

CASE REPORT

Vincristine, doxorubicin and cyclophosphamide chemotherapy induced oral chronic hyperplastic candidiasis and xerostomia in a young patient with Ewing's sarcoma: A case report

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A common primary bone malignancy in childhood and adolescence is Ewing's sarcoma. Here we report multidisciplinary approach in the management of chronic hyperplastic candidiasis and xerostomia secondary to chemotherapy with vincristine, doxorubicin and cyclophosphamide (VDC) in a pediatric male patient with Ewing's sarcoma of Ethmoid sinus. The initial diagnosed oral lesion was treated with topical clotrimazole 1%w/v for two weeks and Sucralfate 1g/10mL oral rinse for one month. Upon subsequent VDC chemotherapy cycle, the patient developed grade IV oral mucositis, severe neutropenia and associated oesophageal candidiasis. Treatment included combination of topical clotrimazole 1%w/v and Fluconazole 300mg/day (IV for 5 days and Tablet for 14 days). To prevent caries risk, pit and fissure sealants were applied and topical fluoride therapy was given; patient was encouraged to have frequent sips of water and prescribed kids xylitol gum for 15 days to minimize xerostomia. At 5-week follow up, reduction in burning sensation and resolution of white lesion was noted.

Keywords: Ewing's tumour, antineoplastic chemotherapy protocol, mandible, opportunistic infections, oral candida

Received 21 July 2022 / Accepted 12 January 2023

Introduction

Ewing's sarcoma (ES), first described by James Ewing is a rare yet highly malignant small round cell tumour [1,2]. The presence is predominant in males (male: female ratio of 1.5:1) with peak incidence noted at 10-15 years [3-5]. Isolated cases in head and neck region are uncommon (1%-4%) [1-6] with even rarer cases reported of sinonasal ES [5-7]. In addition, about 15-30% exhibit likelihood of lung and bone metastases present at the time of diagnosis [5]. A multidisciplinary approach involving surgery along-with adjuvant radiotherapy and chemotherapy entails effective management of ES depending on the severity of lesion [1]. A standard chemotherapy regimen with alternating cycles of vincristine-doxorubicin cyclophosphamide and ifosfamide-etoposide is recommended [8]. Further, it is a well-known fact that chemotherapy due to its lack of selectivity, acts on tumour cells as well as multiplies normal cells rapidly [9-11]. Consequently, oral cavity due to its high-cellular turn-over rate, complex and diverse oral microflora and oral tissue trauma occurring during normal oral function is increasingly susceptible to direct and indirect effects of chemotherapy [10,11]. Therefore, it is critical to assess the patient's oral condition and to stabilise any conditions of oral disease before treatment for cancer is provided. In order to mitigate the possibility of oral complications and other associated systemic complications, oncological patient care must be viewed both from a preventive and therapeutic point of view. Although

metastasis of Ewing sarcoma in the oral cavity is reported previously [12], a literature search revealed no case report of chemotherapy induced chronic hyperplastic candidiasis in oropharyngeal region in paediatric patient with Ewing's sarcoma. The present case report is intended to describe a case of chronic hyperplastic candidiasis and xerostomia in a 10-year-old pediatric male patient as an oral adverse-effect of vincristine, doxorubicin and cyclophosphamide (VDC) chemotherapy.

Case Report

An 11-year-old male patient was referred from Department of Paediatrics, Kasturba Medical College, Mangalore, India to the outpatient Department of Paediatric and Preventive Dentistry, Manipal College of Dental Sciences, Mangalore, India complaining of white coating on tongue with burning sensation of mouth on consuming bland food since two-weeks. The medical history revealed the patient was a known case of Ewing's sarcoma of Ethmoid sinus diagnosed at the age of 10 years for which he had undergone twelve episodes of chemotherapy with VDC in the past year. Past family history was non-contributory and the patient was thin built, conscious and cooperative.

