

An Unusual Case of Chronic Relapsing Tetanus Associated with Mandibular Osteomyelitis

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Abstract

A 55-year-old man underwent radiation therapy due to malignant lymphoma of the neck. Eight years after the therapy he developed tetanus. It appears that the radiation therapy resulted in mandibular necrosis, and that this lesion may have been the infectious focus of tetanus. Treatment with penicillin G was very effective in the acute stage, and chronic administration of metronidazole prevented relapse of the disease. However in spite of injections of tetanus toxoid, symptoms of tetanus returned when the administration of metronidazole was discontinued because the infectious focus could not be completely removed. This is the first report of chronic relapsing tetanus associated with radiation-induced mandibular osteomyelitis, and demonstrates that tetanus can occur due to mandibular focus but the chronic administration of metronidazole can prevent relapse.

Key words: chronic relapsing tetanus, mandibular osteomyelitis, metronidazole, ⁶⁷Ga scintigraphy

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Introduction

Tetanus is currently a rare disease in advanced countries, but even so it still remains endemic within the older populations. This disease is caused by an anaerobic gram-positive rod, *Clostridium tetani*, with diagnosis being based on history of penetrating trauma and specific clinical symptoms (1). However this disease sometimes occurs due to occult trauma. The disease is very often lethal, and requires early and precise diagnosis. Here, we report an unusual case of chronic relapsing tetanus resulting from mandibular necrosis following radiation therapy for malignant lymphoma.

Case Report

A 55-year-old man who never had tetanus nor history of

vaccination with tetanus toxoid was diagnosed with B cell non-Hodgkin's lymphoma on the left side of the neck. Following chemotherapy and a total of 50 Gy of radiation therapy complete remission was achieved. However, at age 63, he was hospitalized due to dysphagia followed by painful stiffness in the right leg, opisthotonos, and generalized convulsive seizure. Laboratory data revealed the following: white blood cell (WBC) count 13,400/ μ L (normal range, 4,000-10,000/ μ L); C-reactive protein (CRP) 1.1 mg/dL (<0.3 mg/dL); and creatine kinase (CK) 1,163 U/L (14-170 U/L). He was diagnosed with tetanus and received treatment that included tetanus toxoid, human anti-tetanus immunoglobulin and benzylpenicillin (administration for five days). His symptoms gradually ameliorated and he was discharged one month after initiation of the therapy. However, his infectious focus remained unknown and he had never experienced any trauma causing puncture wounds normally associated with

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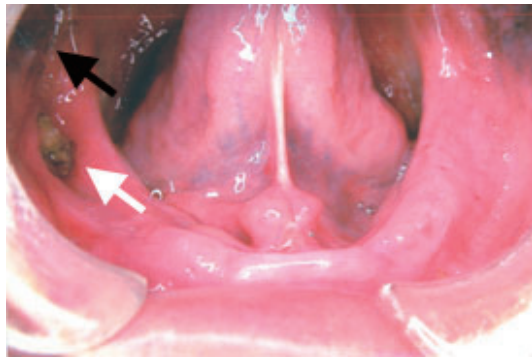


Figure 1a. Note exposure of the mandible (white arrow) from the gingiva caused by necrosis of the buccal mucosa (black arrow).

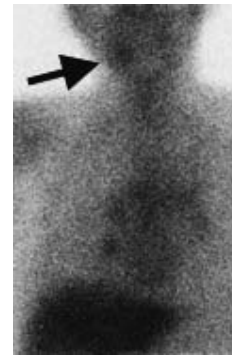


Figure 1b. The findings of ^{67}Ga scintigraphy. Abnormal accumulation is observed in the right mandible (arrow).

tetanus infection.

Nine months later, he noticed right gingival swelling and visited our department of dentistry and oral surgery where he was diagnosed and treated for right mandibular osteomyelitis. One month later, he developed dysphagia and trismus, and he was admitted to our department. The mandible was exposed from the gingiva due to necrosis of the buccal mucosa in the right side of his oral cavity (Fig. 1a). He was mildly incoherent (Glasgow Coma Scale, 14), and had bilateral blepharoptosis, trismus, and swallowing difficulties. He also complained of diplopia resulting from slight abduction of the left eye. General muscle tonus was increased, and he displayed remarkable opisthotonos induced by touching his forehead. Results of laboratory studies included the following: CRP 0.3 mg/dL (<0.3 mg/dL); and CK 702 U/L (14-170 U/L). Swab culture from the necrotic buccal mucosa and mandible showed no growth of *Clostridium tetani*. The findings of ^{67}Ga scintigraphy displayed abnormal accumulation in the right mandible (Fig. 1b).

