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Strawberry Gingivitis: Rare Early Manifestation of Relapsing Granulomatosis with Polyangiitis

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A 38-year-old man was referred to a dentist with strawberry-like gingivitis (Figure 1a). A biopsy of the gingivitis revealed hyperplasia and inflammatory cell infiltration (Figure 1b). The patient had a 6-year history of granulomatosis with polyangiitis (GPA), previously referred to as Wegener's granulomatosis. Six years prior to the current admission, the patient had presented with fever, joint pain, epididymitis, mononeuritis multiplex, sinusitis, and erythema, and his blood tests had revealed a positive result for myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) (61 U/ml; reference range, 0-19) and elevated C-reactive protein (CRP) level (124.2 mg/l; reference range, 0-3.0). Thus, the patient had been diagnosed with ANCA-associated vasculitis, specifically GPA, due to the presence of epididymitis. The patient had been treated with prednisolone [(PSL); 80 mg/day], which led to the resolution of symptoms. However, when the PSL dosage was tapered to 18 mg/day, the patient experienced a recurrence of joint pain and erythema, with CRP levels fluctuating between 20 to 60 mg/l. Four years prior to the current admission, the PSL dosage was increased to 40 mg/day, and methotrexate (MTX) and intravenous cyclophosphamide (1000 mg/body monthly, for a total of 7 cycles) were initiated. Nevertheless, when the PSL dosage was reduced to 25 mg/day, the joint pain recurred and the CRP levels increased (10-40 mg/l). Consequently, intravenous cyclophosphamide was discontinued 3 years before the current admission, and infliximab (IFX) therapy was initiated because rituximab and azathioprine had not been approved for GPA in our country at that time. Because the patient's symptoms improved, the PSL dosage was tapered.

Before admission, the patient was being administered 9 mg/day of PSL, 7.5 mg/week of MTX, and 6 mg/kg of IFX every 4 weeks. He developed osteoporosis-related complications. Thus, he was prescribed minodronic acid hydrate (50 mg every 4 weeks) and alfacalcidol (5 µg/day). There were no other symptoms or laboratory findings indicative of GPA recurrence. After experiencing 7 months of gingivitis, he was admitted to our hospital for a 10-day history of fever and dry cough.

Laboratory findings at the time of admission revealed elevated levels of PR3-ANCA (51.3 U/ml; reference range, 0-3.4) and CRP (101.7 mg/l; reference range, 0.1-1.4) and a creatinine level of 0.65 mg/dl (reference range, 0.6-1.1). Proteinuria and hematuria were within the normal limits. The chest computed tomography (CT) revealed multiple lung nodules that were rapidly increasing in size (Figure 1c). Furthermore, the patient developed respiratory failure that required oxygen supplementation. The head CT revealed fluid in the ethmoid, maxillary, and sphenoid sinuses. The patient was diagnosed with recurrent GPA and was treated with a combination of methylprednisolone pulse therapy and rituximab. The lung and sinus lesions and the swollen gingiva gradually improved (Figure 1d, e). Written informed consent was obtained from the patient.

Strawberry gingivitis is a relatively rare manifestation that is characterized by a swollen and red gingiva. It is reportedly observed in only 2% of patients with GPA.[1] The typical pathological findings associated with strawberry gingivitis in GPA are pseudoepitheliomatous hyperplasia, microabscesses, and multinucleated giant cells. Necrotizing vasculitis of small vessels and granulomas are infrequently observed in GPA-related strawberry gingivitis.[2] The presence of strawberry gingivitis does not necessarily lead to a definitive diagnosis. This is because the etiology of strawberry gingivitis is diverse, encompassing infections (e.g., bacterial, fungal, and tuberculosis), medications (e.g., MTX, tumor necrosis factor-alpha inhibitors, phenytoin, cyclosporine A, calcium channel blockers, and oral contraceptives), leukemic and malignant tumor infiltration, sarcoidosis, and Crohn's disease.[3-6] Our differential diagnoses for the oral and lung lesions were primarily

