



“Krokodil” drug - Related osteonecrosis of midface: A case series

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ABSTRACT

Krokodil is a cheap and effective home-made substitute for heroin. It is widely used over the territory of the former USSR (Russia, Ukraine, Armenia and others).

Krokodil drug-related midface ON often occurs as a complication of maxillary ON.

Treatment of Krokodil drug-related ON of the midface is challenging. It is difficult to determine the ON zone preoperatively and intraoperatively, due to the complex anatomy of the midface and the different periods of the disease onset in different areas.

The aim of this study is to show variations of the clinical course and treatment options of Krokodil drug-related ON of the midface.

In this study, 3 cases of Krokodil drug-related midface ON are reported. The main clinical feature of midface ON is extraoral fistula in the midfacial zone with purulent discharge or extraoral exposure of zygomatic bone. Surgery is the main treatment method for Krokodil drug-related midface osteonecrosis. Surgery includes necrotic bone removal and defect closure. Usually an extraoral approach is used to expose necrotic bone. Intraoral maxillary sinus floor defect is closed with the use of a buccal fat pad to prevent formation of oroantral communication.

Drug withdrawal, radical necrectomy, and proper closure of formed defects are the main factors that lead to successful treatment of Krokodil drug-related midface ON patients.

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1. Introduction

Krokodil is a cheap and effective home-made substitute for heroin. It is widely used over the territory of the former USSR (Russia, Ukraine, Armenia and others) (Malanchuk et al., 2007; Tymofieiev and Lesova, 2009; Basin and Medvedev, 2013; Hakobyan, 2013). The main drug component of Krokodil is desomorphine. For the synthesis of Krokodil, cheap and widely available substances are used, for example codeine-containing analgesics, iodine, soda, red phosphorus (from match boxes), hydrochloric acid and gasoline.

Osteonecrosis of the jaws (ONJ) is a common complication in Krokodil users. Involvement of other skull bones (palatal bones, vomer, minor wings of sphenoid bones, nasal bones, zygomatic bones etc.) may also be found in Krokodil users (Hakobyan, 2013; Medvedev et al., 2016).

Zygomatic bone ON often occurs as a complication of maxillary ON. Incidence of zygomatic bone involvement in Krokodil drug-related ON patients is 4.4% (Hakobyan, 2013). Primary Krokodil related osteonecrosis of zygomatic bones are rare. Isolated ON of zygomatic bone was never found. ON of adjacent structures (zygomatic processes of temporal and frontal bones, frontal process of maxilla, ethmoidal bone, orbital floor, maxilla etc.) is always revealed (Hakobyan, 2013; Medvedev et al., 2016). So, it is proper to use the term “midface ON” rather than “zygomatic bone ON” to describe these patients.

Treatment of Krokodil drug-related ON of the midface is challenging. Due to the complex anatomy of the midface and the different periods of the disease onset in different areas, it is difficult to determine the ON zone preoperatively and intraoperatively. This may make the surgery planning more difficult, especially when the orbital floor and skull base are involved. In such cases, involvement of a neurosurgeon may be needed. In more complicated cases, radical necrectomy may be life-threatening or impossible.

There is too little information in the literature about midface ON of any origin. So, the results of every new treated case are

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important. The aim of this study is to show variations of clinical course and treatment options of Krokodil drug-related ON of the midface.

2. Case report

2.1. Case 1

A 38-year-old HCV positive male patient was admitted to the department of maxillofacial surgery with Krokodil drug-related ON of the right midface and maxilla. All complaints occurred after tooth extraction at a private dental clinic a year ago. The patient noted use of Krokodil for a year. The last use was 14 months prior to examination.

During extraoral examination, two fistulas with purulent discharge were revealed in the malar and infraorbital regions (Fig. 1a). The surrounding skin was hyperemic.

Intraoral exposure of the maxillary alveolar process was revealed distal to tooth 13 (Fig. 1b). The defect of vestibular mucosa was found in full height. Teeth 13, 12, 11, 21, and 22 were mobile and the surrounding mucosa was hyperemic (Fig. 1b).

On CBCT images, the zone of bone destruction with clear demarcation was found (Fig. 1c). Total opacification of the right maxillary sinus was also revealed.

