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Presence of Phlebitis in Aseptic Nasal Septal Abscess Complicated with Ulcerative Colitis; Possible Association with Granulomatosis with Polyangiitis: A Case Report

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Although nasal septal abscesses are uncommon, their cosmetic complications can be severe. Hence, prompt diagnosis and treatment are important. Here, we report a case of aseptic nasal septal abscess in a patient with proteinase 3-antineutrophil cytoplasmic antibody (PR3-ANCA)-positive ulcerative colitis (UC), in which phlebitis was observed and granulomatosis with polyangiitis (GPA) might co-exist. A 27-year-old female suffered from intermittent abdominal pain and diarrhea for several years. She visited our hospital complaining of worsening swelling and pain in the middle forehead and fever lasting 2 weeks. Physical examination and computed tomography revealed severe swelling of the nasal septum. The patient was diagnosed with nasal septal abscess, and incision drainage and biopsy from the bilateral nasal septum were performed, which showed severe ulcerative neutrophilic mucositis with phlebitis. Simultaneously, blood examination yielded slight positivity for PR3-ANCA. Colonoscopy, including biopsy, revealed severe inflammation without vasculitis nor granuloma, which led to the diagnosis with PR3-ANCA-positive UC. Phlebitis in the nasal mucosa and elevated PR3-ANCA suggested co-existing GPA; hence, she was treated with glucocorticoids and rituximab. Following treatment, the nasal septal abscess and digestive symptoms disappeared. She was discharged on day 25 without symptom recurrence or major nasal deformity. For the prevention of nasal deformity due to persistent inflammation, prompt administration of immunosuppressive therapy should be considered with adequate evaluations for systemic diseases, including UC and GPA.

Keywords: antineutrophil cytoplasmic antibody; granulomatosis with polyangiitis; nasal septal abscess; ulcerative colitis; vasculitis
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Introduction

Nasal septal abscess is an uncommon condition defined as the accumulation of purulent material between the cartilaginous or bony septum and overlying mucoperichondrium or mucoperiosteum (Ambrus et al. 1981). Classically, it can occur secondary to trauma, nasal surgery, dental infections, and sinusitis, particularly in immunocom-

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promised patients and those with uncontrolled diabetes mellitus (Ambrus et al. 1981; Salam and Camilleri 2009; Cheng et al. 2019). Moreover, recent studies showed that systemic diseases, such as ulcerative colitis (UC), could cause nasal septal abscesses (Yilmaz et al. 2011; Chang 2018; Tomioka et al. 2018; Yu et al. 2020). In this article, we report a rare case of an aseptic nasal septal abscess in a patient with proteinase 3-antineutrophil cytoplasmic antibody (PR3-ANCA)-positive UC, in which phlebitis was observed and granulomatosis with polyangiitis (GPA) might co-exist.

Case Presentation

A 27-year-old female suffered from intermittent abdominal pain and diarrhea for several years. She had lost 6 kg for three years. Approximately 6 months prior to visiting the hospital, her symptoms worsened and were also accompanied by bloody stools. She visited our hospital with complaints of worsening swelling and pain in the middle forehead and fever lasting 2 weeks, despite treatment with antibiotics. She did not have history of trauma, nasal surgery, diabetes mellitus, or other systemic diseases. Physical examination revealed a slight swelling and tenderness of the nasal root and severe swelling of the nasal septum (Fig. 1). Body temperature was 39.1℃. There were no evident otitis media, skin lesions, or neuropathy. Blood examination demonstrated anemia (hemoglobin 10.6 g/dL) and elevation of white blood cell counts (11,190/μL), C-reactive protein levels (9.59 mg/dL), and erythrocyte sedimentation rate (63 mm/h), which suggested severe inflammation. Serum creatinine level was 0.54 mg/dL, and urinalysis did not show hematuria or urinary protein. In addition, the T-SPOT (interferon gamma release assay for tuberculosis) and β-D glucan tests were negative. Computed tomography revealed swelling of the nasal septum, including low-density areas on both sides of the nasal septal cartilage, without apparent bone destruction (Fig. 2). She was admitted to our hospital on that day (day 0), and we initiated treatment with ceftriaxone.

