Literature Review

Noma: a neglected tropical disease

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ABSTRACT

Background: Noma is an orofacial gangrene often manifesting in malnourished children in developing and tropical countries. Epidemiological data on noma are hard to find, but it is estimated that the global incidence of noma is 30-40,000 cases per year, with estimated mortality rate of about 85%. **Purpose:** To discuss the pathogenesis, diagnosis, prevention, and treatment of noma. **Literature review:** The cause of noma is multifactorial, but is often found in conjunction with malnutrition and with other diseases such as measles, malaria, and the human immunodeficiency virus (HIV), along with poor oral hygiene. The pathogenesis of noma includes a rapidly spreading noninfectious gangrene infection of the face, often preceded by acute necrotizing gingivitis, and stomatitis. Microbiological studies show opportunistic infections caused by imbalance of normal intraoral microorganisms. The key to prevention is to increase food hygiene, improving vaccination program against measles, prevention of malaria and HIV, and early detection and treatment of necrotic gingivitis and stomatitis. Early treatment with antibiotics can prevent gangrene formation or reduce the extent of the lesions. Late treatment consists of surgical rehabilitation, which is often hard to conduct. **Conclusion:** Noma is an infectious disease that can cause wide gangrenous wounds. Recognizing and understanding the symptoms and characteristic signs of noma is important so that comprehensive prevention and management can be given as early and optimally as possible to provide complete recovery for patients.

Keywords: noma, neglected tropical disease, orofacial gangrene, acute necrotic gingivitis

ABSTRAK

Latar belakang: *Noma adalah gangren orofasial yang menyerang anak-anak kekurangan gizi terutama di negara-negara berkembang dan negara-negara tropis. Data epidemiologi tentang noma sangat langka, tetapi perkiraan kejadian global saat ini adalah 30-40.000 kasus per tahun, dengan tingkat kematian sekitar 85%.* ***Tujuan:*** *Membahas patogenesis, diagnosis, pencegahan, dan tatalaksana noma.* ***Tinjauan pustaka:*** *Penyebab noma multifaktorial, namun sering ditemukan bersamaan dengan malnutrisi dan dengan penyakit lain seperti campak, malaria, dan* human immunodeficiency virus (HIV). *Sering pula terjadi bersamaan dengan higiene mulut yang buruk. Patogenesis noma meliputi infeksi gangren tidak menular, yang menyebar cepat di daerah wajah, sering didahului oleh gingivitis nekrotikans akut, dan stomatitis. Studi mikrobiologi menunjukkan adanya infeksi oportunistik yang disebabkan oleh ketidakseimbangan mikroorganisme intraoral normal. Pencegahan dapat berupa nutrisi yang baik, vaksinasi campak, pencegahan malaria dan HIV, termasuk deteksi dini dan pengobatan gingivitis nekrotikans dan stomatitis. Pengobatan dini dengan antibiotik dapat mencegah terjadinya gangren atau mengurangi luasnya lesi. Perawatan lebih lanjut berupa rehabilitasi bedah, yang seringkali tidak mudah dilakukan.* ***Kesimpulan:*** *Noma adalah penyakit infeksi yang dapat menimbulkan defek luka gangren luas. Penting untuk mengenali dan memahami gejala serta tanda karakteristik noma, sehingga pencegahan dan tatalaksana secara komprehensif dapat diberikan sedini dan seoptimal mungkin, agar dapat memberikan kesembuhan sempurna untuk pasien.*

Kata kunci: *noma, penyakit tropik terabaikan, gangren orofasial, gingivitis nekrotik akut*

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INTRODUCTION

Noma (cancrum oris) is orofacial gangrene that often occurs in malnourished children in developing countries who are simultaneously affected by various other diseases. The mortality of patients with noma is very high and those who survive often suffer from severe facial deformities. This often results in people with noma being ostracized by society and their families. The epidemiology, pathophysiology, and etiology of this disease are still often debated even though this disease has existed since ancient times.[1,2]

Noma is a disease that has been known to mankind for a long time. Many classical writers in the United States and Europe had often wrote or described about this disease. At the end of the 19th century, cases of noma began to decrease and disappear from Europe and the United States as the welfare of the people on these two continents continued to improve.[3] In the 20th century, cases of noma became increasingly common, while bacteriologists at that time still struggled to find a definite organism causing this disease. In 1912, Steward finally discovered that noma was not caused by a specific infection, but opportunistic infection of normal flora in the mouth.[4] Shortly after the discovery of sulfonamides and penicillins in the 1940s, antimicrobial therapy was successful in reducing the mortality of the disease from about 85% to 15%. On the other side of treatment, concepts regarding reconstructive surgery for noma had only started to be developed about 50 years ago.[5]

The purpose of this review is to discuss causes, risk factors, prevention, pathogenesis, diagnosis, and treatment of noma.

