Strawberry Gingivitis: An Isolated Manifestation of Wegener's Granulomatosis?

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Sir,

Wegener's granulomatosis (WG) is a form of systemic necrotizing vasculitis of small and medium vessels leading to granuloma formation. It belongs to the spectrum of syndromes with anti-neutrophil cytoplasmic antibodies (ANCA) production (1, 2). The disease can be rapidly progressive or mild and indolent (3). WG is often difficult to diagnose when involvement is limited and the recognition of a distinctive sign would help in early diagnosis. In these cases laboratory abnormalities such as elevated erythrocyte sedimentation rate (ESR), elevated white blood cell count, normocytic normochromic anaemia and thrombocytosis may support the establishment of a diagnosis (3–5). Intra-oral manifestations have been well described in WG; however, they are not the usual presenting sign (2–6). Gingival lesions as a manifestation of WG are extremely rare, but when present they are clinically and histopathologically very suggestive of the disease (6). In such situations a good collaboration between clinicians and pathologists may speed up the diagnosis with impact on early treatment and prognosis (3–6). The present report describes a patient with strawberry gingivitis without any systemic signs and symptoms of WG. The case is very suggestive of early manifestation of WG.

CASE REPORT

A 45-year-old Caucasian woman presented with an 8-month history of gingival lesions. The patient reported no improvement of the condition regardless of previous periodontal treatment. Intra-oral examination showed an exophytic mass with ill-defined margins, presenting a granular and haemorrhagic surface on the mandibular gingiva, accompanied by teeth mobility (Fig. 1A).

There was no evidence of cervical or submandibular lymphadenopathy; the patient was in apparently good health and without other symptoms. At the physical examination no lesions were clinically detected on the skin or in the upper respiratory tract.

Periapical and panoramic X-rays revealed diffuse bone destruction with ill-defined margins of the left mandibular molars (Fig. 1B, arrow). X-rays and computed tomography of the nasal cavity and facial sinuses showed no alterations. Haematological and serological tests were conducted, including complete blood cell counts, anti-nuclear antibodies, ANCA, renal function, ESR; all were negative or within normal range. Chest X-ray and urinanalysis showed no abnormalities.

An incisional biopsy from the lesion was obtained. Histological examination of the specimen revealed gingival mucosa with an epithelium showing marked inflammatory pseudoepitheliomatous hyperplasia, focal epithelial degeneration and presence of micro-abscesses filled with haemorrhagic exudate, neutrophils and eosinophils (Fig. 1C–E). In the lamina propria an intense inflammatory infiltrate was detected, consisting of histiocytic component admixed with plasmocytes, neutrophils and numerous eosinophils. Multinucleate giant cells were found (Fig. 1E, arrow). There was no evidence of granuloma formation. Focal necrosis, haemorrhage and vascular dilation were observed, with many capillaries displaying endothelial swelling, although vascular wall necrosis and inflammation were lacking. Special stains revealed no fungi or acid-fast bacilli.

Clinico-pathological correlations led us to the most likely diagnosis of WG. The patient was treated with oral prednisone (60 mg/day) and cyclophosphamide (100 mg/day) and after 2 months the lesions had cleared completely. At 1-year follow-up the patient remains free of disease and medication has been gradually tapered.

DISCUSSION

WG was first described in 1936 by Friedrich Wegener, and consists of the triad of systemic necrotizing vasculitis, granulomatous inflammation of the respiratory tract and renal glomerular disease. The aetiology is unknown (7, 8). Serological tests can be of help in the establishment of a diagnosis, especially the identification of high titres of c-ANCA. Cytoplasmic pattern of ANCA (c-ANCA) is 80–100% specific for WG; these antibodies are thought to be of pathogenic relevance, however, c-ANCA may be negative in up to 33%

