Oral Oncology 99 (2019) 104343

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Letter to the editor

Medication related osteonecrosis of jaw in a leukemia patient undergoing systemic arsenic trioxide therapy: A rare case report

ARTICLE INFO

Keywords:
Medication-related osteonecrosis of the jaw
Osteonecrosis of the jaw
Arsenic trioxide
Side effects
Necrosis
Combination chemotherapy
Complications

ABSTRACT

Osteonecrosis of the jaw is a potential side effect of certain pharmaceutical agents used in the field of medicine. Early diagnosis and effective management of this condition can be challenging to the clinicians. Bisphosphonates and other anti-angiogenic agents are the most common drugs that are attributed to cause medication-related osteonecrosis of the jaw. In the past, arsenic-based compounds were commonly used local agents for pulp devitalization therapy. Arsenic is also one of the components of the chemotherapeutic regimen in the management of refractory leukemia. Although local diffusion of the arsenic compounds is known to cause osteonecrosis, there are no reports of the same caused by its systemic administration. Here, we present the first ever case of mandibular bone necrosis in a patient with acute promyelocytic leukemia who underwent systemic arsenic trioxide therapy.

Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) with a rapid, fatal course. This disorder is characterized by a marked increase in the number of promyelocytes in the bone marrow. There is severe bleeding tendency due to hyper fibrinolysis and disseminated intravascular coagulation (DIC), which is further worsened by chemotherapy [1]. The standard care of treatment for APL consists of a combination with all-trans retinoic acid (ATRA) and anthracycline-based chemotherapy. However, high-risk category and cases of relapse are managed with dual therapy of arsenic trioxide (ATO) and ATRA [2–4]. Studies have also proven the role of arsenic trioxide as a single effective agent in the management of APL [5]. However, chemotherapy with ATO is known to cause side effects like hepatitis, ventricular arrhythmias, renal failure and mucositis [3,6]. Here, we present the first ever case of mandibular osteonecrosis in acute promyelocytic leukemia patient on systemic arsenic trioxide therapy.

Case report

A 27-year-old female reported to the Oral Diagnosis department with a complaint of dull pain in the right lower back tooth region since the past one week. She was diagnosed with acute promyelocytic leukemia - high risk with molecular emission three months back and underwent daily-dual therapy of intravenous arsenic trioxide (10 mg) and oral all-trans retinoic acid capsule (40 mg) for 50 days. After the completion of treatment, she developed pain in the right lower back tooth, which was sudden in onset, continuous and moderate in intensity. On intraoral examination, a localized area of exposed necrotic bone was seen on the lingual aspect of right lower second molar tooth region (Fig. 1). The teeth in the area of exposed bone were firm and non-carious. Intra oral periapical radiograph did not reveal any bony changes. Since the area of exposed bone was localized and minimal, symptomatic management was done by thorough debridement of the exposed site with betadine solution and antiseptic mouthwash was prescribed. Patient was advised to maintain meticulous oral hygiene and she obtained significant relief of symptoms though the lesion did not resolve completely. She was kept on regular follow up for one year.

Discussion

Arsenic compounds were once considered as potent carcinogens for skin and lung cancer but later known to have medicinal properties. The use of arsenical compounds originated from Chinese medicine as a pulp-devitalizing agent. Additionally, it was also used in the management of psoriasis, rheumatoid arthritis, syphilis and trypanosomiasis involving the nervous system. The principle behind the use of arsenic is “targeting a toxin with another toxic agent” [6]. The side effects of systemic arsenic trioxide include mucositis, enterocolitis, hyperpigmentation, reactivation of herpes zoster and herpes simplex, ventricular arrhythmias and myelosuppression. Intravenous arsenic trioxide therapy is better tolerated than oral form.

Medication-related osteonecrosis of the jaw (MRONJ) refers to the condition, which manifests as exposure of bone in the maxillofacial region due to long-term use of drugs like bisphosphonates, anti-resorptive agents like denosumab and anti -angiogenic agents [7]. Till date, arsenic trioxide and arsenical compounds are not included in the list of medications that are known to cause MRONJ even though rare case reports of mandibular alveolar bone necrosis due to the local contact of arsenic-based pulp devitalizing agent have been reported earlier [8–10]. However, this is the first ever-case report of systemic ATO therapy, causing mandibular bone necrosis. Our clinical experience suggests the addition of arsenic trioxide as one of the potential agents, which could cause MRONJ. As treatment options for this condition are quite limited, it is imperative to emphasize on the preventive dental care, strict oral hygiene maintenance and regular dental follow up to reduce the incidence of MRONJ [11,12].

https://doi.org/10.1016/j.oraloncology.2019.06.024
Received 12 June 2019; Received in revised form 21 June 2019; Accepted 23 June 2019
Available online 26 June 2019
1368-8375/

Fig. 1. Intraoral photograph showing the exposed lingual alveolar bone in the mandibular right second molar tooth region.

Declaration of Competing Interest

None declared.

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