

Short Case Report

Chronic lymphocytic leukemia revealed by a rare complication: Noma. First description from Togo

Komlan Mawabah Bouassalo^{1,*}, Edem Komi Mossi², Esohana Padaro³, Mathieu Gunepin⁴, Elise Weber⁵

¹ Service d'odontostomatologie CHR-Dapaong, BP 57, Dapaong, Togo

² Service de Médecine Interne CHU Sylvanus Olympio de Lomé, Lomé, Togo

³ Service d'Hématologie du CHU Campus de Lomé, Université de Lomé, Lomé, Togo

⁴ Centre médical des armées de Paris, antenne médicale de Balard, CS 21623, 75509 Paris Cedex 15, Paris, France

⁵ Service de Chirurgie Maxillo-Faciale – Centre Hospitalier Régional Universitaire de Besançon, 3 boulevard Alexander Fleming, 25030 Besançon Cedex, Paris, France

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Abstract – Introduction: Noma is defined as a gangrenous ulcerative stomatitis whose starting point is endobuccal. Its exact etiology remains unknown, but many risk factors have been described (malnutrition, poor hygiene, etc.). Chronic lymphoid leukemia (LLC) is a lymphoproliferative syndrome characterized by medullary proliferation of a B lymphocyte clone. It is not considered as a risk factor for noma disease. **Observation:** A 43-year-old patient is admitted in the odontostomatology unit of the Dapaong Regional Hospital Centre (Togo) for a deep lesion of the left cheek. The clinical examination allows to conclude the presence of a noma. Biological examinations also show a LLC at Binet stage C. In our patient, the LLC is associated with an immunosuppression and the development of infections due to the late diagnosis of the LLC. **Comment:** The immunosuppression and the development of infections are described in the literature as risk factors for noma disease. An association between LLC and noma could therefore exist. However, such association has been reported to date only once in the literature in 1976. **Conclusion:** Our observation suggests that the LLC could be a risk factor for noma disease. However, further studies based on large samples are necessary to conclude a causal association between LLC and noma.

Introduction

Noma or *cancrem oris* is defined as a gangrenous ulcerative stomatitis with an intraoral origin. It results in soft tissue damage, followed by bones structure destruction via its rapid expansion from the oral cavity to the skin [1,2].

Epidemiological data on noma are sporadic because of the high mortality rate of this diseases in the absence of treatment (90%) [3], the lack of health facilities in the areas where the majority of noma cases occur, and patient isolation due to the social stigma associated with this disease [3]. The global annual incidence of noma is estimated at 140,000 cases and the prevalence at 770,000 cases [3–5]. Noma mainly affects young children (2–6-year old) [3,6]. It is commonly found in populations suffering from extreme poverty, severe malnutrition, unsanitary water consumption, poor hygiene (especially oral hygiene), high infant mortality, and limited access to quality health care [3]. Therefore, noma is often called “the

face of poverty” [2,7,8]. Most cases of noma are reported in the so-called “noma belt,” which is located south of the Sahara and runs across Africa, from Senegal to Ethiopia [3]. The exact etiology of noma remains unknown. It is considered to be multifactorial in nature [3]. Literature analysis suggests that in the context of poor oral hygiene, factors such as malnutrition, compromised immune system, and history of viral infections favor the development of an oral ulcer, constituting an entry for the pathogens to cause noma [3,9]. In children, noma often occurs due to severe undernutrition combined with viral (measles) or parasitic (malaria) infections [8]. In adults, noma occurs due to immunosuppression, especially in HIV patients, in whom it is considered an opportunistic infection [10,11].

Chronic lymphocytic leukemia (CLL) is a lymphoproliferative disorder characterized by the medullary proliferation of a B lymphocyte clone secondarily invading the blood and lymphoid organs [12]. CLL is one of the world's most common malignant hemopathies. In France, its incidence is close to 3/100,000 inhabitants/year [12]. In Nigeria, Mounkaila *et al.* have reported CLL in 33.33% of the cases

* Correspondence: bmawaba@yahoo.fr

in a study of 90 hematological malignancies [13]. In France, men are predominantly affected with an average age of 72 years [12], while in Africa women are predominantly affected with an average age of 53 years [14,15]. In Togo, epidemiological data on CLL are rare; however, Kueviakoe *et al.* have reported 25 cases of CLL over a period of 14 years [15]. Primary CLL complications include the risk of infection, occurrence of cytopenia, bone marrow failure, and Richter's syndrome.

Here, we report the case of a 43-year-old woman presenting with noma and CLL concomitantly. To our knowledge, concomitant presence of noma and leukemia in adults is exceptionally rare in the literature [2], with only one case reported in 1976 [16].

Observation

A 43-year-old homemaker consulted the Odontostomatology Department of Dapaong Regional Hospital on November 30, 2017, because of a deep wound on the left cheek. The first symptoms had appeared 10 days before the consultation, with a cheek swelling that fistulized giving way to a deep wound. Upon clinical examination, the patient showed a general altered state. Examination of the left cheek revealed swelling with a purulent, foul-smelling, ovoid, deep, and gangrenous jugulomandibular wound about eight centimeters in diameter. The wound communicated with the oral cavity and revealed the necrotic mandibular bone (presence of sequestra) and teeth (Fig. 1). The wound edges were edematous.

These lesions led to the diagnosis of noma. Examination of the right cheek was normal. The rest of the clinical examination revealed a tight trismus, sialorrhea, significant peripheral tumor syndrome with homolateral superficial cervical adenopathies of 5 cm, Hackett's Grade 4 splenomegaly (present for five years according to the patient), discrete hepatomegaly, and lower limb edema.