On day 1, puncture of the swelling of the nasal septum revealed the presence of pus. Thus, the patient was diagnosed with nasal septal abscess, and we performed incision drainage and biopsy from the bilateral nasal septum. Upper and lower gastrointestinal endoscopy showed diffuse gastrointestinal inflammatory findings. In particular, the colonoscopy showed extensive inflammation, suggesting inflammatory bowel diseases (IBD), such as UC (Fig. 3). By day 4, after the incision drainage of the nasal septal abscess, the nasal swelling and the inflammatory index of blood examination were slightly decreased. Nevertheless, the forehead ache and the digestive symptoms persisted. Immunological study revealed that the levels of PR3-ANCA were 4.4 U/mL (reference value < 3.5 U/mL), suggesting an association with UC or co-existence with GPA. Ophthalmologic examination revealed no abnormalities including uveitis. Contrast-enhanced magnetic resonance imaging did not show hypertrophic pachymeningitis, and contrast-enhanced whole-body computed tomography

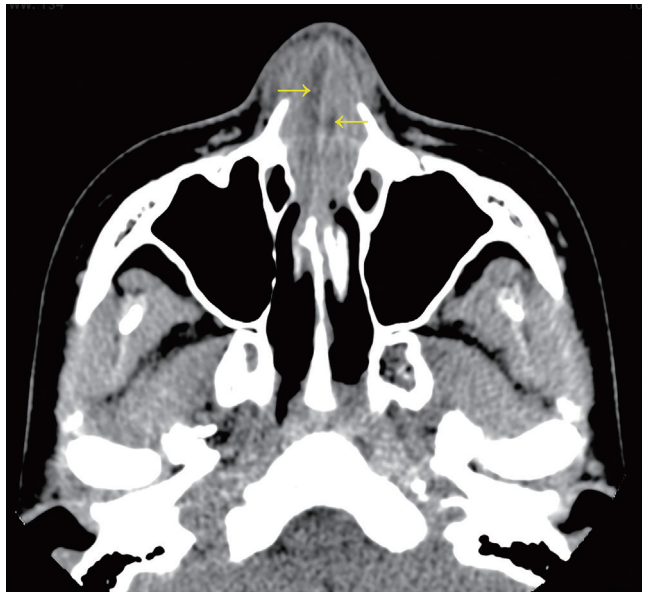

Fig. 2. A pre-treatment computed tomography image of the nose.
The nasal septum was severely swollen, including low-density areas on both sides of the nasal septal cartilage (arrows).

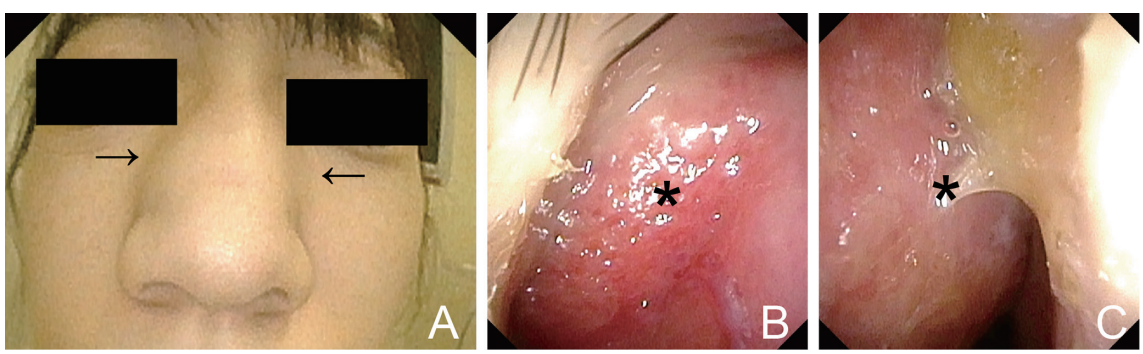

Fig. 1. Pre-treatment photographs of the face and nasal cavity.
(A) Both sides of the nasal root were swollen (arrows). (B, C) Bilateral nasal septum was severely swollen: B, right side; C, left side; asterisks, nasal septum.

