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Necrotising gingivitis as a manifestation of Richter syndrome



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Background: Richter syndrome describes the development of high-grade, non-Hodgkin lymphoma (NHL) through transformation from chronic lymphoid leukaemia. This report describes the case of a 77-year-old patient with a history of chronic lymphoid leukaemia, who presented initially with a gingival condition that was characteristic of necrotising gingivitis.

Methods: Histological staining with haematoxylin and eosin of a gingival biopsy of the intra-oral lesion revealed diffuse sheets of malignant cells, which were confirmed as being lymphoid cells of B cell lineage using immunostain with CD20 marker. The Ki67 proliferation fraction was about 50%, which supported a diagnosis of a high-grade lymphoma, and the overall features confirmed a diagnosis of a diffuse, large B-cell lymphoma.

Results: Periodontal treatment was largely ineffective but the introduction of a CHOP-R chemotherapy regime resulted in dramatic and instantaneous resolution of the oral ulceration and associated symptoms.

Conclusions: The report demonstrates that the clinical signs of gingival ulceration and necrosis can, albeit rarely, represent a manifestation of an underlying, insidious general pathology which in this instance, transformed into a diffuse, large B-cell lymphoma.

■ Introduction

Richter syndrome (RS), also known as Richter transformation (RT), describes the development of high-grade, non-Hodgkin lymphoma (NHL) in patients with chronic lymphoid leukaemia (CLL). The syndrome was first described in 1928 in a patient with rapidly fatal, generalised lymphadenopathy and hepatosplenomegaly associated with CLL¹.

The reported incidence of transformation to RS in patients with CLL ranges from 2.2% to 8%². The molecular mechanism involved in the transformation of CLL to RS is poorly understood. The large cell lymphoma clone occurs either by transformation of the original CLL clone or as a separate and independent neoplasm, as shown by characterisation of immunoglobulin heavy-chain gene rearrangements and light-chain isotype analyses³. Triggers such as viral



Fig 1a Initial presentation showing a necrotising gingivitis localised to the remaining lower anterior dentition.



Fig 1b Appearance approximately 3 months following hygiene phase therapy, scaling and prophylaxis. Note the extension of the ulceration and necrosis apically and laterally.

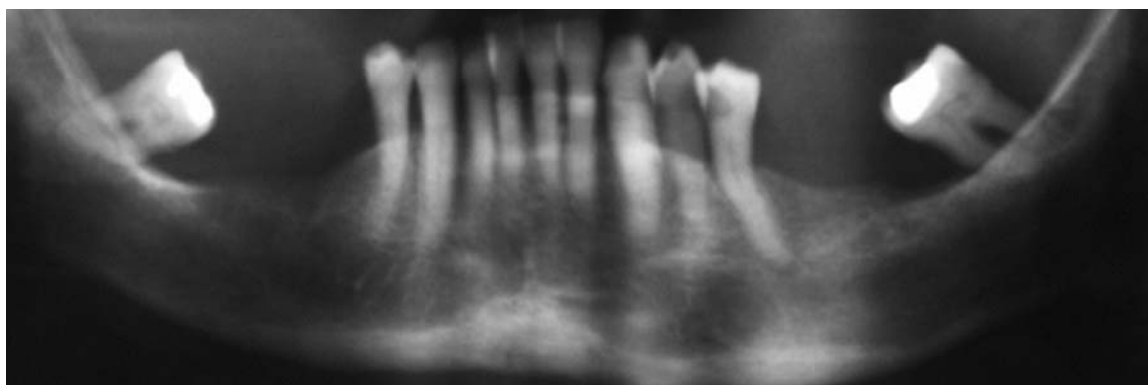


Fig 2 Panoramic radiograph shows a condition consistent with chronic periodontitis.

infections with Epstein Barr virus (EBV), which are common in immunosuppressed patients, have been described.

Karyotypic changes, including trisomy 12, chromosome 11 abnormalities, and multiple cell cycle regulator disruptions, have also been found in patients with RS. Although these genetic defects are believed to cause CLL cells to proliferate and, by facilitating the acquisition of new genetic abnormalities, transform into RS cells, none appears predominantly responsible for the transformation.