LITERATURE REVIEW

Epidemiology

Most noma cases are reported in children between the age of 2-7 years living in Africa (mainly in the harsh environment of sub-Saharan Africa). Noma cases are also often found in very poor countries with very low rates of measles vaccination.[6] The incidence of noma globally is assumed around 30,000-140,000 people. With a survival rate of about 15%, and an estimated life expectancy of about 40 years, it is calculated that the global number of survival of the disease is over 210,000 people.[2,7,8] Many noma cases are not recorded nor even get medical services due poor health systems, lack of knowledge of noma, negative stigma, and abandonment of patients with this condition. Children with noma often die without a definitive diagnosis, health care services, and without a death record. This happens due to the fact that noma often struck the poorest children in remote areas without good health service and medical staff's low knowledge of the disease.[2]

The risk factor for noma continues to increase due to economic inequality, lack of food, hunger, malnutrition, climate change, immune-compromising disease (HIV), and ignorance. The estimated mortality rate for noma is around 85%, as most children with this condition could not get medical services. Incidence and mortality data in three different sub-Saharan countries show that the noma accounts for 0.5–3% of mortality in children.

Worldwide, it is estimated that about 0.5% of children may die from noma.[1]

In Indonesia, there were several publications reported the incidence of noma. One case report wrote about a patient of noma with non-Hodgkin lymphoma in Bandung.[9] One case was also found in a child from the Korowai tribe in Asmat district, Papua. In this 5 year old child, risk factors such as malnutrition and poor oral hygiene contributed to the occurrence of noma.[10] Because the case is rarely found in Indonesia, it could be possible that cases of noma will be unidentified due to lack of knowledge about this disease.

Figure 1. Patient with noma from Afimabul village, Asmat district, Papua.[10]

Etiology, risk factors, and microbiology of noma

Noma occurs due to plenty of causes. One of the prerequisites for the occurrence of noma is malnutrition, which often occurs due to extreme poverty. However, in some cases other factors were also found, such as several concomitant diseases, and gingivitis that occurred due to poor oral hygiene. Malnutrition is often closely related to immunity, which in turn can cause nutritionally acquired immune deficiency syndrome.[11] Noma was also found to be very prevalent in preterm infants and babies born with low body weight. The timing of noma's occurrence can be correlated to the nutritionally susceptible condition present during the weaning period, which obviously presents higher threat to underweight babies. It is also important to note that the weaning period is usually associated with the onset of diseases that weaken and cause immune disorders (such as malaria and measles).[12]

Social factors also play an important role in the emergence of noma, especially those with large families, or mothers who have a large number of children and poor nutritional status. There is a possible correlation between the incidence of noma and maternal malnutrition during pregnancy. This may be related to the increased likelihood of preterm birth and the likelihood of an underweight baby leading to chronic malnutrition, and thus inducing noma. In addition, several types of diseases have also been found that are closely related to the incidence of noma, this includes malaria, typhus, measles, chickenpox, tuberculosis, and HIV.[13] Malaria and measles were the diseases most frequently reported before the onset of noma. Both diseases often occur during weaning and have serious immunosuppressive effects. Lack of oral hygiene can also lead to the appearance of necrotizing gingivitis which is characterized by the presence of periodontal pathogens which sometimes cause the appearance of noma.[14,15]

