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CASE REPORT

A RARE CASE OF METHOTREXATE-RELATED OSTEONECROSIS OF MANDIBLE WITH AGGRESSIVE COURSE (CASE REPORT)

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ABSTRACT

Methotrexate-related osteonecrosis of the jaws is a rare disease. It is usually diagnosed in patients with rheumatoid arthritis treated with methotrexate. The most common trigger of MTX-ONJ is odontogenic infection. Common clinical findings in these patients are exposed alveolar ridges and fistulas with purulent discharge, redness, and edema of surrounding soft tissues. Stage-1 and -2 cases are usually found. Stage-3 cases are too rare. On CBCT scans, sequestrums and bone destruction are common.

The period of sequestrum formation is not prolonged as in BRONJ patients. After sequestrum formation, surgical treatment is effective, with low recurrence rates. Usually, sequestrum removal and bone debridement are proper.

This study presents a rare case of stage 3 MTX-related ON of the mandible with a pathological fracture. Mandible segmental resection under general anesthesia was proper for the treatment.

***Keywords*:** MTX-related ON of the mandible; mandible pathological fracture; MRONJ.

INTRODUCTION

Medication-related osteonecrosis of the jaws (MRONJ) is an important complication of certain medications and drugs. Bisphosphonates and RANKL inhibitors are the most common drugs that may lead to MRONJ development[1].

Krokodil and antiangiogenic drugs are the next common substances associated with MRONJ development[2].

Recently, methotrexate has been implicated in the development of ONJ[3-5].

Methotrexate (MTX) is a disease-modifying anti-rheumatic drug (DMARD) used in the treatment of rheumatoid arthritis (RA). At therapeutic doses, MTX inhibits bone formation and mineralization. It increases bone resorption, as shown by increased osteoclast density[6,7].

MTX has several side effects in addition to its therapeutic effect. The most common adverse effects of MTX use are cytopenia, infections, liver damage, synovitis, myelopathy, interstitial pneumonia, and MTX-associated lymphoproliferative disorders (MTX-LPD) [3,4].

Recently, rare cases of MRONJ related to MTX use have been reported in the literature [3-5].

2. CASE REPORT

A 53-year-old female patient, with a history of RA, was admitted to the Department of Maxillofacial Surgery complaining of pain, swelling on the left mandible, and lip numbness. During the initial examination, swelling at the left mandible angle was found. No inflammatory masses were found after palpation. Intraorally, deformation of the mandible alveolar ridge was found. No fistulas were found either extraorally or intraorally.

Cone beam computed tomography (CBCT) scans revealed a pathological fracture and formed sequestrums of the left mandible angle (Fig 1 and 2).

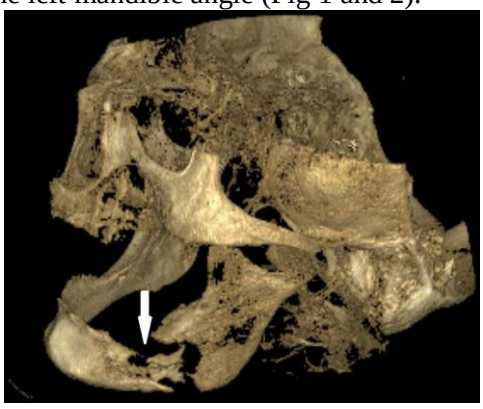

Figure 1. 3D view of the patient's skull. Formed

sequestrums (white arrow) with pathological fracture of the mandible left angle are seen.

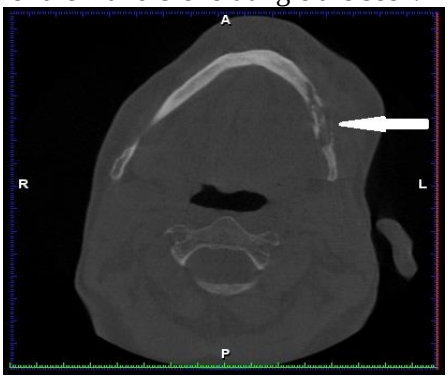

Figure 2. CT scan of the patient's mandible. Formed sequestrums (white arrow) with pathological fracture of the mandible left angle are seen

The patient noted an abscess formation on the left edentulous mandible seven months ago, which was drained in another clinic. A possible trigger of the abscess formation was an ulcer from the removable dentures. After a month, an abscess recurrence was found on the same side, which was again drained in another clinic. At this period, CBCT was done, on scans of which no evident bone changes were found. After another three months, the patient noted swelling, pain in the left mandible, and lower lip numbness.