RS is characterised by the development of systemic symptoms such as fever, weight loss, and drenching night sweats, sudden clinical deterioration, and, usually, a rapid increase in the size of a lymphoid mass at one site. Patients may have abdominal symptoms due to increasing splenomegaly and/or hepatomegaly, or symptoms related to other sites of disease involvement. The lymphomatous clone in RS frequently arises in lymph nodes or bone marrow and disseminates to other

organs. Rarely, RS may present with extranodal involvement⁴. Extranodal sites of involvement include the gastrointestinal (GI) tract, central nervous system, skin, eye, testis, and lung or kidney. Most patients with extranodal RS in the GI tract represent a true secondary neoplasm, but less frequently a clonal relationship between CLL and GI RS has been shown by clonality studies⁵.

■ Case Report

■ Presentation and history

A 77-year-old female patient was referred initially to the Department of Periodontology at Newcastle Dental Hospital by her general dental practitioner with symptoms of painful, ulcerated gingiva and a provisional diagnosis of necrotising gingivitis. The patient was a vague historian but mentioned a history of recent weight loss that had been attributed

to the painful gingiva. She also reported a non-specific, abdominal pain and more detailed questioning revealed a 15-year history of chronic lymphoid leukaemia which was subsequently confirmed following consultation with her haematologist. Indeed, the weight loss and abdominal symptoms had been investigated with an abdominal ultrasound scan and upper and lower GI endoscopies, which had all been normal other than to confirm the presence of mild splenomegaly that was attributed to the long history of CLL.

Intra-oral clinical examination revealed an upper complete denture and 11 remaining lower teeth: 48, 44, 43, 42, 41, 31, 32, 33, 34, 35 and 38. The labial gingiva associated with the anterior teeth showed marginal ulceration and necrosis that was characteristic of necrotising gingivitis (Fig 1a). There was no palpable lymphadenopathy. A sectional panoramic radiograph revealed a horizontal pattern of bone loss affecting approximately 50% of the root lengths, and consistent with chronic periodontitis (Fig 2). A haematological and nutritional screen (full blood count, haematinics, electrolytes, liver enzymes, c-reactive protein and auto antibodies) revealed only mild lymphocytosis that was attributed to the long-standing CLL.

Management

The patient was initially referred to a dental hygienist for hygiene phase therapy, scaling and root surface instrumentation of the lower teeth and the oral symptoms and the extent and severity of the ulceration improved in the short term. The patient returned after 3 months, however, complaining of 'severe pain from her gums', and clinical examination revealed a far more extensive distribution of the gingival ulceration than had previously been observed (Fig 1b). The ulceration failed to respond to a course of metronidazole. Palliative treatment included the application of topical lignocaine (lollipops) and use of 0.2% chlorhexidine mouthwash.

Microbiological swabs of the necrotic ulcers were taken for culture and sensitivity, although these revealed only the presence of non-specific, anaerobic bacteria. A biopsy of one of the sites of gingival ulceration was performed to exclude malignancy. Histological staining with haematoxylin and eosin revealed diffuse sheets of malignant cells (Fig 3a),

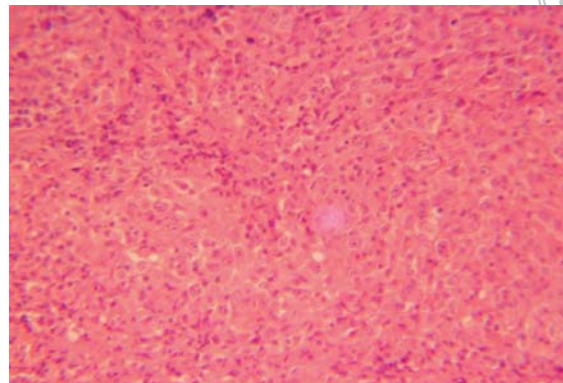


Fig 3a Low magnification of biopsy specimen stained with haematoxylin and eosin shows diffuse sheets of malignant cells.

