FIRST CASE OF CANCRUM ORIS (NOMA) IN AN HIV-POSITIVE PATIENT IN BULGARIA

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Abstract. We present a case of a necrotising disease of the orofacial tissues, the so-called noma, in a female patient with AIDS in a stage of severe immune deficiency. To our knowledge, this is the first time a case like that has been reported in Bulgaria. The patient received an antibiotic course of treatment with a triple combination to good effect on the inflammatory process, and began also HAART. Within 3 weeks, the patient's general condition improved. However, despite the treatment, a demarcation line was formed, and a defect on the lower lip occurred. Noma is a manifestation of severe immune deficiency with lasting adverse consequences for the patient: severe deformation of the maxilo-facial region and functional impairment (i.e. difficulties eating and speaking, and salivary leak).

Key words: HIV, noma, immune deficiency, facial disfigurement

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INTRODUCTION

The term “noma” (cancrum oris) has been derived from the Greek word “*nomen*”, which means “to devour” [1]. It is a gangrenous disease affecting the tissues of the mouth, which as a rule begins as a catharrhal or fibrous gingivitis, followed by necrosis of the mucosa and submucosa of the mouth, jaws, and periodontium [2, 3, 4]. Noma occurs mainly in children below the age of 6 years. Risk factors include social and demographic status, malnutrition, compromised immune system, and factors pertaining to microorganisms (viral and bacterial) [5]. Noma is not transmitted from one person to another; it is not a contagious disease [6]. The worldwide incidence is between 100,000 and 140,000 persons per year [6, 7]. The disease is an important health problem in countries with malnutrition. The majority of the cases occur in Africa: across Western and Central Africa, and especially in Nigeria and Senegal. Noma

affects also children in Latin America and Asia. It has been a common disease in Europe until the end of the 19th century. With improvements in hygiene and nutritional status, throughout the 20th century noma has altogether disappeared in developed countries, except for the cases in the concentration camps of Bergen-Belsen and Auschwitz during World War II [4, 8]. However, over the past two decades, there has been an increase in the incidence of noma in association with immunosuppressive therapy, and in patients with HIV infection and AIDS [4, 9, 10, 11]. The so-called noma-like lesions are a form of the disease that occurs in immunocompromised adults, manifested by the typical orofacial lesions seen in noma [12].

The disease is localised in parts of the body exposed to direct contact with the external environment on which a bacterial infection has been superimposed. The ischaemia caused by the obstruction of the vessels contributes to the development of necrosis [6,

14]. Noma is a polymicrobial opportunistic infection. Currently, there is no consensus regarding the causative microorganisms. *Atopobium* spp., *Prevotella intermedia*, *Peptostreptococcus* spp., *Streptococcus pyogenes* and *Streptococcus anginosus*, *Fusobacterium necrophorum* present a relatively high proportion among the microorganisms associated with the development of noma lesions [19].

The orofacial lesion develops unilaterally in most cases, and rarely bilaterally [4]. The first signs of the disease are the red swollen gums that bleed upon touching or during the brushing of the teeth [14]. The next stage comprises spontaneous bleeding of the gums and painful ulceration, surrounded by hyperaemia and covered with whitish exudate. This ulceration involves one or more interdental papillae. There are also halitosis and excessive salivation. Necrotising ulcerative gingivitis (NUG) develops. NUG, together with necrotising ulcerative periodontitis (NUP) with destruction of the ligaments anchoring the teeth in their sockets, and with necrotising stomatitis, when NUP progresses into the tissue beyond the mucogingival junction, are believed to be noma precursors [10, 15, 17]. The global incidence of HIV/AIDS-associated NUG is approximately 16% [18]. Within a few days, the necrotising infection extends rapidly into the intraoral mucosa, and facial oedema appears. Other features at this stage include soreness of the lips or cheeks, difficulty eating, halitosis, fever, excessive salivation, lymphadenopathy, anorexia. The oedema stage lasts one or two weeks. At this stage, noma could still be seized [15, 16, 17]. The necrotic process leads to extensive destruction of the intraoral soft and hard tissues [10, 15]. A line of demarcation develops along the border between the gangrene and the healthy tissue. This demarcation of the gangrene is followed by a separation of the necrotic tissue, which leaves a hole in the face [15, 16]. As a result, we can see facial disfigurement, sequestration of teeth and bones, trismus, difficulty eating and speaking, salivary leak, nasal regurgitation [15, 17]. The mortality rate without treatment is 90% [13]. The patients die of sepsis, malnutrition, and/or dehydration [6].

CASE PRESENTATION

We present the case of a 27-year-old woman who was proved as HIV- positive in 2012. The patient was of Roma origin, and had received no antiretroviral therapy (ART) prior to the current admission due to non-attendance of the respective appointed visits to the Department. However, she did have a previous hospitalization at the Department for Immune

Deficiency in December 2012 because of left-sided pneumonia with reactive pericarditis. The patient belonged to a risk group intravenous drug users (IVDU), and had a hepatitis C virus (HCV)-coinfection. The reasons for the current hospitalization were complaints of fatigue, pain, and inflammatory changes in the buccal mucosa and the lower lip, whose onset was approximately ten days prior to the admission (Fig. 1).

Fig. 1. The patient 10 days prior to admission

Upon admission, the patient had evidence of cachexia, left-sided pneumonia, a gangrenous inflammatory process of the oral cavity and the lower lip, and oropharyngeal candidiasis. The examination of the local status revealed buccal mucous membranes with whitish pockets and suppurative secretion. In the area below the lower lip, a longitudinal fissure with a pharyngeal secretion was visualized upon the inner and the outer surfaces (Fig. 2).