There are several species of bacteria which often linked with noma due to the rapid evolution of the disease and the odor emitted from the lesions, such as *Borrelia vincenti* and *Fusobacterium fusiformis*.[16] Another theory suggests the etiology of noma as an opportunistic multifactorial that occurs in the presence of relatively normal oral flora in chronically malnourished children.[13] Other studies have shown that there is an imbalance between the normal oral flora and reduced bacterial diversity in general. In acute noma cases there were often found a reduction in *Capnocytophaga* and *Fusobacteria genera* accompanied by an increase in the bacteria of the genus *Prevotella*.[13,17] *Prevotella intermedia* is a bacterium that is well known as a periodontal pathogen in adults, and can even be detected in primary teeth in young children. These bacteria are common in

purulent oral infections and in secondary nosocomial infections.[17,18] It should also be noted that *P. intermedia* usually co-exist with other pathogens and has never been reported as a single infectious agent. Hence the proliferation of *P. intermedia* in noma lesions is likely a consequence of changes in local ecological conditions that occur as the disease progresses.[13,18]

Pathogenesis and clinical stages

Noma is a gangrene disease in children that rapidly damages the soft and hard tissues of the face. Subsequently, this will lead to massive destruction of facial structure which causes functional impairment.[1] This destructive process is divided into several different clinical stages.

The noma usually begins with a small intraoral ulcer, apthous lesion, or acute necrotic gingivitis (ANG). ANG itself usually has signs such as spontaneous bleeding, gingival papillae ulcers, pain, and greyish pseudomembrane.[19,20] In Africa, the prevalence of ANG in children is quite high and reaches 15-60% depending on the region and the level of poverty.[21,22] ANG can also occur due to lack of oral hygiene, but other evidence also suggests that malnutrition alone can cause changes in the oral microflora and cause ANG.[21] Generally, ANG can be cured by improving oral hygiene. The use of antibiotics for ANG needs to be considered in children with malnutrition and children with disabilities to maintain oral hygiene. Without therapy, ANG can develop into necrotic stomatitis and cause damage to the gingival mucosa, oral mucosa, and bone around the lesion. In this phase, antibiotics must be given immediately. If left untreated, it is very likely that the lesion will continue to develop into noma.[23,24]

The onset of the noma is usually marked by the appearance of facial edema and intraoral necrotic stomatitis, accompanied by halitosis. These are pathognomonic signs of noma and last only a few days.

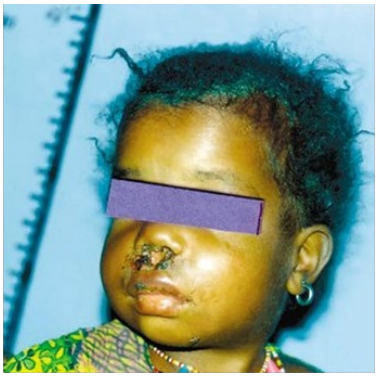

Figure 2. Facial edema due to noma (should be distinguished from abscess).[14]

After the appearance of necrotic stomatitis and facial edema, necrotic infection will spread rapidly to the intraoral mucosa, facial mucosa, skin, maxilla, and mandible. A bluish discoloration of the skin is a sign that the necrosis is starting to spread to the surface. The gangrene of noma has self-limiting characteristics, where the necrosis process will end with a clear demarcation. In certain cases, the body appears to be able to resist and stop gangrene expansion. There were children with relatively small lesions even though they did not receive any therapy, whereas in other children there was extensive facial damage after optimal therapy. This may occur due to differences in the level of impairment of the immune system.[25,26]

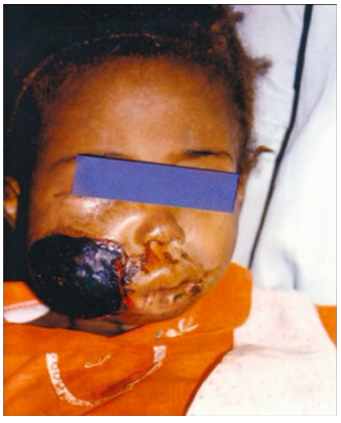

Figure 3. Children aged 3 years old with orofacial noma before sloughing of the necrotic tissue. There was a clear demarcation of necrotic tissue and surrounding healthy tissue.[14]