The patient underwent surgery under general anesthesia. Necrotic bone exposure was achieved through extraoral Kocher-Weber incision (Fig. 1d). After necrotic bone exposure, clear demarcation was seen (Fig. 1d). Necrotic bone was resected about 5 mm behind the demarcation line (Fig. 1e and f). After necrectomy, a large defect of right maxillary sinus floor was formed. Thickened sinus mucosa was removed only from the defect side. The wound was sutured. The intraoral defect was closed only by local mucoperiosteal flaps (during that period we did not use buccal fat pad for maxillary sinus floor defect closure). Postoperative conservative treatment was also performed (antibiotics, analgesics, oral rinses). After suture removal on the tenth day, a large oroantral communication was revealed. No exposed bone areas were seen. The postoperative follow up period was 8 months, during which oroantral communication still persisted with no signs of ON recurrence (exposed bone or purulent discharge) (Fig. 1g and h).

2.2. Case 2

A 43-year-old HCV positive patient was admitted to the department of maxillofacial surgery with Krokodil drug-related ON of the left midface. Disease onset was after recurrence of left maxillary ON surgical treatment 8 months earlier. The patient noted use of Krokodil for 2 years. The last use was a year ago.

During extraoral examination, a soft tissue defect was found in the left malar area with exposure of the left zygomatic bone. Purulent discharge was revealed from the defect. Surrounding soft tissues were hyperemic.

During intraoral examination, only edentulous left maxillary alveolar process revealed without any signs of ON. On CBCT images, a formed sequestrum was found at the left zygomatic bone.

The patient underwent surgery under general anesthesia. Necrotic bone exposure was achieved through extraoral incision. All sequestrums were removed after necrotic bone exposure. Bone debridement was continued in all directions about 5 mm. The wound was sutured and drained. Postoperative conservative treatment was also performed (antibiotics, analgesics, oral rinses). Sutures were removed on the tenth day and a fistula with purulent discharge was found. During a month this fistula turned into a soft tissue defect of a larger size than it was before the surgery. Recurrence of midface ON occurred.

2.3. Case 3

A 50-year-old HCV positive male patient was referred to the department of maxillofacial surgery with Krokodil drug-related ON of the right midface and bilateral ON of the maxillary alveolar process. All complaints occurred after tooth extraction 8 months prior at a private dental clinic. In anamnesis the patient noted use of Krokodil for 3 years. The last use of Krokodil was 8 months prior to the examination.

Extraorally only edema of the right malar area was revealed. Intraoral exposure of the maxillary alveolar process was revealed distal to the right central incisor. The defect of the vestibular mucosa was in full height. Teeth 13, 12, 11, 21, 22, 23, 24, 25 were mobile. Vestibular mucosa was hyperemic at this area.

On CBCT images, formed sequestrums were found at right zygomatic bone, right alveolar process of maxilla, and right frontal process of maxilla. At left maxillary alveolar process, zones of bone destruction were found without clear demarcation.

The patient underwent surgery under general anesthesia. Intraoral midcrestal incision with releasing incisions in both sides were used for necrotic bone exposure. All formed sequestrums were removed. Left maxillary alveolar process was found necrotic until alveola of tooth 24. Necrotic alveolar process was resected until tooth 26. After necrectomy, a large defect of the right maxillary sinus floor occurred. Pathologic sinus mucosa was removed only from the sinus floor area. Vestibular mucoperiosteal flap was mobilized. Buccal fat pad (BFP) was mobilized and relocated into the wound. BFP was fixed to the palatal mucosa over the sinus floor defect. Horizontal mattress sutures were used to close the mucosa, and a secondary running continuous suture was placed over the horizontal mattress sutures. Postoperative conservative treatment also was performed: antibiotics, analgesics, oral rinses. Sutures were removed on the tenth day. Exposure of BFP 5 mm in size was found, which epithelialized over the following month. Postoperative follow up period was 7 months, during which the patient was free of symptoms: no signs of recurrence or oroantral communication were found.

3. Discussion

Jaw ON is a common complication in Krokodil drug users. Krokodil drug-related ONJ presents as alveolar process exposure in the oral cavity. Involvement of only the maxilla is found in 30%, only the mandible in 44.4%, and both jaws in 25.6% of patients (Hakobyan, 2013).

Low levels of serum C-terminal telopeptide (CTX) are found in these patients (Hakobyan et al., 2017), indicating decreased bone turnover, which is the result of Krokodil use (Hakobyan et al., 2017). Thus, Krokodil has an anti-resorptive effect on bone tissue (Hakobyan et al., 2017), which means that ONJ in Krokodil abusers is a new type of medication-related osteonecrosis of the jaw (MRONJ) (Hakobyan et al., 2017).

The radiographic signs of jaw osteonecrosis in Krokodil-addicted patients depend on the terms of drug use withdrawal and the period of disease onset (Poghosyan et al., 2013). In the early period of the disease, radiographic examination can be uninformative as nonspecific signs are often revealed: osteosclerosis, destruction, and empty dental alveoli without demarcation of osteonecrotic zone (Poghosyan et al., 2013).