Her medication history was noteworthy for methotrexate, leflunomide, and metipred use for two years to treat her RA. The patient's history was free of bisphosphonates and RANKL inhibitors. MTX and leflunomide use was interrupted 5 months before the first abscess formation.

MTX-related ON of the mandible with pathological fracture was diagnosed. The patient underwent surgery under general anesthesia. Mandible segmental resection was performed through the extraoral incision (Fig. 3 and 4).

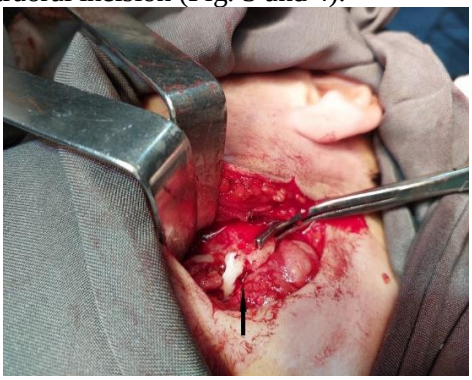

Figure 3. Intraoperational view of the patient's mandible. Formed sequestrums (black arrow) with pathological fracture of the mandible left angle are seen.

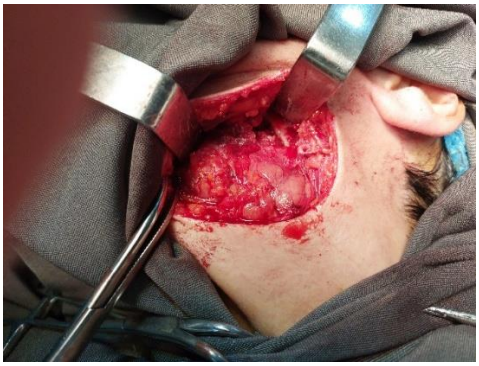

Figure 4. Intraoperative view after mandible left angle resection

The diagnosis was confirmed histologically. The postoperative period included clindamycin, oral rinses with chlorhexidine, painkillers, and wound care. The postoperative follow-up period was 6 months, which was uneventful.

3. DISCUSSION

Nowadays, it is accepted that MRONJ development may be associated with MTX use [3-5]. Interestingly, MTX has the opposite effect on bone tissue than other well-documented MRONJ-associated drugs, such as bisphosphonates and RANK-L inhibitors [6,7]. It is shown that MTX inhibits bone formation and mineralization and increases bone resorption due to increased osteoclast levels [6,7].

In many of the cases presented in the literature, patients used other MRONJ-associated drugs, such as BP [3]. Therefore, it would be wrong to classify such cases as MTX-associated ONJ [8].

In most MTX-ONJ cases, when no BP or RANK-L inhibitors were used, patients noted the use of leflunomide. In vitro studies show that leflunomide inhibits RANK-L-induced differentiation of osteoclasts [9]. However, there is no direct relation between leflunomide use and jaw ONJ development yet.

The most common trigger of MTX-ONJ is odontogenic infection. Common clinical findings in these patients are exposed alveolar ridges and fistulas with purulent discharge, redness, and edema of surrounding soft tissues. Stage-1 and -2 cases are usually found. Stage-3 cases are too rare [3-5]. Sometimes, the ONJ may be associated with MTX-LPD [3-5].

On CBCT scans, sequestrums and bone destruction are common [3-5].

The period of sequestrum formation is not prolonged as in MRONJ patients. After sequestrum formation, surgical treatment is effective, with low recurrence rates [3-5]. Usually, sequestrum removal and bone debridement are proper [3-5].

4. CONCLUSION

Stage-3 MTX-ONJ is a rare and serious complication in RA patients treated with MTX. Due to the lack of information about the pathology of this disease, further research is needed to show the direct involvement of MTX in the development of ONJ.

DECLARATION

Informed consent

Informed consent was obtained from the patient in this study.

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Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

None

Conflict of Interest

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