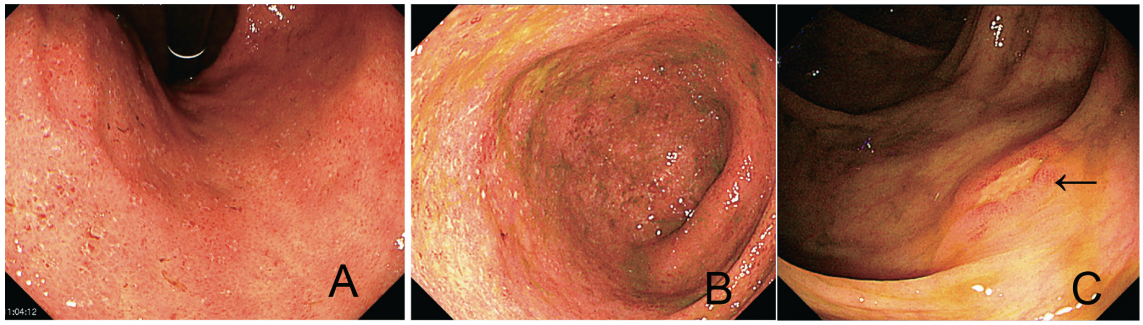

Fig. 3. Gastrointestinal endoscopic findings.
(A) Gastric mucosa with redness and erosion. (B) Erythema and loss of visible vascular pattern in the sigmoid colon. (C) A small ulcer (arrow) in the right side of the colon.

revealed slight gastrointestinal wall thickening without obvious lesions in the lungs or other organs. We promptly initiated treatment with prednisolone (20 mg/day) to test the response to anti-inflammatory therapy, and to prevent deformation of the nose due to persistent inflammation. By day 10, the forehead ache and gastrointestinal symptoms were gradually relieved, and pathological evaluation of the nasal mucosa revealed severe ulcerative neutrophilic mucositis with bleeding, necrosis, and phlebitis (Fig. 4A-D). The gastrointestinal tract pathology revealed mild inflammation from the stomach to the duodenum and severe acute inflammation, including cryptitis, in the colon against the background of chronic inflammatory change without vasculitis or granuloma; these findings were compatible with UC (Fig. 4E, F). Additionally, culture of the pus collected from the nasal septal abscess did not reveal the presence of pathogenic organisms, including mycobacteria, fungi, or anaerobic bacteria, confirming aseptic nasal septal abscess. Therefore, we diagnosed the patient with aseptic nasal septal abscess associated with UC. Although the aseptic nasal septal abscess had been reported as extra-intestinal manifestations of UC (Yilmaz et al. 2011; Chang 2018; Tomioka et al. 2018; Yu et al. 2020), the presence of phlebitis indicated co-existing small-vessel vasculitis, possibly GPA in the context of PR3-ANCA-positivity (Jennette et al. 2013; Robson et al. 2022). The patient was diagnosed with probable GPA according to the diagnostic criteria from Japanese Ministry of Health, Labour and Welfare (MHLW) (Isobe et al. 2020). Therefore, she received treatment with 125 mg of methylprednisolone and 500 mg of rituximab as remission induction therapy. Following treatment, the nasal septal abscess and gastrointestinal symptoms disappeared, and she presented with a slight saddle nose (Fig. 5). After the remission induction therapy, the levels of PR3-ANCA decreased to 1.8 U/mL, and treatment with 25 mg/day of prednisolone *per os* was continued. She was discharged on day 25 without symptom recurrence or major nasal deformity. The patient provided written informed consent for this study.

Discussion

Based on the clinical symptoms, gastrointestinal endoscopy, and pathological findings, we diagnosed the patient with an aseptic nasal septal abscess associated with PR3-ANCA-positive UC. Furthermore, the presence of phlebitis indicated the involvement of small-vessel vasculitis in the nasal septal abscess. Although she fulfilled the diagnostic criteria of Japanese MHLW for probable GPA, it was arguable whether the GPA was involved in this case.