After gangrenous demarcation, the necrotic tissue will begin to slough. In this phase, many patients died from sepsis. Signs of wound healing will begin to appear if the patient survived and the patient's body has eliminated the necrotic tissue through a process of sloughing, suppuration, and sequestration. In the healing phase, granulation tissue begins to form, wound contractures occur, and the mucosa and epithelium starts to form from the end of the wound towards the granulation surface.[16] This process can take weeks to several months depending on the tissue damage and health status of the patient. This healing process could cause trismus, and in severe cases cause fibrous or bony ankylosis in the temporo-mandibular joint. It will generate further disruption of intake and nutrition in children who often have malnutrition.[27]

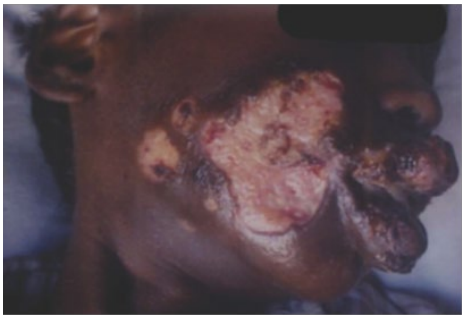

Figure 4. The necrotic tissue begins to peel and granulation tissue could usually be seen at the edge of the skin indicating healing process.[16]

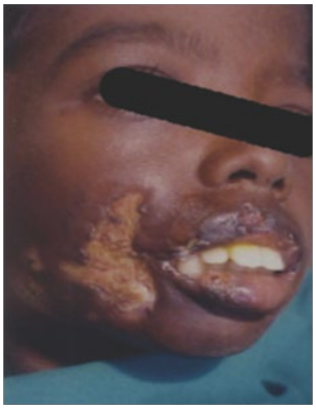

Figure 5. The lesions began to heal without any sign of active infection.[16]

Only about 15% of the children could survive acute noma.[2,7] Almost all survivors of noma will have facial deformations, trismus or mandibular ankylosis which will lead to eating disorders, oral incontinence, speech problems, and other social problems (exclusion, stigma, neglect). As the child grows older, contractures will occurs and results in growth disturbances which again cause damage to facial structures.[28] The psychological impact of noma survivors can be easily understood, but very rarely studied.[2]

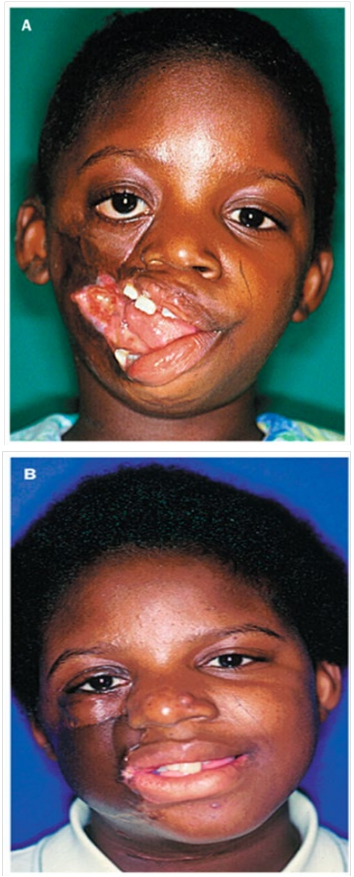

Figure 6. Patients with noma sequelae (A) and 3 months after facial reconstructive surgery (B).[13]

Prevention

Primary medical prevention of noma should be included together with programs for poverty, malnutrition and health education. Economic growth can prevent noma, as this growth can ensure that parents can provide enough food to their children. Medical-

prevention for noma includes treatment for other neglected disease such as measles vaccination program, and prevention and treatment of common diseases such as HIV and malaria.[2,29] Measures needed to prevent noma include administration of nutritious food, exclusive breast feeding during the first three to six months of life, introducing proper oral hygiene practices, immunization against endemic diseases like measles, segregation of animals from human living areas and creating a proper awareness about noma.[26]

Secondary prevention of this disease, as noma is preceded by necrotizing gingivitis, necrotizing periodontitis, and necrotizing stomatitis, so early diagnosis and treatment of any stage in this sequence of progression will prevent the development of noma, but is still difficult to be implemented in poor areas far from health facilities.[2,5]

Tertiary prevention of this disease includes preventing the negative impact of symptoms of this disease (such as disability and death) through medical treatment and rehabilitation.[2]