Surgery is the main method for the treatment of Krokodil drug-related ONJ patients (Poghosyan et al., 2014). Low rates of recurrence are found in patients with drug withdrawal (minimum 1 month prior to surgery) and following jaw resection for a minimum of 0.5 cm into healthy tissue (Poghosyan et al., 2014). After surgery, recurrence of disease was seen in 23% of cases in the mandible, with no cases of recurrence in the maxilla.

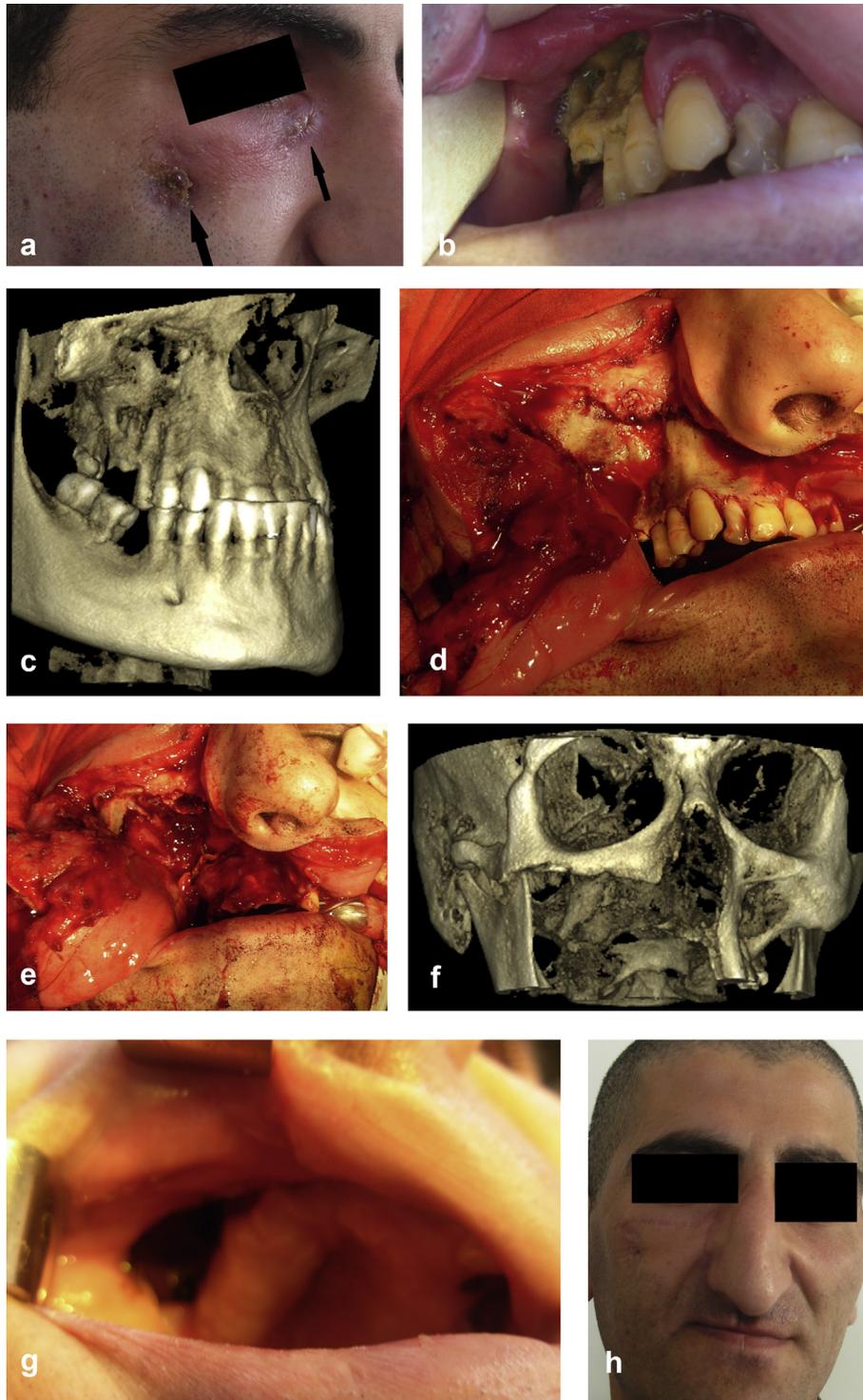


Fig. 1. Case 1. Patient with Krokodil drug - related ON of right midface a) extraoral view of the patient, fistulas with purulent discharge are shown (black arrows); b) intraoral exposure of distal maxillary alveolar process; c) preoperative 3D reconstruction of CBCT images, clear demarcation is seen; d) intraoperative view, clear demarcation of necrosis zone is seen; e) intraoperative view after surgical resection, large defect of right midface is seen; f) postoperative 3D reconstruction of CBCT images, large defect of right midface is seen; g) 8 month postoperative intraoral view, large oroantral communication is seen, without ON recurrence; h) 8 month postoperative extraoral view, no signs of disease recurrence are seen.