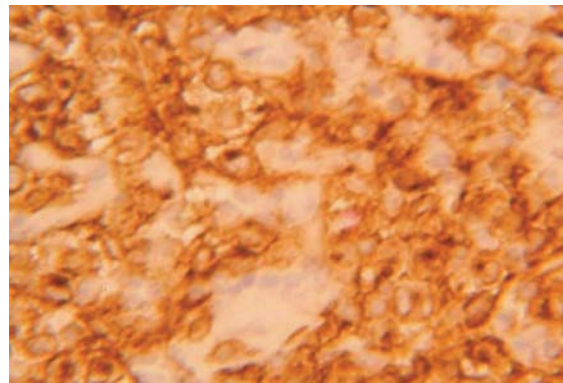


Fig 3b Immunostain with CD20 marker shows lymphoid cells of B cell lineage.

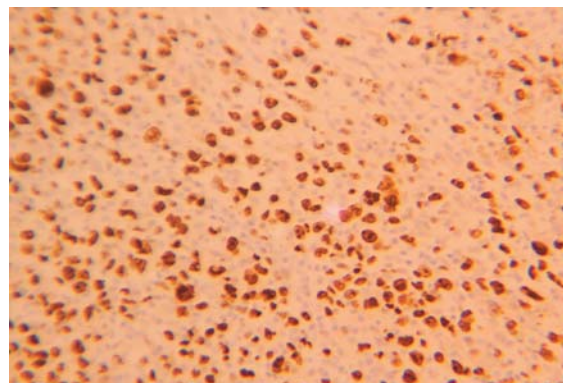


Fig 3c Ki67 proliferation fraction is approximately 50%.

which were confirmed as being lymphoid cells of B cell lineage using immunostain with CD20 marker (Fig 3b). The Ki67 proliferation fraction was approximately 50% (Fig 3c), which supported a diagnosis of a high-grade lymphoma and the overall features confirmed a diagnosis of a diffuse large B-cell lymphoma.

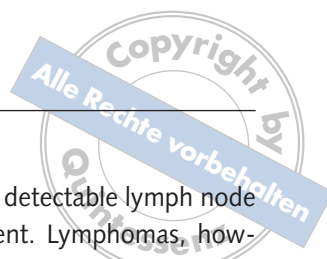


Fig 4 Resolution of ulceration and necrosis following CHOP-R chemotherapy and with no further periodontal management.

The diagnosis was discussed with the patient's consultant haematologist who undertook further prognostic investigations, including staging of the lymphoma, serum $\beta 2$ microglobulin and LDH. Serum uric acid was checked as high cell turnover may lead to deposition of uric acid crystals in the urinary tract, causing renal dysfunction, and in joints, causing gout. These parameters were normal. Bone marrow aspirate confirmed CLL but no other abnormal cells and staging CT chest and abdominal scans confirmed splenomegaly.

Following a lymphoma multidisciplinary team meeting, treatment with three cycles of CHOP-R chemotherapy (cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone, rituximab) was started. The patient made a rapid and remarkable recovery with immediate improvement of appetite and spontaneous resolution of the necrotising gingivitis, but with development of some gingival recession (Fig 4). To date, 14 months after initial oral presentation and 8 months after cessation of chemotherapy, the patient has not presented with recurrence of the oral lesions and remains under long-term management via the lymphoma multidisciplinary team and her General Dental Practitioner.

■ Discussion

Richter syndrome, the transformation of CLL into diffuse large B-cell lymphoma, is a rare condition and we have not been able to find a previously reported case involving the oral cavity. The majority of signs and symptoms of RS were present in this

case although there was no detectable lymph node or bone marrow involvement. Lymphomas, however, have a high predilection for the oral cavity, account for 2–5% of oral malignancies and predominantly affect the Waldeyer ring of tonsillar tissue, the gingiva, alveolus and palate. A prolonged immunodeficient state and extensive use of chemotherapeutic agents may also give rise to opportunistic lesions⁶.

In this case, the presenting signs were those of an ulcerative and necrotising gingivitis; a condition that is associated with a number of systemic and general conditions such as HIV infection, malnutrition and immunodeficiency states. Although the short-term response to periodontal management was promising, the condition proved to be refractory in the longer term and the clinical signs became more extensive and the symptoms more severe. When the diagnosis was confirmed through biopsy, the CHOP-R chemotherapy regime achieved an immediate response, suggesting remission and a favourable longer term prognosis, which is often the case with early treatment of stage 1 lymphoma⁷. The periodontal management regime was almost entirely palliative and perhaps helped to minimise the likelihood of a secondary infection.

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