

Received Date : 01-Sep-2016

Revised Date : 23-Sep-2016

Accepted Date : 29-Sep-2016

Article type : Case Report

Case report:

Dengue related Osteonecrosis of the Maxillary Dento-Alveolar Bone

Running title: Dengue haemorrhagic fever and osteonecrosis

Al-Namnam N M¹, Nambiar P¹, Shanmugasundaram P¹, Harris M²

¹Department of Oro-Maxillofacial Clinical Sciences, Faculty of Dentistry, University of Malaya,
50603 Kuala Lumpur, Malaysia

²School of Medicine and Dentistry, University of Central Lancashire, Preston, United Kingdom.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:

10.1111/adj.12472

This article is protected by copyright. All rights reserved.

* Corresponding author, Al-Namnam NM¹

Email: nis_moh2007@yahoo.com

Acknowledgements

The authors would like to express their sincere thanks to High Impact Research Grant No: UM.C/HIR/MOHE/Dent/19 for partially help us in the preparation of the case and scanning patient.

Abstract

Dengue is a mosquito transmitted flaviviral infection which can give rise to severe haemorrhage (dengue haemorrhagic fever/DHF) and with capillary leakage induces hypovolemic shock (dengue shock syndrome/DSS). Although dengue symptoms and complications have been known for many decades there has only been one documented case of osteonecrosis of the maxilla which was treated by excision of the necrotic bone. In this case of dengue infection, extensive maxillary osteonecrosis and minimal root resorption appeared to follow factitious injury with a toothpick but resolved with nonsurgical management.

Keywords: Dengue haemorrhagic fever, dento-alveolar resorption, osteonecrosis of jaw, Aedes Aegypti mosquito

Introduction

Dengue fever is a painful debilitating mosquito borne disease caused by a flavivirus. These are global human pathogens that primarily cause encephalitis and haemorrhagic disease in tropical and sub-tropical regions and is transmitted by day-biting female *Aedes Aegypti* mosquitoes [1].

The common name for dengue fever is "break bone fever", due to the severe associated myalgia and arthralgia due to the deposition of antibody immune complexes at sites of viral infection in bone, muscle or the synovium.

An estimated 390 million dengue infections occur worldwide each year [2]. It is found in Africa, Americas, Mediterranean region, South-East Asia and the Western Pacific region (Fig.1) [3].

[**Insert Fig. 1 here**]

It is endemic in around 100 countries. Dengue fever is not endemic in Australia, however, epidemic of dengue have probably occurred. The vector of dengue was probably introduced to Australia during European colonization from the late 18th century. International diseases distribution maps show the vector and dengue epidemic activity is widespread in the northeast state of Queensland Australia and travel has probably had the most important impact on its spread. Furthermore, the current proliferation of domestic water storage tanks presents a high potential dengue transmission risk during the warm summers [4].

Dengue fever is generally a benign disease which is characterized by fever with an acute onset of severe headache and myalgia, but can develop into a life-threatening dengue haemorrhagic fever (DHF). DHF arises from damage to lymphatics, with plasma leakage increased vascular permeability, thrombocytopenia, producing impaired haemostasis, epistaxis, and gingival

This article is protected by copyright. All rights reserved.

haemorrhage. The plasma leakage can result in pleural effusion and ascites leading to hypovolaemia and circulatory shock with organ failure. Infected hepatosplenomegaly increases the spleen's mechanical filtration with RBC destruction. These features may progress to massive bleeding, and the dengue shock syndrome (DSS) which is more common in patients during a second episode of infection [5].

Aseptic osteonecrosis of the jaws could be a result of impaired blood supply. However, periodontitis which may arise from the impaired immune response enhancing the subgingival microbiome could be responsible for a bacterial osteitis [6]. The following case is presented as an uncommon maxillary osteonecrosis, periodontitis with root resorption associated with dengue haemorrhagic fever.

