

Chronic graft Vs host disease and dental caries: a pattern of unusual presentation.

Rebecca Iles
StR in Special Care Dentistry

Introduction

Graft Vs host disease (GvHD) is a severe complication following allogeneic haematopoietic stem cell transplantation (HSCT). Chronic GvHD describes a diverse syndrome which mimics forms of autoimmune disease and develops at least 100 days following a HSCT. It affects between 50-70% of patients who have an allogeneic HSCT and may arise as an extension of acute GvHD or *de novo*. Chronic GvHD presents with a multitude of clinical features affecting numerous body systems, including the oral cavity. Ocular, gastrointestinal, pulmonary, skin and neuromuscular manifestations not only negatively impact on quality of life, but significantly increase mortality rate.

The soft tissue oral presentations of GvHD are well reported within the literature; the most prevalent being white reticulated lesions resembling erosive lichen planus which have an increased risk of malignancy transformation, xerostomia, dysgeusia, mucositis, increased susceptibility to oral infections and periodontal disease. Furthermore the treatment for GvHD can also have oral implications, for example methotrexate associated oral ulceration and ciclosporin induced gingival hyperplasia. To date there are few reports of dental caries developing as a complication of allogeneic HSCT and chronic GvHD.

This case describes the unusual pattern of caries progression in a patient with chronic GvHD who was referred to the Sedation & Special Care department at Guys Hospital, London, by her GDP. The patient was also under the care of the Oral Medicine department at Guys, where she had been referred by her dermatology team for management of the oral GvHD manifestations, which are shown in Figure 1.



Figure 1: Initial clinical photographs taken on referral to Oral Medicine department, prior to treatment with cocaine mouthwash, flixonase & nystatin mouthwash, and commencement of ECP treatment

Case Report

Presenting complaint

- Sore tongue –Oral Medicine department at Guys managing oral GvHD lesions
- Has been told by dentist that a number of teeth have cavities. Teeth not currently causing any pain

Medical History

- Chronic GvHD following allogeneic HSCT to treat Acute Myeloid Leukaemia (AML)
- Undergoing extracorporeal photopheresis (ECP) treatment for the management of her GvHD symptoms- 8 weekly cycle
- Failed previous chemotherapy to treat AML
- Pericarditis
- Osteopenia
- Previous TIA (1 year ago)
- Hiatus hernia
- Current medications: **alendronic acid** (4 year use history), **Ruxolitinib**, penicillin V, Cotrimoxazole, Aciclovir, Lansoprazole, **Clopidogrel**
- Previous immunosuppressive medications: prednisolone, azathioprine, ciclosporin

Social History

- 65 year old female
- Retired GP
- Non smoker
- Lives with husband (also a retired doctor)
- Diet: previous PEG fed, cannot eat spicy foods due to oral soreness, not on nutritional supplement drinks, low sugar intake

Dental History

- Regular attender with GDP. Has regular dental hygiene appointments
- Brushes BD with Duraphat 5000 toothpaste
- Uses interdental brushes daily

Examination & Clinical Photographs

Extra oral examination- GvHD skin signs, mild keratosis of lips

Airway assessment:
L Nil of concern
E 3-3-2
M Mallampati I
O No obstructions
N Good neck mobility and extension- full range of movements

Vital Signs:
SpO₂ 96%
BP 119/66 mmHg
PR 85bpm

Intra oral examination-

- Soft tissues:
- Plaque induced marginal gingivitis palatal of upper anterior teeth and right molars
 - Challacombe scale of clinical oral dryness- 8
 - Erythema tip of tongue
 - No current intraoral GvHD related ulceration
 - BPE 222/222

Hard tissues:

- Cervical cavities in multiple teeth: LR7^B LR6^L LR3^B LR4^B UR6^B UL3^B UL4^B LL7^B
- Moderately restored dentition, multiple anterior and posterior crowns and restorations in posterior teeth.

Oral Hygiene - some interproximal and marginal plaque & minimal food debris sticking to teeth



Investigations

Radiographs: DPT and full mouth IOPAs

Justification: caries, bone loss, apical pathology, root morphology
Grade 1

Report:

- Interproximal radiolucent changes affecting crown and root surfaces, in some cases at the margins of restorations
- Advanced or gross dental caries:

