

Up-to Date Review And Case Report

Avascular osteonecrosis of the premaxilla secondary to disseminated intravascular coagulation: a case report

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Abstract – Introduction: Disseminated intravascular coagulation (DIC) is a complex systemic disorder characterized by a widespread activation of the coagulation, that may lead to thrombosis, ischemia and finally, end-organ failure. The clinical presentation of DIC depends on the site of intravascular coagulation and the severity of the disease process. Avascular osteonecrosis is a pathological state, that can occur secondary to DIC and where a reduced vascular supply leads to ischemia and bone necrosis. **Observation:** A 83 years old patient was sent to the oral surgery department for tooth mobility in the premaxilla, following the diagnosis of sepsis and DIC induced acute myeloid leukemia, one month ago. The examination showed an exposed avascular bone behind the 12-11-21. A diagnosis of DIC induced osteonecrosis of the premaxilla was made. A resection surgery was then programmed. **Discussion:** DIC may generate thrombi that might occlude intraosseous vessels in the premaxilla, and lead to bone necrosis. The maxilla is supplied by multiple branches of external carotid artery, therefore, usually, there is a lower risk of osteonecrosis in the maxilla. Nevertheless, since 1993, 4 cases of avascular necrosis of the maxilla secondary to DIC are reported in literature. **Conclusion:** This kind of complication, although being rare, can be dramatic for the patient as bone and aesthetic defects. Early support and management of these complications is necessary.

1 Introduction

Disseminated intravascular coagulation (DIC) is a complex systemic disorder characterized by a widespread activation of the coagulation cascade, that may lead to thrombosis, ischemia and finally, end-organ failure. This may occur from the extrinsic or the intrinsic pathway. DIC can be the consequence of various underlying disease, such as major trauma, head injuries, infections and metastatic neoplasm [1].

The clinical presentation of DIC depends on the site of intravascular coagulation, the severity of the disease process and whether haemodynamic instability occurs predominantly from vascular obstruction or haemorrhage.

End organ failure occurs due to local fibrin thrombus formation that may embolize and obstruct the microcirculation. If the occlusion is proximal and no central circulation exist, ischemia may lead to end-organ failure.

Avascular osteonecrosis is a pathological state where a reduced vascular supply leads to ischemia and bone necrosis. This has been reported in orthopedic literature [2,3] but only few cases described maxillary bone necrosis, in particular secondary to DIC. With regard to the oro-maxillo-facial sphere,

avascular necrosis of the midface is a rare condition due to rich blood supply from the bilateral branches of the external carotid artery [4].

However, as DIC is mostly a vital emergency and because of its major symptoms in early stage (multiple organ dysfunction, massive haemorrhage), the oral consequences are often diagnosed later and may lead to major bone defect.

2 Observation

A 83 years old patient was admitted at the emergency department, for a severe alteration of general state with anorexia since one week. Patient's record indicates no history of medical trouble or surgery. The first examination showed a dyspnea stage III of the New-York Health Association, hypothermia at 36.5 °C. The blood pressure was 139/56. There was no evidence of chest pain, oral hemorrhage, weightloss or sign of shock.

Blood test were performed and showed a platelet count at 23 G/L, white blood cell at 246 G/L, hemoglobin at 6.8 g/dL, D-dimer over than 20 000 ng/L, fibrinogen at 3.7 g/L, C-reactive protein level at 120.5 mg/L, Protein C at 2.7 µg/L, a prothrombin time of 61s, and an international normalized ratio (INR) of 1.61.

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Fig. 1. Orthopantomographic showing moderate generalized alveolar bone loss.

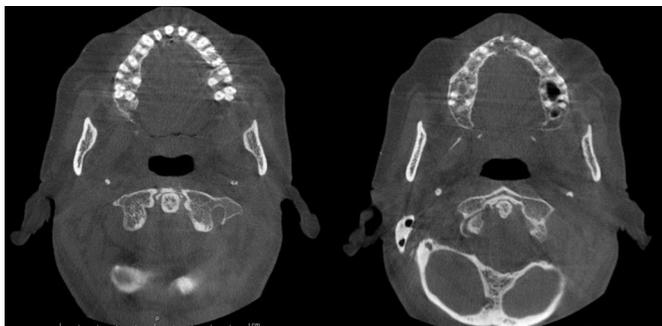


Fig. 2. Computer tomographic views in axial section showing the osteonecrosis.

A diagnosis of Acute Myeloid Leukemia was made over the abnormally high white blood cells count, and low platelet level [5].