Diagnosis and Treatment

Fresh cases of noma are seen primarily in the 1 to 4 age group. Systemic manifestations of noma include fever, tachycardia, lymphadenopathy, high respiratory rate, anorexia, general edema and ascites. Medical history reveals a parasitic or viral infection (measles, malaria) in the recent past, recurrent fever and diarrhea, and swelling in the face with foul-smelling discharge from the mouth in malnourished children. Blood examination reveals a low hemoglobin concentration and white blood cell count, elevated erythrocyte sedimentation rate and hypoalbuminaemia. The appearance of facial gangrene a few days later will confirm the diagnosis of noma, but during this stage antibiotic therapy often does not reduce the extent of gangrenous lesions.[2,26]

There are several clinical features of other diseases similar to noma such as those found in Buruli ulcer, tooth abscess, herpetic stomatitis, and local cellulitis. Other ulcerative lesions to be considered in the differential diagnosis of noma include leprosy, leishmaniasis, skin tuberculosis, agranulocytic angina, malignant oral lesions, squamous cell carcinoma, midline granuloma of the face, and trauma.[2,4,14]

Medical therapy for noma consists of three main elements: antibiotics, hydration, nutrition, and management of other concomitant diseases and deficiencies to prevent death. The potential damage caused by facial gangrene can be prevented if antibiotic therapy is started in the early phase. The choice of antibiotic is done empirically, usually amoxicillin and metronidazole. Common concomitant diseases include respiratory infections, gastrointestinal infections, malaria, and HIV. Wound care is also mandatory for noma lesions, this includes changing the dressing frequently, debridement of the wound, and sequester extraction.[2,30]

Surgical management of noma sequelae is aimed at improving function and aesthetics of the face. The basic principles of surgical management include treating trismus or ankylosis and replacing the lost tissue with a flap of localized tissue or from another part of the body (especially if the tissue lost is extensive).[2,28] Usually such treatment can only be done in tertiary health facilities, which are not available in areas where noma is found.

DISCUSSION

Noma or orofacial gangrene is a noncontagious infectious disease that often occurs in malnourished children in developing countries, who are also affected by various other diseases. This disease often attacks the children of poor families in remote areas far from good health service.[2] One of the

preconditions for the occurrence of noma is malnutrition, which often occurs due to extreme poverty. It also found closely related to several types of diseases such as malaria, typhus, measles, chickenpox, tuberculosis, and HIV. The pathophysiology of the disease is an opportunistic multifactorial that occurs in the presence of relatively normal oral flora in chronically malnourished children.[13]

The noma usually begins with a small intraoral ulcer or acute necrotic gingivitis (ANG), with symptoms such as spontaneous bleeding, gingival papillae ulcers, pain, and greyish pseudomembrane.[19,20] ANG needs to be treated with antibiotic, otherwise it could developed into necrotic stomatitis and cause damage to the gingival mucosa, oral mucosa, and bone around the lesion, and will continue to become noma.[24] The pathognomonic sign of the noma is the appearance of facial edema and intraoral necrotic stomatitis, accompanied by halitosis, and it lasts for several days. Subsequently the necrotic infection could spread rapidly to the intraoral mucosa, facial mucosa, skin, maxilla, and mandible.[25]

Medical therapy for noma consists of three main elements: antibiotics (amoxicillin and metronidazole), hydration, nutrition, and management of other concomitant diseases.[30] Wound care is also mandatory for noma lesions, such as changing the dressing frequently, debridement of the wound, especially on the skin, and sequester extraction.[2]

Surgical management of noma sequelae is aimed to correct the deformities and to improve the function of the face, but usually surgical reconstruction and functional rehabilitation should await healing and fibrosis process, which might take up to 1 year.[1,5,28]

In conclusion, medical practitioners need to realize the debilitating health, psychological, and socio-economic impact that resulted from noma. Attention needs to be given to maintain the patient's quality of life through prevention, early diagnosis, prompt treatment, and proper rehabilitation. Prevention of noma could be achieved through the promotion of oral hygiene and food safety. Medical practitioners can identify this disease by looking at the risk factors and early pathognomonic signs and symptoms, such as necrotic stomatitis and facial edema. Prompt treatment with sufficient antibiotics, and resolution of sequelae with reconstructive surgery and rehabilitation should be considered for all noma patients and survivors.

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