

Oral Medicine Case Book 56:

Oral manifestations of aplastic anaemia

SADJ February 2014, Vol 69 no 1 p26 - p27

S Padayachee¹, H Holmes², WP Dreyer³

CASE REPORT

A 22-year old female patient was referred to the Oral Medicine Clinic from the Haematology Ward at Groote Schuur Hospital for evaluation of a painful oral ulcer, which had been present for three weeks. The patient reported that, six weeks ago, she had sought treatment from her own dentist for painful and bleeding gingivae. The dentist performed a scale and polish and prescribed a combination of amoxicillin and metronidazole, at normal adult doses, for seven days. The gingival bleeding had not resolved by the time she presented for her recall visit, two weeks later. The patient also reported the presence of "small, purple spots" on her lower limbs and trunk.

On the basis of the poor response to treatment and the presence of petechial haemorrhage, the attending dentist referred her to the Haematology Department at Groote Schuur Hospital for further investigation and management.

On arrival at the Oral Medicine Clinic, the patient presented her laboratory results which revealed pancytopenia with very low values for red blood cells (anaemia), white blood cells (leukopenia) and platelets (thrombocytopenia). The referral note from Haematology stated that a diagnosis had been reached of aplastic anaemia of unknown etiology. Intra-oral examination revealed the presence of a crateriform ulcer on the right palatal fauces, measuring approximately 2cm in diameter. The margins were erythematous with a pale yellow centre (Figure 1). Marginal gingivitis was present around several teeth and in addition, tooth 36 showed the presence of punched-out gingival papillae on the lingual side. Plaque and calculus deposits were present on the lingual surfaces of the anterior mandibular teeth.

Consultation with the referring haematologist revealed that management of the patient's aplastic anemia would entail either a transplant (bone marrow and blood) or, should no donor be available, anti-thymocyte globulin treatment. At the

time of the initial consultation, the required medication was still awaited and the patient was being managed by regular platelet administration.

A scaling and polishing was performed on the same day the patient received platelets. A doxycycline mouth-rinse was prescribed, to be used twice daily, for one week. The patient presented for a follow-up visit two weeks later and by this time, the original gingival inflammation and ulceration had completely resolved (Figure 2). However, a new painful ulcer, of approximately 0.2cm in diameter, had developed on the right margin of the tongue, close to the tip. The ulcer had a red border with a whitish-yellow base (Figure 3). It was decided that the lesion be monitored and further consultation with the attending haematologist sought, should the lesion persist and a biopsy be required. In the interim, the patient was requested to maintain good plaque control and to use a 0.2% chlorhexidine gluconate mouth rinse, twice daily and to return should further oral problems arise.

DISCUSSION

Aplastic anaemia is a relatively uncommon condition occurring mostly in the teens and twenties, but also among the elderly. It was first described by Elrich in 1888¹ and is a condition in which multi-potential myeloid stem cells are suppressed, leading to hypo-cellularity of the bone marrow and resulting in a pancytopenia, with a deficiency of erythrocytes, granulocytes and platelets.² A pancytopenia is diagnosed when two of three criteria are met: a neutrophil count of less than 0.5×10^9 cells/L, a platelet count less than 20×10^9 cells/L and a reticulocyte count less than 1%. When the neutrophil count is less than 0.2×10^9 , the disease is then characterised as severe.²

Aplastic anaemia is classified as acquired or congenital. The congenital type is rare and usually associated with Fanconi's anaemia and dyskeratosis congenita.³ In more than 50% of the acquired cases of aplastic anaemia, the cause is unknown. In some cases, exposure to myelotoxic agents, such as drugs or chemicals, or a viral infection such as Hepatitis C virus and infectious mononucleosis, are implicated.^{2,4} Although aplastic anaemia has traditionally been associated with exposure to various drugs and chemicals, the risk is relatively minor, considering the large number of people using such drugs. Drugs that have been implicated are various non-steroidal anti-inflammatory drugs, antibiotics (especially sulphonamides), anti-thyroid drugs, cardiovascular drugs,

1. **S Padayachee:** MChD, BChD. Division of Oral Medicine and Periodontics, Faculty of Dentistry, University of the Western Cape.
2. **H Holmes:** MChD, BChD. Division of Oral Medicine and Periodontics, Faculty of Dentistry, University of the Western Cape.
3. **WP Dreyer:** BDS, HDipDent, PhD, Division of Oral Medicine and Periodontics, Faculty of Dentistry, University of the Western Cape; Professor Emeritus, Stellenbosch University.

Corresponding author

WP Dreyer:

PO Box 1285, Sedgefield 6573, e-mail: wpd@sun.ac.za



Figure 1: The patient presented with a painful chronic ulcer on the right palatal fauces and with gingivitis around the right lower molar teeth.



Figure 2: At the time of the follow up visit, two weeks later, the ulcer and gingivitis had fully resolved.