PR3-ANCA is considered a highly specific biomarker for GPA (Lüdemann et al. 1988; Pagnoux 2016). However, elevations in PR3-ANCA have also been reported in cases of IBD, drug-induced vasculitis, autoimmune liver disease, arthritis, systemic lupus erythematosus, infections, and neoplasms (Savige et al. 2000; Shirai et al. 2009). A recent study reported positivity for PR3-ANCA in 44.5% of UC cases, most of which were not diagnosed with GPA (Imakiire et al. 2022). Besides, ANCA-associated vasculitis can occur secondary or concurrent to IBD (Sy et al. 2016). Therefore, in case of positivity for PR3-ANCA, treating physicians should consider the possibility of GPA, IBD, or their co-occurrence, particularly in patients with gastrointestinal symptoms.

Among ANCA-associated vasculitis, GPA often includes upper respiratory tract lesions (70-100%) (Comarmond and Cacoub 2014). In particular, the nasal cavity and the paranasal sinuses are the most common sites of involvement in the head and neck area (85-100%) (Greco et al. 2016). Classic nasal manifestations of GPA include crusting rhinorrhea, blood-stained discharge, sinusitis, saddle nose, septal perforation, and granulomatous lesions (Comarmond and Cacoub 2014; Greco et al. 2016; Sattui and Lally 2020). However, to the best of our knowledge, a case of nasal septal abscess has not been reported thus far.

UC is a chronic inflammatory condition that causes continuous mucosal inflammation of the colon. Currently, there is no gold standard for the diagnosis of UC. Consequently, patients are diagnosed with UC based on clinical, laboratory, imaging, endoscopic, and histopathological parameters (Magro et al. 2017). Although vasculitis in the gastrointestinal tract can mimic IBD (Kasuga et al. 2008; Grigg et al. 2012; Sato et al. 2021), the history of bloody diarrhea for approximately 6 months suggested a non-ischemic nature in this case, which corresponded to