Case report

In November 2014, a 30-year old male patient presented in Taize, Yemen with high fever, epistaxis, gingival bleeding and severe headache. The patient tested positive for anti-NS1 antibodies which is diagnostic for dengue infection. The full blood count revealed leukopenia (3600 WBC μ l) and thrombocytopenia of less than 90.000 per mm^3 . After 3 days, the platelet count dropped to less than 20.000/ mm^3 and the patient developed hypoxia, generalized oedema, hepatosplenomegaly and impaired renal function. The symptoms progressed to haemorrhage and shock for 14 days. Supportive care consisted of paracetamol (500 mg, 6 times/day), isotonic fluid, platelets and blood replacement was provided until complete recovery a month later.

The patient's history, revealed that he contracted dengue fever 4 years earlier with leukopenia and thrombocytopenia (90,000 / mm^3) but mild dengue symptoms.

Throughout the features of dengue haemorrhagic fever, the patient injured his interdental gingiva when he attempted to remove impacted food between the upper right canine and first premolar with a toothpick. This led to severe bleeding, pain, and gingival swelling for 2 months. However, the teeth were non-carious and did not exhibit any mobility. The pain was reduced by oral analgesics (paracetamol; 500 mg), however the gingival swelling and bleeding persisted for over 2 months. A bone biopsy consisting of 2 x 2 cm fragments of grey and light brown tissue removed for histology from the right upper alveolar bone showed fragments of bone devoid of osteoclasts with a mononuclear infiltration of lymphocytes, plasma cells, and histiocytes. There was no evidence of any specific pathology or infection. Furthermore, mobility of the right maxillary canine, premolars and molars was noted and ipsilateral submandibular lymphadenitis. A panoramic radiograph and computed tomography, showed evidence of decreased bone density involving the right maxillary alveolar bone extending from the canine to the second molar region (Fig. 2 (A& B)). Widening of the periodontal space was also noted around the canine root.

[Insert Fig. 2 here]

Amoxiclav (500 mg amoxicillin & 149 mg clavulanate potassium) 3 times a day 400 mg of metronidazole 2 times a day and chlorohexidine mouth wash 2 times a day were administered for 14 days.

The patient recovered completely over 4 months from the dengue clinical features and the tooth mobility reduced significantly.

8 months later the CT scan confirmed marked reduction in the radiolucent areas (Fig. 3).

[Insert Fig. 3 here]

At 9 months there was no mucosal hyperaemia, swelling or fistula. and all the right maxillary teeth were firm except the canine with grade-II mobility. Periapical and occlusal images showed an increase in bone density with trabecular restoration, apical root resorption of the right canine tooth and to a lesser extent the premolar and mesiobuccal molar roots which had not been evident in earlier radiographs (Fig. 4 & 5).

[Insert Fig. 4 here]

[Insert Fig. 5 here]

Discussion

The oral manifestations of dengue fever are haemorrhagic with varying degrees of swollen bleeding gingiva, tongue, lip, buccal mucosa, and post-extraction haemorrhage [7, 8]. Purpura, and ecchymoses will reflect platelet levels.

Microbiological laboratory testing may show virus segregation in cell cultures, nucleic acid demonstrated by polymerase chain reaction (PCR), and serological detection of viral antigens [9].

At the outset of a dengue infection, the virus enters the blood stream and penetrates macrophages and monocytes which enable reproduction in the circulation [10]. These leukocytes release cytokines and interferons, which are responsible for the viral symptoms. Halstead (1980)

proposed that vascular permeability gives rise to the dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) [11], and the vascular permeability is amplified by a cascade of cytokines which include, T-lymphocyte cytotoxic factor (CF) and a macrophage cytotoxin (CF2) factor [10]. The cytokines also cause thrombocytopenia, leukopenia and trigger off intravascular coagulation and fibrinolysis [12]. The thrombocytopenia and fibrinolysis are responsible for the haemorrhage and the widespread capillary permeability, gives rise to oedema with, pleural effusion and ascites and the risk of circulatory organ failure. This complex cytokine interaction produces bone marrow suppression and osteonecrosis [13]. The exact cause of the bone necrosis is still not conclusive, but could be marrow suppression and intraosseous haemorrhage leading to bone infarction and periodontal infection.

This case presented with osteonecrosis of the right maxilla and resorption of the canine root apex. He had no evidence of other unrelated causes of osteonecrosis and no prior periodontal disease. The histopathology report excluded bacterial osteomyelitis and malignancy but a crucial feature of his medical history was dengue viral infection 4 years earlier in 2010.