Besides, a sepsis was suspected, given the alteration of general state, dyspnea, hypothermia, abnormal white blood cell count, and elevated plasma level of C-reactive protein. Blood culture confirmed the diagnosis, being positive to *E. Coli* (anaerobic bacteria) [6].

Furthermore, there was many signs that showed underlying DIC: low platelet count, diminution of prothrombin time, increased level of D-Dimer (fibrin split products), low concentration of protein C [1].

She was immediately transferred to haematologic department, and received two globular pellets, and a platelet concentrate transfusion. She was treated under ceftriaxone 2g per day and cytarabine, with a positive evolution 3 days later of the thrombocytopenia (platelet count at 56 G/L), acute myeloid leukemia (white blood cell at 23 G/L) and DIC (diminution of D-Dimer).

Three weeks later, the patient complained about tooth mobility in the premaxilla region, with discrete gum haemorrhage. Nevertheless, the patient did not complained about any pain. She was sent to the oral surgery department.

The interrogation did not report history of any systemic or prolonged disease, any trauma, long term corticotherapy, bisphosphonate, denosumab or anti-angiogenic treatment, radiotherapy, recent extraction or dental care. There was also no history of any drug allergy.

The extra oral examination did not reported swelling or fistula over the maxilla.

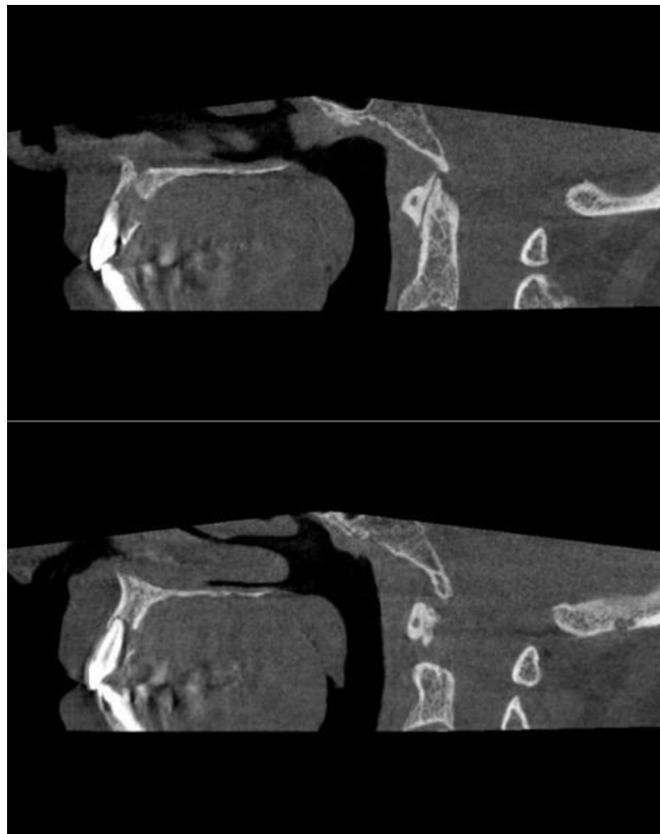


Fig. 3. Computer tomographic views in sagittal section showing the osteonecrosis.

The intra oral examination showed an exposed avascular bone behind the maxillary incisors and canines, clinically visible. It was 2 cm long. This bone was firm, brown, and asymptomatic. It was tenderness to touch and associated exsudate was not exhibited. The upper incisors were grade III mobile, and exquisitely tender to percussion. All of the involved teeth were vital. Probing was positive all around the anterior maxillary alveolar bone, showing peeling of the periosteum, even if oral hygiene was good with a healthy and stable periodontium.

Orthopantomographic radiographic showed a partially dentate adult dentition, a generalized moderate horizontal bone loss, and an angular periodontal bone loss located to the 24, 25 and 26 (Fig. 1).

A cone beam computer tomography showed the extent of osteonecrosis, which was from right lateral incisor to left lateral incisor (Figs. 2 and 3).

A diagnosis of osteonecrosis was made over the clinical examination. The diagnosis of ulcero-necrotic periodontitis was dismissed because of the peri-osseous probing, the good hygiene, the missing pain and absence of signs of ulcero-necrotic gingivitis (healthy and safe papillas). DIC was assumed to be responsible for the osteonecrosis, given that no other possible causes were present (radiotherapy, denosumab, bisphosphonate, long term corticotherapy, anti-angiogenic treatment).