He was therefore clinically diagnosed with tetanus, and treated with tetanus toxoid, human anti-tetanus immunoglobulin and benzylpenicillin. The treatment with benzylpenicillin was continued for 36 days, resulting in improved lucidity, and disappearance of all symptoms. The mandible lesion gradually improved with administration of benzylpenicillin and thus debridement of the necrotic tissue was performed rather than removing the mandible since the procedure itself might be life-threatening. He then received another injection of tetanus toxoid, approximately four weeks after admission. Administration of benzylpenicillin was replaced with metronidazole (500 mg/d), and his condition became stable five days after initiation of administration of metronidazole and he was discharged.

His symptoms were stable for approximately fourteen months, at which time he stopped taking metronidazole of his own volition. Eight months later, he started to feel that his whole body became rigid and opisthotonos was induced when he touched his face. A diagnosis of tetanus relapse was made, and he was readmitted to our department. Laboratory studies revealed normal levels of WBC count, CRP,

erythrocyte sedimentation rate and CK. Treatment with tetanus toxoid, human anti-tetanus immunoglobulin and benzylpenicillin (administration for 24 days) followed by administration of metronidazole was effective in abolishing all symptoms. Continuous administration of metronidazole has subsequently prevented his symptoms from relapsing, and he is currently in a stable condition. Tetanus antibody was not examined through the disease course.

Discussion

The present case was clinically diagnosed with tetanus, although *Clostridium tetani* was not detected, and he developed symptoms of the disease on three independent occasions. Before he developed the disease, he had never experienced any trauma causing tetanus other than the mandibular osteomyelitis. Despite injections of tetanus toxoid, the disease relapsed when metronidazole was discontinued. Therefore the disease was thought to have arisen from an osteomyelitis lesion of the right mandible, resulting from radiation therapy for malignant lymphoma. The inability to detect *Clostridium tetani* may have been due to the difficulty in culturing this bacteria (2) as tetanus has previously been shown to be associated with anaerobic lesions in the oral cavity (3). Several cases of recurrent tetanus have been reported and most cases are a result of new and different wounds (2, 4, 5), and relapse rarely occurs due to the same infectious focus (6, 7) as the present case.

This report is the first to demonstrate the use of ^{67}Ga in the diagnosis of tetanus. ^{67}Ga accumulates in lesions of inflammation, as well as in tumors (8), and was therefore able to show osteomyelitis of the right mandible in the present case. This shows the usefulness of this examination, especially in cases where the infectious focus of tetanus is unknown.

Bates reported a case that developed tetanus twice and recommended that wound debridement should be carried out early if there is any suspicion that a foreign body is present (9). Because the mandible itself could not be removed in the present case, chronic infection of *Clostridium tetani* appears to have led to relapsing tetanus. Administration of metroni-

dazole was effective in preventing relapse of the disease. Although metronidazole is normally given for 7-10 days (1), long-term administration may be necessary in cases where tetanus occurs due to chronic inflammation. The present case study highlights that chronic administration of metronidazole can be a very effective treatment for tetanus cases where surgical removal of the infectious focus is difficult.

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References

1. Attygalle D, Rodrigo N. New trends in the management of tetanus. *Expert Rev Anti Infect Ther* **2**: 73-84, 2004.
2. Cook TM, Protheroe RT, Handel JM. Tetanus: a review of the literature. *Br J Anaesth* **87**: 477-487, 2001.
3. Burgess JA, Wambaugh GW, Koczarski MJ. Report of case: reviewing cephalic tetanus. *J Am Dent Assoc* **123**: 67-70, 1992.
4. Praharaj KC. Recurrent tetanus. *J Indian Med Assoc* **58**: 11-12, 1972.
5. Spenny JG, Lamb RN, Cobbs CG. Recurrent tetanus. *South Med J* **64**: 859 passim, 1971.
6. Sahadevan MG. Recurrent tetanus. *Br Med J* **2**: 492-493, 1968.
7. Bhatt AD, Dastur FD. Relapsing tetanus (a case report). *J Postgrad Med* **27**: 184-186, 1981.
8. Habibian MR, Staab EV, Matthews HA. Gallium citrate Ga 67 scans in febrile patients. *JAMA* **233**: 1073-1076, 1975.
9. Bates I. "Relapsing" tetanus. *Trop Doct* **18**: 192, 1988.