The interdental application of tooth pick (once) with marrow suppression may have caused a periodontal abscess, loss of the adjacent lamina dura, widening of the periodontal ligament (PDL) space and blunting of the canine apex.

The general management of dengue is of primary importance. Plentiful oral fluid supplementation is essential but intravenous fluid administration is mandatory in cases of shock, severe vomiting, and dehydration. Low platelet counts, are a serious concern for bleeding and are best managed by transfusion of fresh whole blood. However prophylactic platelets may be given at a level of $<10,000/\text{cu mm}$ in the absence of bleeding manifestations

Conclusion

Osteonecrosis and associated dental root resorption are unusual oral manifestations of dengue haemorrhagic fever despite the innumerable risk factors, but should still be considered a potential complication. Optimum maintenance of periodontal health must complement symptomatic dengue treatment and appears to allow the osteitis to heal uneventfully without radical intervention. Careful interdental hygiene with a fine brush is desirable. This case will be followed up to ensure complete bone healing with the elimination of tooth mobility.

References

1. Wilder-Smith A, Schwartz E. Dengue in travelers. *N Engl J Med* 2005; 353: 924-932.
2. Gould E, Solomon T. Pathogenic flaviviruses. *Lancet* 2008; 371: 500-509.
3. Kay MT, Tyler MS, Harold SM. CDC Health Information for International Travel. Infectious Diseases Related to Travel. 2016. Oxford University Press.
<http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/dengue>
4. Dengue and severe dengue: Fact sheet, World Health Organization; 2016.
<http://www.who.int/mediacentre/factsheets/fs117/en/>
5. Halstead SB. Pathogenesis of dengue: challenges to molecular biology. *Science*. 1988; 239: 476.
6. Hong BY, Araujo MVF, Strausbaugh LD, Terzi E, Ioannidou E, Diaz PI. Microbiome Profiles in Periodontitis in Relation to Host and Disease Characteristics. 2015.
<http://dx.doi.org/10.1371/journal.pone.0127077>
7. Ahmed S, Mohammad WW, Hamid F, Akhter A, Afzal RK, Mahmood A. The 2011 dengue haemorrhagic fever outbreak in Lahore—an account of clinical parameters and pattern of haemorrhagic complications. *J Coll Physicians Surg Pak* 2013; 23: 463-467.
8. Pontes FS, Frances LT, Carvalho Mde V, Fonseca FP, Neto NC, do Nascimento LS, Pontes HA. Severe oral manifestation of dengue viral infection: a rare clinical description. *Quintessence Int* 2014; 45: 151-156.
9. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, Hunsperger E, Kroeger A, Margolis HS, Martínez E, Nathan MB, Pelegrino JL, Simmons C, Yoksan S, Peeling RW. Dengue: a continuing global threat. *Nat Rev Microbiol* 2010; 8: S7-S16.
10. Chaturvedi UC, Dhawan R, Khanna M, Mathur A. Breakdown of the blood-brain barrier during dengue virus infection of mice. *J Gen Virol* 1991; 72: 859-66.
11. Halstead S. Dengue haemorrhagic fever—a public health problem and a field for research. *Bull World Health Organ* 1980; 58 : 1-21.
12. Indurkar MS, Sethi R. An Unusual Case of Osteonecrosis of Jaw associated with Dengue fever and Periodontitis. *Aust Dent J* 2015. doi: 10.1111/adj.12308.

This article is protected by copyright. All rights reserved.

13. Chuansumrit A, Chaiyaratana W. Hemostatic derangement in dengue hemorrhagic fever. *Thromb Res.* 2014; 133: 10-6.

Figure legend

Fig. 1: Distribution of dengue.

Fig. 2: Axial CT (A) and three-dimensional rendering (B) shows marked bone destruction in the right alveolar region of the maxilla. (Jan 2015)

Fig. 3: Volume rendering showed significant healing of the maxillary alveolar region. (Oct 2015)

Fig. 4: Increase in bone density with trabecular restoration and apical root resorption of the right canine tooth and to a lesser extent of the premolar and mesiobuccal molar roots. (Nov 2015)

Fig. 5: Oblique occlusal view of the maxilla showing the healing alveolar region (Nov 2015)