7 ^{MD}	6 ^{MD}	5 ^{MD}	4 ^M	6 ^D	7 ^{MD}
7 ^{MD}	6 ^{MD}	5 ^{MD}	4 ^{MDB}	3 ^B	6 ^D
					7 ^{MDB}

- Early carious lesions UL5 LL45

Vitality testing

LR45 UR45 negative
response to cold spray

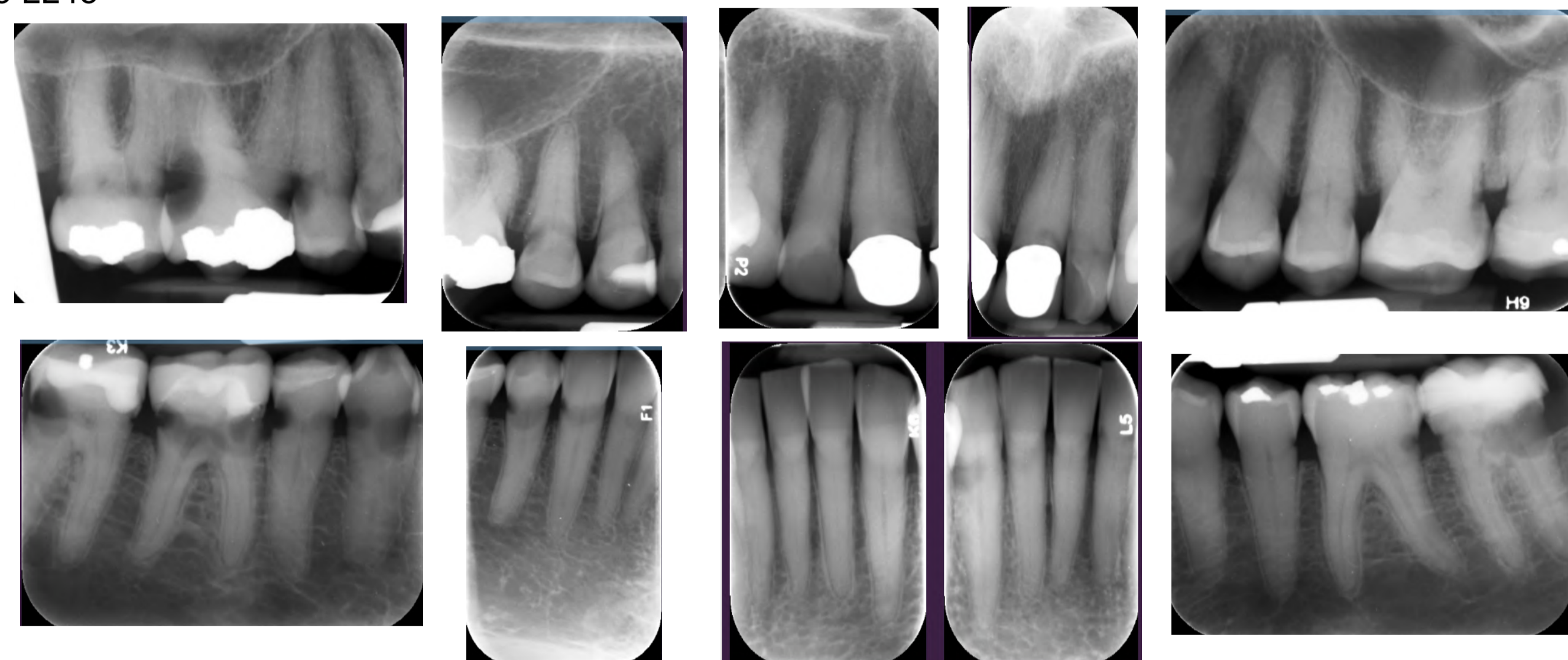
Blood results

Neutrophils 9.9 x 10⁹
WBC 12.8 x 10⁹
Platelets 693 x 10⁹
Hb 129 g/L



Figure 2: DPT

Figure 3: Full mouth intra oral periapical radiographs



Diagnoses

- Oral GvHD
- Plaque induced gingivitis
- Dental caries UR4567 UL34567 LR34567 LL67

Treatment Plan

- Prevention (in line with DoH 2014) :
 - Diet Advice
 - OHI
 - Fluoride
 - Saliva substitution
- Full mouth scaling
- Investigation of teeth with questionable prognosis:
 - UR45 LR45- found to be unrestorable
- Restorative treatment:
 - UL34, UR3, LL3 LR3 restored with GIC or RMGIC
 - LR6 restored with amalgam
- Staged extractions under IVS:
 - UR4567, LR4567, LL7
 - Time with ECP therapy
 - Review of healing 8/52 following extractions
- Immediate acrylic resin P/P
- Replacement of missing teeth:
 - Referral to restorative department for Implant assessment
 - Provision of definitive P/P

Treatment considerations

Risk Assessment

- Infection risk due to immunosuppression
- Bleeding risk
 - GvHD liver involvement and associated thrombocytopenia
 - Clopidogrel
- MRONJ risk – alendronic acid and monoclonal antibody use

Appropriate dental care

- Emergency dental treatment only during acute phase
- Invasive treatment best performed in a hospital environment (Scully)