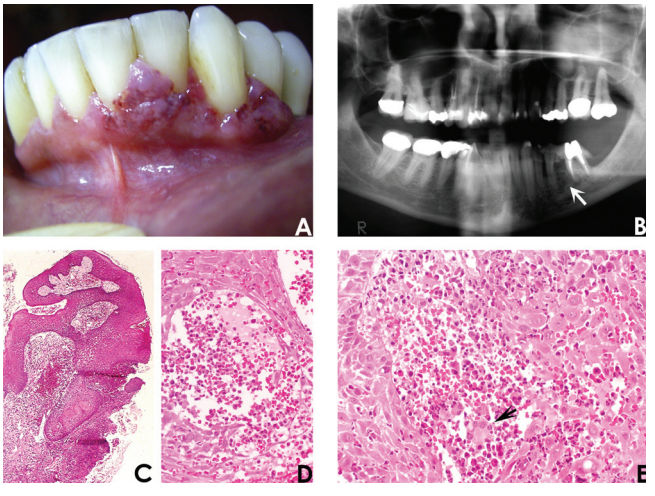

Fig. 1. (A) Clinical presentation of strawberry gingivitis. (B) Panoramic X-ray revealing diffuse bone destruction with imprecise limits on the left mandibular molars (arrow). (C) Histological findings showing pseudoepitheliomatous hyperplasia and a mixed inflammatory infiltrate with abundant neutrophils and eosinophils (H&E ×25). (D) Micro-abscesses within the pseudoepitheliomatous hyperplastic epithelium (H&E ×250). (E) Inflammatory infiltrate featuring multinucleate giant cells (arrow) (H&E ×250).

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of patients, particularly in those cases without renal disease (3–5, 8).

Mucocutaneous findings are present in up to 66% of cases and include purpura, necrosis, ulcers, papules, nodules, petechiae, superficial erosion, bullae, erythema and oral lesions (1, 5, 8). Oral manifestations have been reviewed previously (9) and include palatal and lingual ulcerations, aphthae and non-healing extraction sockets. Gingival lesions, known as 'strawberry gingivitis' because of their granular and haemorrhagic aspect, are very rare with only a few cases reported (6, 8–13). This specific gingivitis is typically accompanied by alveolar bone rarefaction and tooth mobility (9, 10). In the absence of additional findings they are very suggestive of early disease that precedes visceral lesions (10).

The present case was diagnosed as WG by the positive correlation of the following key features: (*i*) vegetating haemorrhagic gingival lesions that resembled over-ripe strawberries, accompanied by alveolar bone rarefaction; (*ii*) histopathological appearance in the gingival biopsy specimen. In these very early stages c-ANCA titre may prove non-contributory for the diagnosis as it was in our case (3).

Histological features of WG are distinct from those seen in non-specific gingivitis or periodontitis but also differ from WG in other organs due to the lack of unequivocal necrotizing vasculitis. This is probably related to the absence of large enough vessels in gingival tissues (13). Therefore, histopathological criteria for this specific lesion are the combination of pseudoepitheliomatous hyperplasia, epithelial micro-abscesses, intense mixed inflammatory infiltrate, with striking presence of neutrophils, eosinophils and multinucleate giant cells and focal necrosis in the absence of a demonstrable pathogen.

Although regarded as non-specific, the pseudoepitheliomatous hyperplasia, the intense infiltrate of neutrophils and eosinophils with the formation of micro-abscesses and the presence of multinucleate giant cells are seen in few other conditions affecting the gingiva. Routine histochemical stains excluded fungal infections such as histoplasmosis and paracoccidioidomycosis. Conditions such as Crohn's disease and sarcoidosis were ruled out by the presence of polymorph infiltration, micro-abscesses and the formation of pseudoepitheliomatous hyperplasia (14). Eosinophilic granuloma (Langerhans' cell histiocytosis) may produce red swollen, painful gingiva with a dense infiltrate of Langerhans' cells, which was lacking in our case (15). The degree of epithelial proliferation may suggest a squamous cell carcinoma; however, the overall pattern is more that of a reactive rather than a neoplastic process as atypical epithelial cells were not present.

Most authors acknowledge that the clinicopathological complex of strawberry gingivitis accompanied by histopathological features of pseudoepitheliomatous hyperplasia, micro-abscesses and multinucleate giant cells is highly suggestive of WG, as the classic criteria of vasculitis, granulomas and necrosis are rarely found in gingival biopsy specimens (3, 5, 6, 8, 9), which is in agreement with our experience.

This characteristic gingival lesion might be the earliest manifestation of WG, and early diagnosis accompanied by aggressive treatment is important for a better outcome in this potentially lethal disease (8). Therapy consists of variable schemes of cyclosphamide and prednisone in combination and long-term follow-up (1). In the case presented herein, the patient is well and free of any gingival and oral lesions or systemic manifestations after a 1-year course of therapy with the above-mentioned treatment scheme.

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