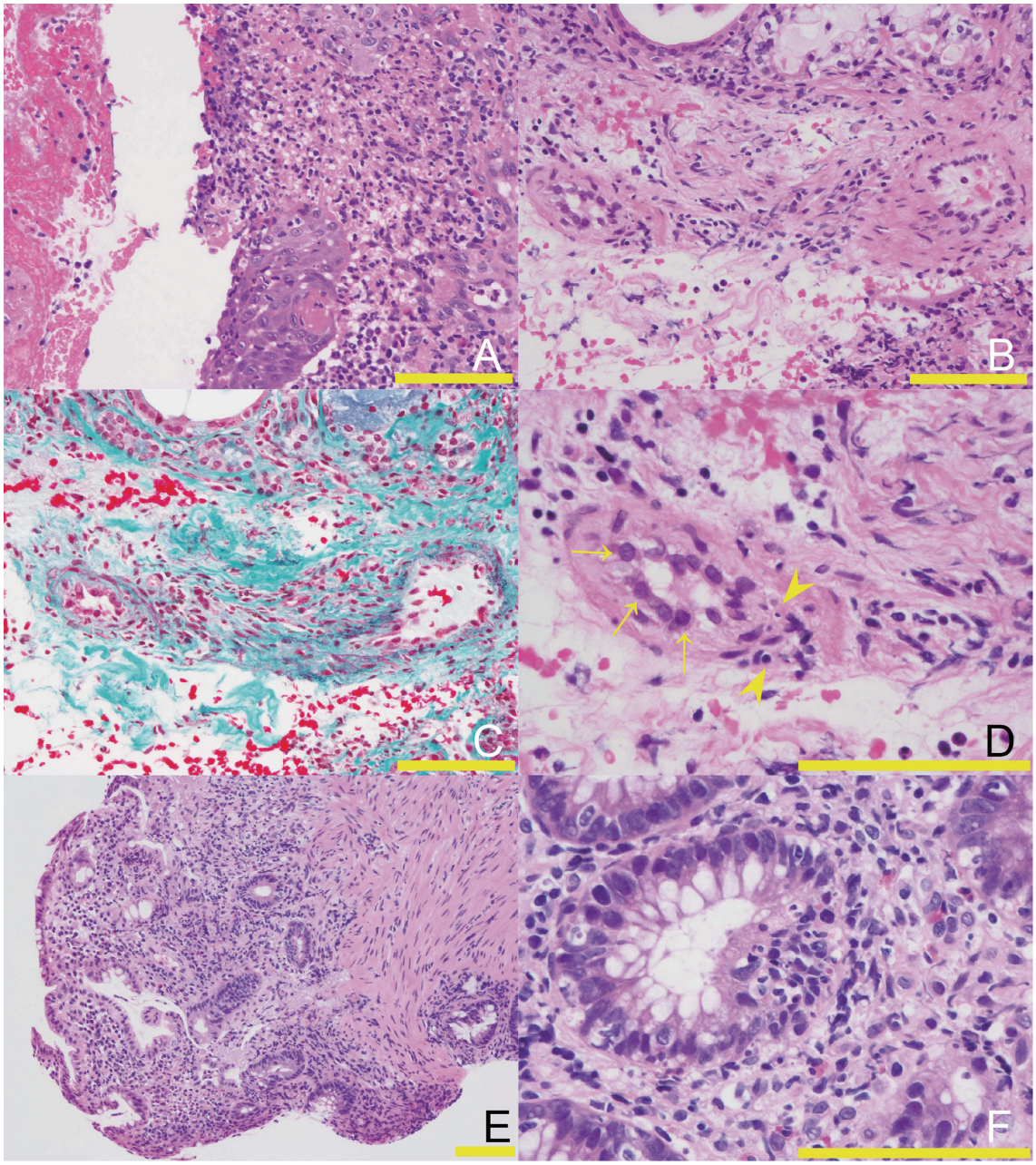

Fig. 4. Pathological findings of the nasal mucosa (A-D) and the colon (E, F).
(A) Severe ulcerative neutrophilic mucositis. (B-D) Endothelial cell swelling (arrows) and lymphocyte infiltration into the venous wall (arrowheads) suggested small-vessel vasculitis (phlebitis). (E) Moderate infiltration of inflammatory cells into the lamina propria and the decrease in crypts and goblet cells suggested chronic inflammation. (F) Cryptitis suggested severe acute inflammation.
(A, B) Hematoxylin and eosin staining (HE), × 200; (C) Elastica-Masson staining, × 200; (D, F) HE, × 400; (E) HE, × 100; scale bars = 100 μm.

UC than vasculitis. Representative extra-intestinal manifestations of UC include anemia, arthropathy, uveitis, hepatobiliary disease, and pyoderma gangrenosum (PG) (Magro et al. 2017). Recently, aseptic nasal septal abscess has also been reported as a rare manifestation of PG in patients with UC (Yilmaz et al. 2011; Chang 2018; Tomioka et al. 2018; Yu et al. 2020) (Table 1). Additionally, leukocytoclastic vasculitis (a form of small-vessel vasculitis) is one of the extra-intestinal manifestations of UC, and it has been reported that 41% of patients with UC complicated with leukocytoclastic vasculitis are positive for ANCA (Pantic et al. 2022). Therefore, patients with PR3-ANCA-positive UC are prone to develop small-vessel vasculitis.

The pathological analysis of the nasal mucosa showed ulcerative neutrophilic mucositis and phlebitis, and there are three possibilities regarding phlebitis in this case: 1) one of the extra-intestinal manifestations of UC; 2) partial manifestations of GPA; and 3) the secondary phenomenon to