The extra-oral examination revealed changes associated with chemotherapy, including loss of hair from scalp and eyebrow and discolouration of skin near dorsum nasi. Intra-oral hard-tissue examination revealed mixed dentition, Grade III mobile lower left primary canine (pre-shedding mobility) and deep pits and fissures on all permanent first molars. Further, intra-oral soft-tissue examination revealed the presence of curdy-white, homogenous, smooth,

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plaque-like non-scrapable deposits dispersed on the dorsum of the tongue (middle third and posterior one-third) (Figure-1A) No similar lesion was noticed on other areas of oral cavity. Additionally, the tongue blade sign for xerostomia was positive. Based on the history, clinical presentation of lesion and the incidence of candidiasis being common in immunocompromised patients, a working diagnosis of chronic hyperplastic candidiasis (CHC) with grade two moderate level of xerostomia (as per National Cancer Institute Common Terminology Criteria for Adverse Events) was given. Other white oral cavity lesions, such as oral leucoplakia, oral hairy leucoplakia, white sponge nevus, oral lichen planus, lichenoid reactions and chemical burns, were considered for differential diagnosis and disregarded since the patient responded to antifungal therapy given later described below. Further, the probability of metastasis to mandible was ruled out with an orthopantomograph.

As a part of an interdisciplinary approach to provide treatment for patient, therapeutic diagnostic approach was followed with an integrated team, involving paediatrician, paediatric dentist and a specialist in oral medicine.



Fig. 1. A. Showing presence of widespread, homogenous, non-scrapable, curdy-white, plaque-like deposits on the dorsum of the tongue. B. Showing mild resolution of white lesions at five-week follow-up.

The management involved application of topical antifungal therapy to confirm the therapeutic diagnosis. Topical clotrimazole 1%w/v to be applied at the site of lesion after food 3-4 times/day for 14 days, post hand hygiene, was advised to be continued until the end of chemotherapy. A suspension of Sucralfate 1g/10mL; swish and spit or swish and swallow the suspension thrice daily to relieve burning sensation in mouth. Later, the paediatrician informed patient underwent a cycle of VDC chemotherapy (during the time topical anti-fungal therapy was being given) due to which he developed grade IV mucositis and culminated in severe neutropenia. Subsequently, he complained of decreased food intake, odynophagia and pharyngitis due to spread of infection to his throat i.e., oesophageal candidiasis. It was then determined that anti-fungal combination treatment with topical clotrimazole and systemic therapy should be introduced. Topical application of clotrimazole was continued with Injection Fluconazole 300mg/day for 5 days. Subsequently, when the patient was able to consume drugs after days orally, topical clotrimazole application was continued with Tab Fluconazole 300mg/day for 14 days. Eventually, a reduction in the burning sensation of the mouth and the extent of white non-scrapable lesions was found during a 5-week follow-up. (Figure 1B)

Further, preventive therapies were carried out to limit the risk of carious lesions that may act as foci of infection in future. Pit and fissure sealants on all permanent first molars followed by first application of full mouth fluoride varnish was completed and was to be continued once in every three-months. Also, the patient and his parents were counselled and educated regarding the importance of oral hygiene maintenance in order to reduce common oral sequelae secondary to cancer therapies. To minimize the effect of xerostomia, patient was encouraged to have frequent sips of water and prescribed kids xylitol gum for 15 days. The timeline of the management is shown in Figure 2.