Some patients restart the use of Krokodil after treatment. In these patients the formation of the new ON lesions may occur in previously operated zone of the maxilla. If this new maxillary ON lesion is not treated, zygomatic bone and other adjacent bone structures may be involved, and midface osteonecrosis may

develop. Zygomatic bone involvement may also occur after untreated maxillary ON (Hakobyan, 2013; Medvedev et al., 2016). Primary midface ON is rare (only one case in our practice). Krokodil drug-related ON of the midface is a new stage of facial bone osteonecrosis. It has a specific clinical course, and diagnostic and

treatment approaches different from those of maxillary ON. The main clinical feature of midface ON is extraoral fistula in the mid-facial zone with purulent discharge or extraoral exposure of zygomatic bone. Edema and redness of infraorbital and malar regions may also be found. Intraorbital abscess may occur in case of pus drainage failure intra- or extraorally.

The intraoral view depends on the previous treatment, if:

- midface ON is the result of the recurrence of the previous surgery on maxilla, there is a maxillary defect of different size, granulation tissue growth, and exposure of different bone structures (inferior wall of orbit, maxillary tuber, nasal septum etc.).
- midface ON is the result of the complication of the untreated maxillary ON, the intraoral view is according to the maxillary ON.
- there is a primary midface ON, maxillary alveolar process may be intact.

Depending on the periods of the disease onset and Krokodil drug withdrawal on CBCT images, the following signs may be found:

- no demarcation of ON zone
- demarcation of ON zone
- formed sequestrums in affected area.

Usually there is a combination of these three findings due to the complex anatomy of the midface and the different periods of the disease onset in different areas. When there is no demarcation it is difficult to plan the bone volume which needs to be removed. Thus, there may be cases when the total necrosis zone can be identified only intraoperatively. This may make the surgery planning more difficult, especially when the orbital floor and skull base are involved.

Surgery is the main method of treatment for Krokodil drug-related midface osteonecrosis. Surgery includes necrotic bone removal and defect closure. Usually an extraoral approach is used to

expose necrotic bone. Intraoral maxillary sinus floor defect is often formed. The use of a buccal fat pad is an effective method to prevent formation of oroantral communication. Due to different problems, many patients reject surgery. However, a few patients underwent surgery with a successful result.

4. Conclusion

Drug withdrawal, radical necrectomy and proper closure of formed defects are the main factors that lead to successful treatment of Krokodil drug-related midface ON patients.

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Conflict of interest

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References

- Basin EM, Medvedev YuA: Principles of maxilla osteonecrosis in patients with drug abuse. *Pac Med J* 1: 87–89, 2013
- Hakobyan KA: Clinical picture, diagnosis and treatment of facial bones osteonecrosis at patients who use the drug 'Krokodil'. Yerevan State Medical University, 2013 Dissertation
- Hakobyan KA, Poghosyan YuM, Poghosyan AYu: C-terminal telopeptide level in «Krokodil» drug-related jaw osteonecrosis patients. *New Armenian Med J* 11(3): 57–61, 2017
- Malanchuk VA, Kopchak AV, Brodetsky IS: Clinical features of jaw osteomyelitis in drug addicted patients. *Ukr Med Jour* 4(60): 111–117, 2007
- Medvedev YuA, Basin EM, Serova NS, Korshunova AV, Babkova AA, Kureshova DN: Total jaw osteonecrosis among drug addicts. *Rossiyskiy stomatologicheskij zhurnal* 20(4): 183–189, 2016
- Poghosyan YM, Hakobyan KA, Gasparyan LL: Radiographic diagnosis of jaw osteonecrosis at patients who use the drug 'Krokodil'. *Issue Theor Clin Med* 2(78): 44–47, 2013
- Poghosyan YM, Hakobyan KA, Poghosyan AY, Avetisyan EK: Surgical treatment of jaw osteonecrosis in 'Krokodil' drug addicted patients. *J Cranio Maxillo Facial Surg* 42: 1639–1643, 2014
- Tymofeiev AA, Lesova IG: Phosphoric necrosis of jaws at narcodependent patients using substitute awareness-inducing "Screw". *Mod Stomatol* 5(49): 94–98, 2009