Since the tooth mobility hindered the diet, and because it represented a potential infectious lesion, not compatible with current myeloid leukemia and chemotherapy, resection

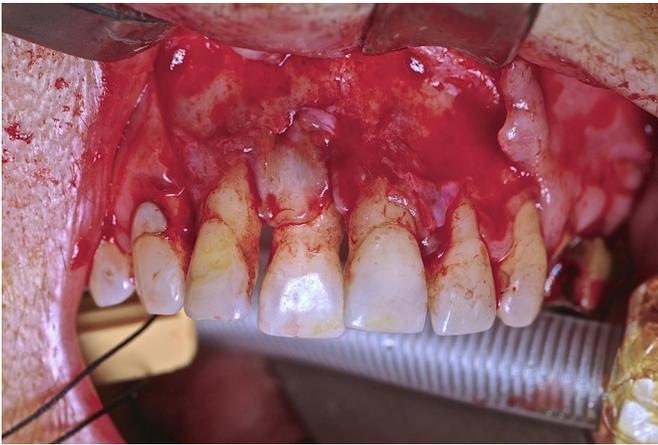


Fig. 4. Vestibular view after realising the flap.

surgery was then programmed under general anesthesia. However, by the time of the surgery, the bone defect had already been naturally expelled. The surgery consisted on large flap from canine to canine, with distal discharge (Fig. 4). The surgical access showed disappearance of the vestibular and palatal cortical bone around 12-11-21-22. The incisive bloc was extracted (12-11-21-22) as well as the first upper left premolar and the first lower right molar's root, which were not in good condition (active carious lesion). A large debridement was initiated. Sutures were then done to close the flap, with a vicryl 3/0 floss (Fig. 5). As the osteonecrosis bone had already been expelled, no anatomic-pathological analysis was able to be performed. The surgery was completed with an antibiotherapy (amoxicilline 3 g per day for 10 days), an analgesic treatment (paracetamol 1g, 4 per day, tramadol 50 mg 4 per day) and an antiseptic treatment (chlorhexidine 0.2% 3 times a day). The patient was seen at J1, J7, J15, one month later and two month later.

There was a positive evolution with good healing, few pain and no gum haemorrhage.

Three month later, although there was a positive response to chemotherapy during first days the patient passed away because of myeloid leukemia.

3 Discussion

DIC is a systemic complex disorder characterized by a widespread activation of the haemostasis system, that may generates to thrombosis and ischemia of organs and soft tissues. The depletion of clotting factors, platelets and fibrinogen lead to massive haemorrhage, and secondary, activation of the plasminogen pathway.

This can occur *via* the extrinsic pathway, through the activation of thromboplastin and factor VII, or by the intrinsic pathway, where vascular damage secondary to trauma, local tissue injuries or gram negative sepsis (such as E. Coli) can activate factor VIII [7].

The diagnosis of DIC is commonly made by a combination of Platelet count, D-Dimer, fibrinogene and INR levels on biochemistry.

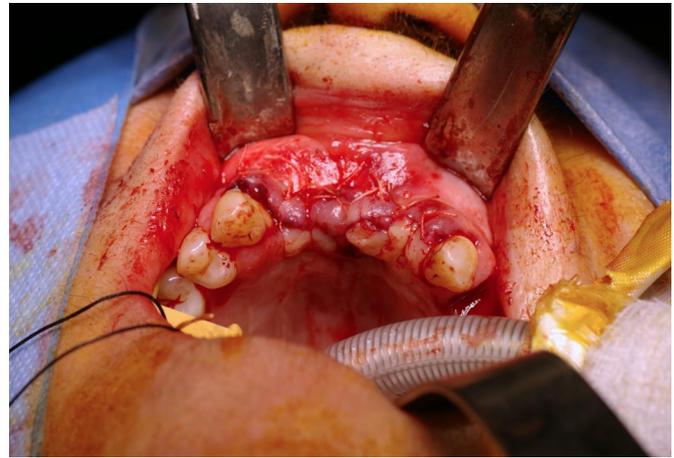


Fig. 5. Endobuccal view of the surgery site after closing.

It is well-known that some underlying disease, such as malignant neoplasm, infection, injuries burn and shock may lead to DIC [8]. DIC can be triggered by modification of bone marrow function, and chemotherapy. In other patients, it can result from a severe systemic inflammatory response syndrome caused by a sepsis. In those with a severe infection, DIC may have developed from the hypercoagulability causes by abnormal high activity of inflammatory chemical mediator [8].

With regard to end-organ dysfunction, the kidney are most commonly affected, followed by hepatic, respiratory and central nervous system [9].