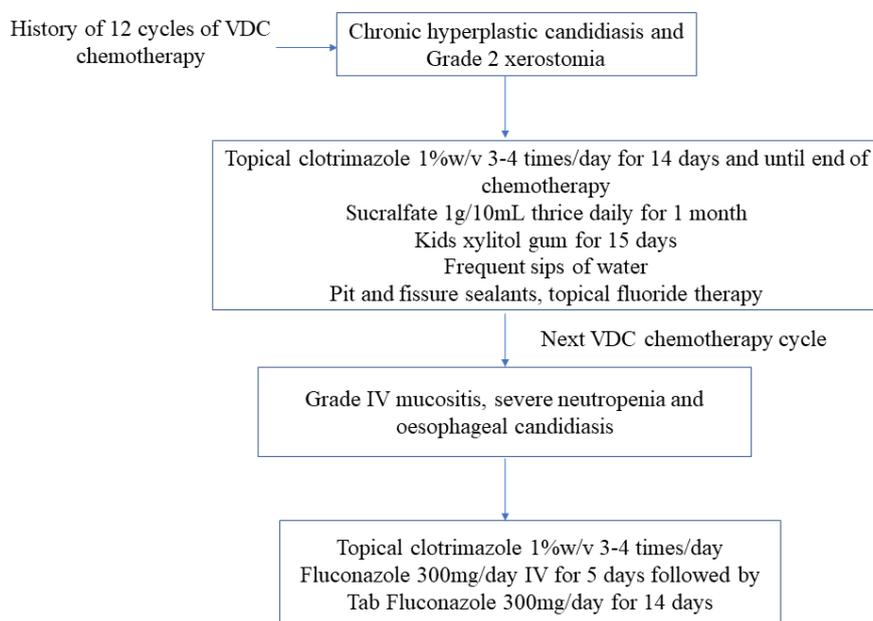


Fig. 2. Flowchart showing timeline of management

Discussion

Ewing's sarcoma (ES) though uncommon in the head and neck region, has reported cases in mandible with predilection in posterior body, the angle, and ramus areas [13]. Due to tendency of metastasis to other bones, likelihood of jaw involvement should be ruled out by dental clinicians [14, 15]. In the present case, an OPG was taken to rule out any bony lesions. The clinical features seen in the maxillofacial region include expansion of bone, swelling, pain, mobility of teeth, paraesthesia, ulceration and trismus [13]. Albeit interdisciplinary management has enhanced ES prognosis [13], antineoplastic treatment still predisposes younger populations to a variety of oral adverse effects [11, 16] such as mucositis, aphthous ulcerations, xerostomia, sialadenitis, poor oral hygiene, gingival bleeding and secondary fungal or candida infections.

Oral candida (OC), otherwise normal commensal in oral cavity, due to compromised host-defence, mucosal inflammation or disruption with prolonged severe neutropenic episodes can cause candidal infections [17] (17). Diagnosis is based on medical and dental history, identification of clinical signs and symptoms with various tests including culture indicating its presence [18, 19]. In our case described above, a therapeutic diagnostic approach was followed and no further investigations were done to confirm the diagnosis. Biopsy, due to its invasive nature and immunocompromised state of patient was not done. However, in cases wherein it may be indicated, (cases where the lesion does not subside with antifungal medication) an oral pathologist should be included for formulation of treatment plan.

A comprehensive management involves communication between paediatric dentist and paediatricians where former implements mandatory oral review prior to chemotherapy initiation. With thorough and comprehensive therapy, oral candidiasis has a favourable prognosis. Relapse occurs due to inadequate adherence to medication or inability to overcome infection's causative issues. In our case, spread of oesophageal candidiasis that may have proven to be life-threatening [20] to the patient was controlled with a multidisciplinary approach and should be encouraged in daily practice.

Conclusion

For pediatric patients undergoing chemotherapy due to malignancies such as Ewing's Sarcoma, early identification of oral signs and symptoms of the adverse effects of chemotherapy, with interdisciplinary management approach by paediatrician, paediatric dentist and oral medicine specialist is essential. Periodic dental examinations may significantly reduce the occurrence of such lesions, thereby reducing the morbidity in these immunocompromised young patients. A therapeutic diagnostic approach as described in the present case is a minimally invasive approach that helped in improving patient's oral health quality of life.

Authors' contribution

HS - Supervision, Investigation, Methodology, Writing – original draft

CT - Supervision, Writing – original draft, Writing – review & editing

AB - Supervision, Investigation, Methodology

MK - Supervision, Investigation, Methodology

SBS - Supervision, Writing – review & editing

Conflict of interest

None to declare.

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