Fig 2. The patient upon admission. The examination of the local status revealed buccal mucous membranes with whitish pockets and suppurative secretion. In the area below the lower lip, a longitudinal fissure with a pharyngeal secretion was visualized upon the inner and the outer surfaces

The laboratory tests (haematological and biochemical) revealed the following pathological findings: anaemia (haemoglobin of 93 g/l, erythrocyte count of $4.59 \times 10^{12}/l$, MCV of 91.9 fL), and slightly elevated liver enzymes (ASAT of 90 U/l; ASAT of 86 U/l). As far as the immunological and virological parameters were concerned, an extremely severe immune deficiency (a CD-4 count of 5 cells/mm³, a CD-8 count of 206 cells/mm³, a CD4/CD8 ratio of 0.02), and a high viral load (VL) of 567,552 copies/ml were particularly worth noting.

The microbiological examinations found significant amounts of *Candida albicans* in the nasal secretions, with no other pathological microorganisms from the throat swab, sputum, urine, and feces. The radiological examination of the lungs and heart showed inflammatory infiltrates in the left upper and middle pulmonary fields.

Antibiotic therapy was administered with a combination of Ceftriaxone, Amikacin, and Metronidazole, followed by Clyndamycin. The patient began antiretroviral therapy with Emtricitabine/Tenofovir Disoproxil fumarate + Darunavir/Cobicistat.

During the hospital stay (22 days), the overall condition of the patient improved, and so did the inflammatory changes in the pulmonary parenchyma. As to the local status, the inflammatory changes subsided, but a wide demarcation line along the lower lip with a minimal peduncle on the right side persisted. The lower lip remained vivid, pale, and pink. Between the lip and the skin of the chin there was granulation and a defect, 5 cm in size (Fig. 3). In addition to the facial deformations present, there were also problems with talking and the intake of liquids and food.

Fig. 3. Following the antibiotic treatment, the inflammatory changes subsided; however, a wide demarcation line along the lower lip with a minimal peduncle on the right side persisted. The lower lip remained vivid, pale, and pink. Between the lip and the skin of the chin there was granulation and a defect, 5 cm in size

Eight months later, the patient was in good overall condition. The oral defect had been filled, but the

lower lip remained deformed (Fig. 4). The laboratory tests revealed a persisting anemia, with no other abnormalities in the laboratory work-up. The patient had achieved optimal viral suppression (a viral load < 40 copies/μl) and good immunological response (CD4: 132 cells/μl; CD8: 906 cells/μl; ratio CD4/CD8: 0.15).

Fig. 4. The patient at eight months follow-up. The oral defect had been filled, but the lower lip remained deformed

DISCUSSION

As mentioned in the introduction, the causative agent of noma remains unclear. It has been known that there is an association between noma and factors such as malnutrition, a compromised immune system, and infection of the oral cavity [4, 17]. In our patient, a specific cause was not established either. Other related factors include poor environmental sanitation, unsafe water supply, and dehydration [17]. Our patient (representative of the Roma population) lived in poor sanitary conditions and exhibits signs of malnutrition, as well. A combination of immune deficiency and poor oral hygiene has also been associated with the onset of the disease. Our patient had extremely advanced immune deficiency. Heroin addiction and HCV co-infection are essential aggravating factors. The patient also developed typical signs of the process described in the scientific literature [10, 15, 16, 17]: necrotising ulcerative gingivitis (NUG), necrotising ulcerative periodontitis (NUP), and necrotising stomatitis. The necrotising process extended rapidly into the mucosa and the submucosal tissue with destruction of the latter. A line of demarcation was formed. That zone of inflammatory reaction separated a gangrenous area from the healthy tissue. A lower lip defect was established. In accordance with literature data [15, 17], feeding difficulties, speech problems, and salivary leak occurred.

The treatment depends on the stage of the inflammatory process. The progress of this necrotising process required the use of broad spectrum antibiotics, correction of the dehydration and the electrolyte balance, analgesics, appropriate nutrition, and disinfection measures, i.e. mouthwashes. A triple course of antibiotics was given to our patient. Several teeth

were extracted. After a period of at least 6 to 18 months, surgical correction should be initiated.

The cases of noma in adults are less frequent. There are few publications which demonstrate the development of noma in patients with HIV/AIDS [20]. Acute necrotising gingivitis and acute necrotising periodontitis (observed in our patient), considered precursors of noma, are among the seven cardinal oral manifestations of HIV infection together with oral candidiasis, hairy leukoplakia, Kaposi sarcoma, linear gingival erythema, and non-Hodgkin lymphoma. The formation of lesions runs parallel to the drop in CD4+ T-cells' levels and the increase in HIV viral load, which are independent indicators of disease progression [20, 21, 22]. HIV-positive patients tend to have a deregulated cytokine profile, a decrease in Langerhans cells' counts, and progressive loss of cell-mediated immune response [23]. As a result, there is a deregulation of the immune responses to oral microorganisms. All this contributes to the development of a necrotising process in the oral cavity [12, 16]. The cases described in the literature have been observed in patients with advanced immunodeficiency, as was the patient we presented. In conclusion, although infection with HIV could be a predisposing factor, there are other factors such as poverty, malnutrition, comorbidity, recurrent infections, etc., that could contribute to the development of the disease.

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