Pain and anxiety control

- Local anaesthesia**- care must be taken if active lesions in the mouth
- Conscious sedation**- pulmonary function may be compromised due to GvHD
- General anaesthesia**- high risk due to complications of GvHD and primary disease

Challenges

This was a challenging case to plan and manage for a number of reasons. Firstly, the patient was not experiencing any pain from her teeth, nor had she previously been aware of any dental problems. She was, understandably, therefore very shocked and upset by the number of teeth which were shown to be grossly decayed on the radiographs, particularly as looking in the mouth the teeth appeared mainly sound and she had always given high priority to maintaining good oral health. Being a doctor, the patient understood the infection risk of leaving the heavily decayed teeth. It was agreed with the patient that teeth with questionable prognosis we would attempt to save in order to minimize the number of extractions required. Unfortunately on investigation many teeth were not restorable. The patient was extremely anxious about having dental extractions, this was largely due to the fact that she had undergone a lot of treatment for her medical condition and had experienced may subsequent side effects which had already significantly impacted her quality of life (such as alopecia, PEG feed, skin and ocular lesions, recurrent infections requiring hospital admission). She did not feel she could manage having extractions unless she was sedated. This patient did not have any GvHD related pulmonary involvement and therefore IV midazolam was provided using an elderly regime.

Discussion

Few cases have been reported in the literature specifically concerning the dental implications of HSCT. Of those published, caries development following HSCT appears to be interproximal and cervical (Castellarin 2012), with no single identifiable factor being correlated with the development of rampant caries. It has been reported that caries develops more frequently in patients who have a history of acute GvHD, prolonged hospitalization, poor general health, impaired oral hygiene, restricted dietary intake and reduced salivary function (Heimdahl 1985). The pattern of dental caries observed in this patient is not dissimilar to that of radiation caries, and further research into this area is warranted in order to help us understand the pathophysiology. Routine pre-HSCT dental assessment and early preventative measures are paramount in reducing the need for future invasive dental treatment, which no doubt presents a number of potential complexities and complications to consider when planning and delivering dental treatment. Furthermore, preservation of oral health related quality of life is of utmost importance for these patients suffering from this debilitating condition.

Conclusion & Reflection

Older patients undergoing allogeneic HSCT may experience higher morbidity than younger patients (El-Jawhri *et al* 2014). Additionally, older patient age is associated with an increased risk of chronic GvHD (Flowers *et al* 2011). It is important that dental professionals are aware of the oral complications of chronic GvHD and the significant risks which may be associated. In addition to pain, infection, and a number of considerations which must be taken regarding dental treatment, multiple extractions can result in compromised aesthetics and impair both functional and social aspects of life. This patient remains high risk (NICE 2004) for dental disease and therefore regular examinations should be carried out and preventative measures reinforced. A shared care approach, between primary and secondary care, would be appropriate for this patient in the future, having check ups and simple treatment in general practice, and invasive treatment and sedation in a hospital setting. It was fortunate for this patient that she was able to receive Oral Medicine and Special Care input at the same hospital where she was receiving medical care for her GvHD. This allowed good communication between all teams, access to relevant investigations, and resulted in good patient care.

References

- Albuquerque R, Khan Z, Poveda A, Higham J, Richards A, Monteiro L, Jané-Salas E, Lopez-Lopez J, Warnakulasuriya S (2016) Management of oral Graft versus Host Disease with topical agents: A systematic review. *Med Oral Patol Oral Cir Bucal*. 1;21(1):e72-81.
- Department of Health (2009) Delivering better oral health: an evidence based toolkit for prevention - second edition. *Department of Health and the British Association for the Study of Community Dentistry*
- Heimdahl A, Johnson G, Danielsson K, *et al.* (1985) Oral condition of patients with leukemia and severe aplastic anemia: follow-up 1 year after bone marrow transplantation. *Oral Surg Oral Med Oral Pathol*, 60: 498-504
- Castellarin P, Stevenson K, Biasotto M, Yuan A, Woo S, Treister N (2012) Extensive Dental Caries in Patients with Oral Chronic Graft-versus-Host Disease. *Biology of Blood and Marrow Transplantation*, 18
- El-Jawhri A, Pidala J, Inamoto Y, Chai X, Khera N, Wood W, Cutler C, *et al.* (2014). Impact of age on quality of life, functional status, and survival in patients with chronic graft-versus-host disease. *Biology of blood and marrow transplantation: journal of the American Society for Blood and Marrow Transplantation*, 20(9), 1341-1348.
- Flowers M, Inamoto Y, Carpenter PA, *et al.* (2011). Comparative analysis of risk factors for acute graft-versus-host disease and for chronic graft-versus-host disease according to National Institutes of Health consensus criteria. *Blood*. 117(11):3214-3219.