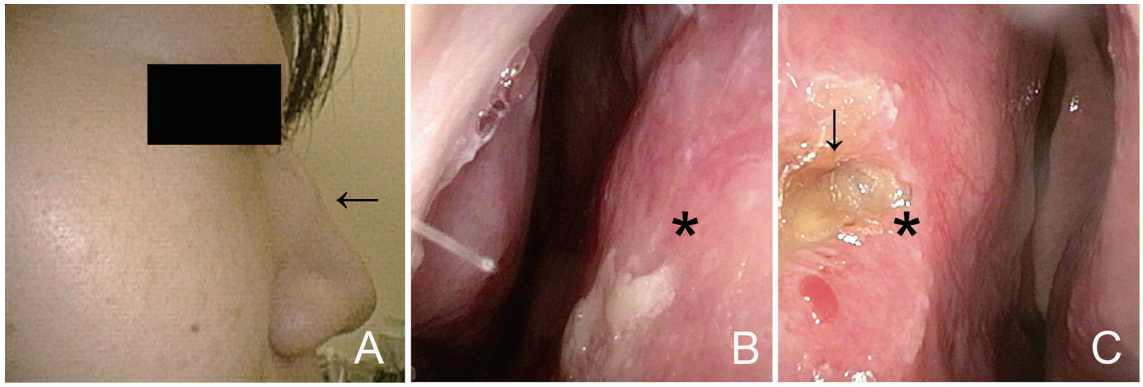

Fig. 5. Post-treatment photographs of the face and nasal cavity.
(A) The patient presented with a slight saddle nose (arrow). (B, C) Swelling of the bilateral nasal septum disappeared: B, right side; C, left side; asterisks, nasal septum; arrow, a scar of incision drainage.

Table 1. Review of nasal septal abscess or pyoderma gangrenosum in patients with systemic disease.

	Age, years	Sex	Vasculitis	Granuloma	ANCA	Diagnosis
Matsumura et al. 1999	65	Male	Negative	Negative	Negative	IgA MG
Isomura et al. 2005	28	Female	Negative	Negative	Negative	IgA MG
Chang 2018	52	Female	Negative	Negative	Negative	UC
Yilmaz et al. 2011	34	Female	NA	NA	NA	UC
Tomioka et al. 2018	33	Female	Negative	Negative	Negative	UC
Yu et al. 2020	28	Female	NA	NA	NA	UC
Present case	27	Female	Phlebitis	Negative	PR3-ANCA(+)	UC possibly with GPA

ANCA, antineutrophil cytoplasmic antibody; GPA, granulomatosis with polyangiitis; IgA MG, immunoglobulin A monoclonal gammopathy; NA, not available; PR3-ANCA, proteinase 3-antineutrophil cytoplasmic antibody; UC, ulcerative colitis.

suppurative inflammation. In this case, the nasal mucosa showed vasculitis without evident necrotizing granuloma, which does not correspond to the strict classical criteria for diagnosing GPA (Jennette et al. 2013). However, upper respiratory tract lesions of GPA often do not show typical pathological features (e.g., necrotizing granulation), posing a challenge to the diagnosis of GPA by pathology in the localized type (Harabuchi et al. 2013; Sattui and Lally 2020). Also, nasal PG in patients with UC and IgA monoclonal gammopathy has been reported (Matsumura et al. 1999; Isomura et al. 2005; Yilmaz et al. 2011; Chang 2018; Tomioka et al. 2018; Yu et al. 2020). However, unlike in this case, vasculitis or elevation of PR3-ANCA was not reported in any cases (Table 1).

The cosmetic complications of nasal septal abscesses can be severe; hence, prompt diagnosis and treatment are important (Ambrus et al. 1981; Tomioka et al. 2018). A previous study reviewed 10 cases of nasal PG and reported that immunosuppressive therapy (including glucocorticoids) was curative for all patients; nonetheless, all available cases presented with a saddle nose or septal perforation (Tomioka et al. 2018). Although early treatment does not invariably prevent the occurrence of nasal complications, an exacerbation of inflammation undoubtedly leads to complications. Thus, prompt diagnosis and treatment are essential.

In summary, we reported a case of an aseptic nasal septal abscess complicated with PR3-ANCA-positive UC, in which phlebitis was observed and co-existence of GPA was possible. For the prevention of nasal deformity due to persistent inflammation, prompt administration of immunosuppressive therapy should be considered with adequate evaluations for systemic diseases, including UC and GPA.

Conflict of Interest

The authors declare no conflict of interest.

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