection including blastomycosis, staphylococcal infection, pemphigus vegetans, and PPV. Biopsy revealed necrotic epidermis, ulcerations, and neutrophilic infiltration (Figure 1C) with negative direct immunofluorescence (DIF). Tissue cultures were negative. Histologic diagnosis was compatible with a neutrophilic dermatosis including PPV.

Given ongoing diarrhea, melena, and skin biopsy compatible with PPV, gastroenterology was consulted. Colonoscopy revealed multiple strictures and large ulcers throughout the colon (Figure 2A). Biopsy of the colonic lesions revealed focal chronic active colitis with ulceration and granulation and no granulomas present (Figure 2B). IBD panel was consistent with Crohn's disease. Given his history and skin biopsy results, it was suspected that the lesions were PPV secondary to IBD. The patient was started on prednisone 40 mg daily with significant improvement of skin and gastrointestinal (GI) symptoms. Vedolizumab infusions successfully controlled GI symptoms after prednisone was tapered, however cutaneous manifestations of PPV recurred. He was eventually switched to infliximab with successful remission of both Crohn's disease and PPV.

## Discussion

PPV is a rare neutrophilic dermatosis that characteristically presents with friable pustules of the oral cavity that form a "snail-track" pattern and papulopustular cutaneous lesions that give rise to vegetating plaques [1]. PPV has a well-documented association with IBD. Although it presents more often as a sequela of ulcerative colitis (UC), it can be seen in Crohn's disease as well, as in our patient [4]. Cases have also been reported with primary sclerosing cholangitis. It is more common for patients to present with GI symptoms prior to the onset of PPV, however skin lesions may appear first in approximately 15% of cases [1]. Although classic PPV involves both the mouth and the skin, involvement of both sites is not required to render a diagnosis. The etiology of PPV remains uncertain, and males between the ages of 20 and 50 are preferentially affected (3:1 male:female ratio) [5].

PPV has characteristic histology including intraepithelial and subepithelial splitting with neutrophilic and eosinophilic microabscesses. It is important to distinguish PPV from auto-immune blistering disorders, including the pemphigus vegetans subtype of pemphigus vulgaris, IgA pemphigus, epidermolysis bullosa acquisita, and dermatitis herpetiformis. Unlike these blistering disorders, DIF is negative in PPV. Additional considerations include cutaneous infections such as blastomycosis-like pyoderma due to *S.aureus*, and endemic dimorphic fungal infections such as blastomycosis, which can be differentiated by positive tissue cultures. Finally, clinical findings of oral ulcers and documented IBD also support the diagnosis of PPV [1,3]. Our patient exhibited characteristic histology of PPV with negative DIF, negative bacterial and fungal tissue cultures, and presence of oral ulcers diffusely on the hard palate with new diagnosis of underlying IBD.

There is no standardized treatment for PPV, and responses to different therapies are extremely variable among patients. To illustrate this, we performed a review of case reports and case series of PPV since 2015 in PubMed detailing patient responses to varying treatment regimens, which is summarized in Table 1. Although there is no standard algorithm for management, corticosteroids are considered efficacious first line therapy. They are used as systemic, intralesional, and topical treatments depending on disease severity. All the cases reviewed that used corticosteroids achieved clearance, however relapse was common when tapering [1-4,6-13]. Other systemic treatments for PPV include dapsone, azithromycin,

cyclosporine, methotrexate, and infliximab, although varying efficacy has been reported with these options. Other topical treatments include tacrolimus, mupirocin, and antiseptic mouth washes for oral involvement.

Often the clinical courses of PPV and IBD are parallel [1], and successful management of the underlying IBD typically results in resolution of PPV [2]. However, there have also been cases in which PPV develops and persists despite well controlled IBD [1,3,4]. Our patient was started on vedolizumab initially for Crohn's disease due to preference over infliximab, however he was eventually switched to infliximab after his skin manifestations continued to flare. Both his skin and GI symptoms have been well controlled with infliximab infusions. Previous reports have shown successful responses of both cutaneous and GI symptoms to infliximab [14], whereas vedolizumab has shown less efficacy in treating cutaneous manifestations of IBD [15].

## Conclusions

In summary, we present a case of PPV that posed a diagnostic challenge, given both the patient's risk factors for infectious cause and unknown underlying Crohn's disease. Our case demonstrates characteristic clinical and histological features of PPV and highlights the necessity to recognize this condition to screen for underlying IBD. A review of the literature revealed the majority of cases clear with corticosteroid treatment, however relapse is common once discontinued. Although PPV has been shown to resolve with management of IBD, this was inconsistent among the reviewed cases and with our patient as well. Responses to other treatments for maintenance of PPV is variable and often requires trial and error to achieve remission.

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