Figure 3: At follow up visit a new painful ulcer of 0.2cm in size was present on the right margin of the tongue, close to the tip.

corticosteroids, penicillamine and allopurinol. The majority of cases of aplastic anaemia, however, are considered to have an immune pathophysiology. T-lymphocytes are thought to be responsible for the haemotopoetic cell destruction and although external exposures, (viruses, drugs, toxins), may trigger the aberrant immune response in some cases, the nature of the antigen responsible for driving this T-lymphocytic response remains uncertain in the majority of patients.^{5,6}

Definitive diagnosis of aplastic anaemia requires bone marrow aspirate smears, or core biopsy specimens. This shows a strikingly fatty bone marrow, indicating aplasia, however, this hypo-cellularity may also be found in other haematological diseases, such as clonal diseases (including myelodysplasia) and single haematopoietic lineage deficiency diseases (agranulocytosis, pure red cell aplasia, amegakaryocytic thrombocytopenia).⁵ The clinical features of aplastic anaemia are associated with the pancytopenia. Anaemia results in weakness, fatigue and pallor. Thrombocytopenia results in gingival bleeding, epistaxis, menorrhagia and purpura and the neutropenia results in increased susceptibility to infection and sepsis.^{1,7} Sepsis and haemorrhage are implicated as the main cause of death in such patients.⁷

Oral manifestations are common in patients with aplastic anaemia and are directly associated with the pancytopenia. These manifestations include petechial haemorrhages, gingival swelling and spontaneous bleeding, ulceration, pallor and severe periodontal disease.^{3,4} Cases of advanced or rapidly progressive periodontitis have been reported to occur with prolonged neutropenia and may be due to several qualitative and quantitative neutrophil defects, including neutropenia, agranulocytosis and leukocyte adhesion deficiency.³ In addition, the thrombocytopenia can induce compromised clotting, so surgical intervention should be delayed until the patient is controlled with platelet administration.³ Brennan⁴ describes the risk factors associated with oral manifestations of aplastic anaemia and suggests that the level of thrombocytopenia is not necessarily indicative of the degree of petechial haemorrhaging. These lesions most likely result from the thrombocytopenia-induced clotting disorder, which causes excessive bleeding even after minor trauma associated with normal oral functioning.

Treatment of aplastic anaemia is directed at suppression of the immune system, or in more severe cases, a bone marrow transplant. The bone marrow transplant aims to replace the bone marrow cells with new multi-potential stem cells from a matching donor. This may effect a cure

in 70% of cases and even higher in younger patients with a matching sibling donor. Graft rejection and graft-versus-host disease remain serious risks, but can be contained by careful patient management.^{2,5} The immune-modulating treatment is based on a short course of anti-thymocyte globulin or anti-lymphocyte globulin and several months on cyclosporin to modulate the patient's immune response.² Cyclosporine, however, may enhance the gingival swelling and bleeding and thus may be of special concern to the oral health care practitioner.⁴ Chemotherapy with agents such as cyclophosphamide and vincristine may also be effective, but these agents can enhance the neutropenia, so severe infections remain a serious risk.⁵ The prognosis of the immune-modulating treatment is relatively high, with 5-year survival rates of up to 75%.⁶

CONCLUSIONS

The present case is a stark reminder that oral health care practitioners should always be on the alert for cases of aplastic anaemia. Any signs of excessive bleeding, or a poor response to the standard treatment of infections and oral ulcerations, should be investigated to rule out a possible presence of pancytopenia. The initial attending dentist in the present case, was astute in recognising the lack of response in the patient and to associate this with the presence of petechial haemorrhage. His early referral of the patient for specialised care will undoubtedly be of considerable value to the patient in the management of this potentially fatal disease.

Declaration: No conflict of interest declared.

References and recommended reading*

1. *Valdez IH, Patton LL. Aplastic anemia: current concepts and dental management. *Spec Care Dentist*, 1990; 10:185-9.
2. Young NS. Acquired aplastic anemia. *Ann Intern Med*, 2002;136: 534-46.
3. Oyaizu K, Mineshima F, Mineshima J, *et al.* Periodontal treatment in severe aplastic anemia. *J Periodont*, 2005; 76:1211-6.
4. Brennan MT, Sankar V, Baccaglioni L, *et al.* Oral manifestations in patients with aplastic anemia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 2001; 92:503-8.
5. *Young NS Current concepts in the pathophysiology and treatment of aplastic anemia. *ASH Educ Book*, 2013, doi 10.1182/asheducation-2013.1.76.
6. Brodsky RA, Jones RJ. Aplastic anaemia. *Lancet*, 2005; 365:1647-56.
7. Sepúlveda E, Brethauer U, Rojas J, Le Fort P. Oral manifestations of aplastic anemia in children. *J Am Dent Assoc*, 2006;137:474-8.