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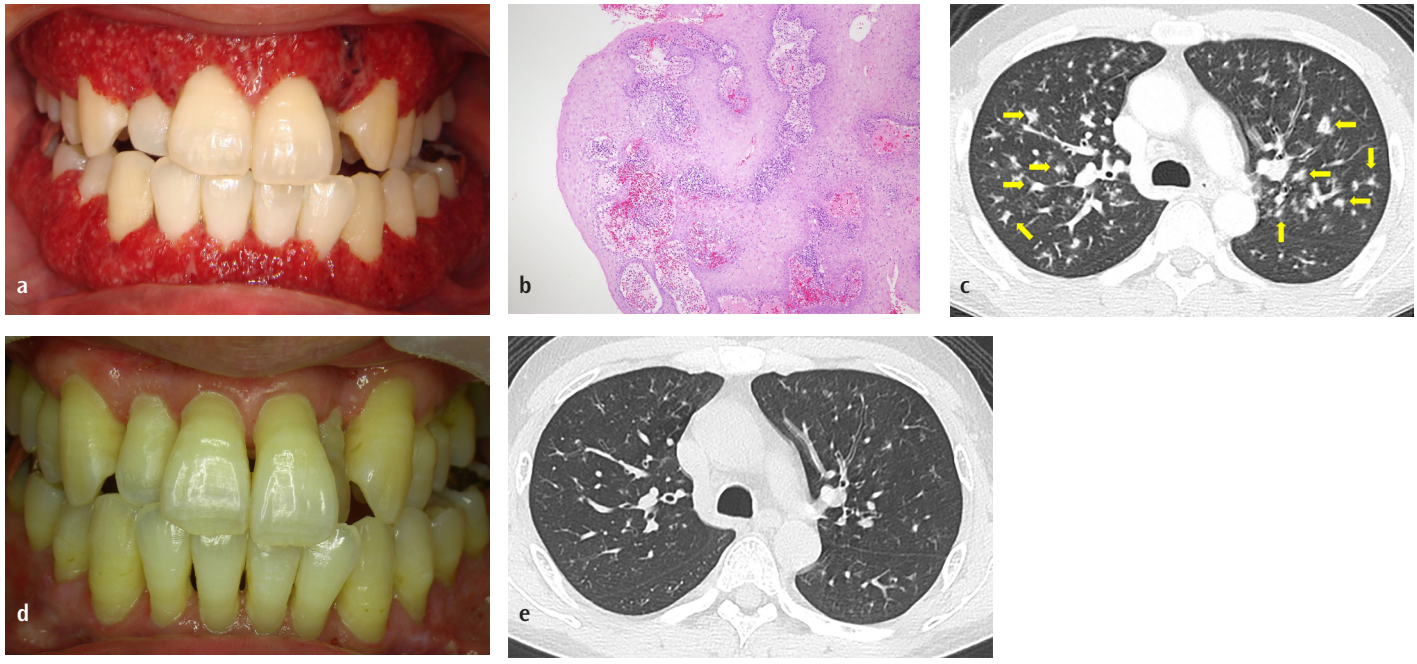

FIG. 1. (a) Gingiva is swelling and red broadly before treatment. (b) The hematoxylin and eosin stained pathology of gingivitis with hypertrophy and interstitial neutrophilic infiltration (40-fold magnification). (c) Lung nodules are observed bilaterally in the lungs (arrows). The image shows motion artifacts caused by the patient's inability to hold their breath due to tachypnea. (d) Swollen red gingiva has disappeared, and roots of teeth are uncovered due to gingiva atrophy after treatment. (e) The lung nodules resolve.

infectious diseases, which were subsequently excluded due to the absence of microorganisms in the bronchial lavage fluid and the lack of response to antibiotics. Furthermore, gingivitis did not recur after MTX and IFX were reinitiated after the induction therapy. No findings indicative of sarcoidosis, such as uveitis, bilateral hilar lymphadenopathy, or elevated angiotensin-converting enzyme levels, were observed.

Although gingivitis itself is not life-threatening, GPA is a systemic disease with a mortality rate of up to 80% without treatment.[7,8] Therefore, if strawberry gingivitis is observed, it is essential to conduct both local and systemic assessments.

Informed Consent: Written informed consent was obtained from the patient.

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