In the present case, the supposed mechanism responsible for osteonecrosis of the premaxilla is thought to be DIC, causing microvascular thrombi. These thrombi occlude intraosseous vessels in the premaxilla, and lead to bone necrosis. The maxilla is supplied by multiple branches of external carotide artery, such as the ascending pharyngeal artery, lesser and greater palatal arteries and alveolar branches of the maxillary artery [10]. Therefore, usually, there is a lower risk of osteonecrosis in the maxilla.

In the present case, the osteonecrosis is supposed to be secondary to the occlusion of the naso-palatal artery, considering the localisation of the bone defect. However, no doppler was performed to confirm this hypothesis.

Orthopedic literature suggested that unless there is a colateral vascularisation, osteoblast and osteocytes become hypoxic and undergo apoptosis, leading to osteonecrosis [11].

Experimental models of bone necrosis, described in orthopedic literature, implicate venous occlusion as a precipitating event, with subsequent increased intraosseous pressure, reduced arterial inflow, ischemia and infarction [12].

Indeed, histologic findings in nontraumatic osteonecrosis usually reveal thrombosis of terminal arteries in subchondral bone, which, due to few collaterals of the arteries, can trigger progressive involvement of venules, veins and arterioles [10].

Although there are some experimental animal models found in literature, the physiopathologic mechanism of bone necrosis secondary to DIC is not yet well understood.

The diagnosis of osteonecrosis was established on the clinical and radiographic finding. Unfortunately, no anatomopathologic analysis could be performed to confirm the diagnosis.

Osteonecrosis may be defined as septic or aseptic. Septic osteonecrosis can occur from a bacterial, viral (herpes zoster), or fungal source (mucormycosis, aspergillosis) [10]. This kind of osteonecrosis may be seen in immunocompromised patients, including those with long term corticotherapy, immunosuppressants, or chemotherapy, and malignancies [10].

In literature, trauma as been described as a frequent cause of osteonecrosis in the maxilla [13–15]. In the present case, no history of trauma was noted, although it is one of the most common cause of nontraumatic osteonecrosis.

To the authors knowledge, from 1993 to 2018, there are only 8 cases reported in the literature about avascular necrosis following disseminated intravascular coagulation (research *via* the Mesh Browser: osteonecrosis + disseminated intravascular coagulation. Data base used were: Pubmed, Cochrane library and Science direct) [4,9,16–21]. Among those 8 cases, 4 concerned the oro-maxillo-facial area, and particularly the premaxilla.

Jagdip Singh Kalsi described in 2012 a case of osteonecrosis in the premaxilla following meningococcal-induced disseminated intravascular coagulation [4]. In 2013, Cooper related a case of Varicella complicated by group A beta-hemolytic streptococcal sepsis and disseminating intravascular coagulation associated with osteonecrosis of the mandible in a 2 year old patient [16]. In 2014, Nguyen described a case of avascular necrosis of the midface secondary to disseminated intravascular coagulation induced by a severe heat stroke, in a 29 year-old man, with no known comorbidities [2]. Indurkar reported in 2015 an unusual bone necrosis of the jaw, associated with dengue fever and periodontitis induced DIC [17].

In these last cases, the diagnosis of avascular bone necrosis secondary to DIC is delayed (from 6 months to 15 months) contrary to our present case, in which, the diagnosis is made over one month. However, because of the primary serious symptoms of DIC, the consequences of it, particularly in the oro-maxillo-facial area are not observed in the early stage, their diagnosis and treatment are often delayed and the results can be fatal, with major bone defect.

In the present case, and besides the serious alteration of the patient's general state (acute myeloid leukemia and current chemotherapy), resection surgery was programmed because osteonecrosis bone was a potential infectious lesion. Furthermore, tooth were grade III mobile and a periodontal splint would not have been sustainable.

The few cases presented in literature showed that dental and more generally oro-maxillo-facial complications can occur secondary to DIC. A special attention must be paid to orodental symptoms as soon as they appear, in order to avoid serious complications and defects, whether they are aesthetic or functional.

4 Conclusion

The oral management of a 83 year old patient presenting an avascular necrosis secondary to sepsis and acute myeloid leukemia induced DIC is reported. Considering the general state of the patient and its underlying disease, we focused on the eradication of possible infectious lesion. The physiopathology of osteonecrosis following DIC is not yet well understanding, and only few similar cases are reported in literature. Early detection and management of oro-maxillo-facial complications is necessary for patient who had suffered from a severe DIC, and may help to prevent the need for invasive surgery and complex treatment.

Conflicts of interest: The authors declare that they have no conflicts of interest in relation to this article.

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