Blood tests during consultation revealed hypochromic normocytic anemia at 61 g/L, hyperleukocytosis at 329 G/L, hyperlymphocytosis at 174.4 G/L, and thrombocytopenia at 36 G/L. Erythrocyte sedimentation rate was very high during the first hour (130 mm). Hepatic assessment revealed elevated transaminases (AST [312 UI/L], and ALT [48 UI/L]). Renal outcome was normal. HIV serology was negative. Abdominal ultrasound detected a homogenous normoechoic splenomegaly associated with the dilation of the portal and splenic veins without portal thrombosis (Fig. 2), a homogenous hyperechoic hepatomegaly associated with moderate hepatic vein expansions without bile duct anomalies (Fig. 3), ascites in the Morrison's pouch, and absence of deep lymphadenopathy.

Because of these hematological anomalies, the patient was referred to the Hematology Department of the University Hospital Campus Lomé. Immediately blood smear revealed morphologically homologous hyperlymphocytosis comprising small mature lymphocytes, with a high nucleo/cytoplasmic ratio. Immunophenotyping of blood cells (Cerva Laboratory,



Fig. 1. Appearance of the jugulomandibular wound after cleansing, demonstrating cutaneo-oral communication and part of the necrotic mandibular bone.

France) confirmed the diagnosis of type B CLL: CD5+, CD19+, CD23+, negative FMC, low surface area immunoglobulin, low CD79b (Matutes score 5/5). These test results led to the diagnosis of Binet stage C CLL.

Therapeutic management of the patient involved local care of the cheek wound, antibiotic treatment (ceftriaxone + metronidazole), analgesic treatment (tramadol + paracetamol), parenteral rehydration, setup of a nasogastric feeding tube, and isogroup isorhesus red blood cell transfusion. Specific CLL management was performed via monochemotherapy with chloraminophen.

Treatment progress was marked by an improvement in the patient's general state and a favorable progress of the cheek wound, leaving room for an orostoma (Fig. 4). Hematological examination revealed increased platelets (105 G/L), decreased leukocytes (284.5 G/L), decreased lymphocytes (164.4 G/L), and elevated hemoglobin level (86 g/L).

The treatment was interrupted on the 38th day of hospitalization due to the inability of the patient to bear the healthcare cost, and the patient died 2 weeks thereafter.

Discussion

We encountered the case of a 43-year-old patient with noma concomitant with Binet stage C CLL. CLL diagnosis was made based on the results of biological tests (blood count and lymphocyte immunophenotyping) 17 days after noma



Fig. 2. a: Longitudinal section of the left hypochondrium passing through the spleen. b: Cross-section of the left hypochondrium passing through the spleen (splenomegaly, measurement).

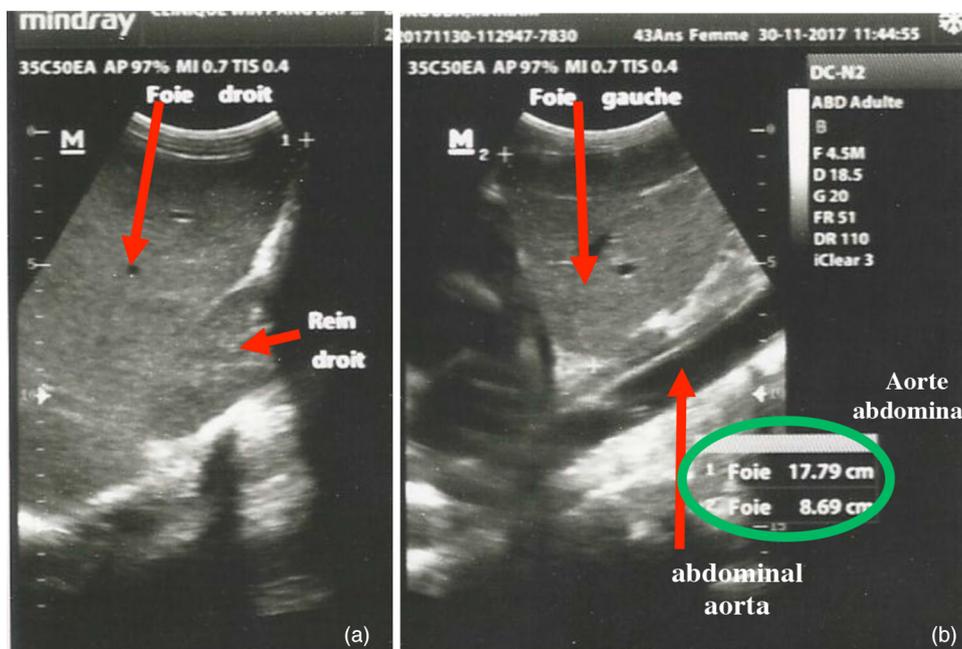


Fig. 3. a: Longitudinal section of the right hypochondrium passing through the liver in renal axis. b: Longitudinal section passing the liver in the abdominal aorta axis (hepatomegaly, measurement).

diagnosis. Although oral mucosal damage during hematological malignancies has been reported in several studies [17], appearance of noma with CLL is very rare. Two hypotheses can explain the association between CLL and noma in our patient:

- Alteration of the immune function related to CLL and abnormalities of B lymphocyte population (quantitative and qualitative abnormalities of the T-cell subpopulation [18]). Immunosuppression renders the mucosa structurally fragile,

promoting its destruction by microbial endotoxins. Any trauma (food or fall) can cause an oral wound on a weakened mucosa. However, such a wound can be a gateway for the microorganisms that cause noma [2]. Immunosuppression, induced in our case by CLL, can therefore be described as a contributing factor for noma occurrence [2,10,11].

- Late CLL diagnosis. Global hypogammaglobulinemia becomes evident later stages of CLL progression in 60%–70% of the patients. This promotes bacterial infections, especially

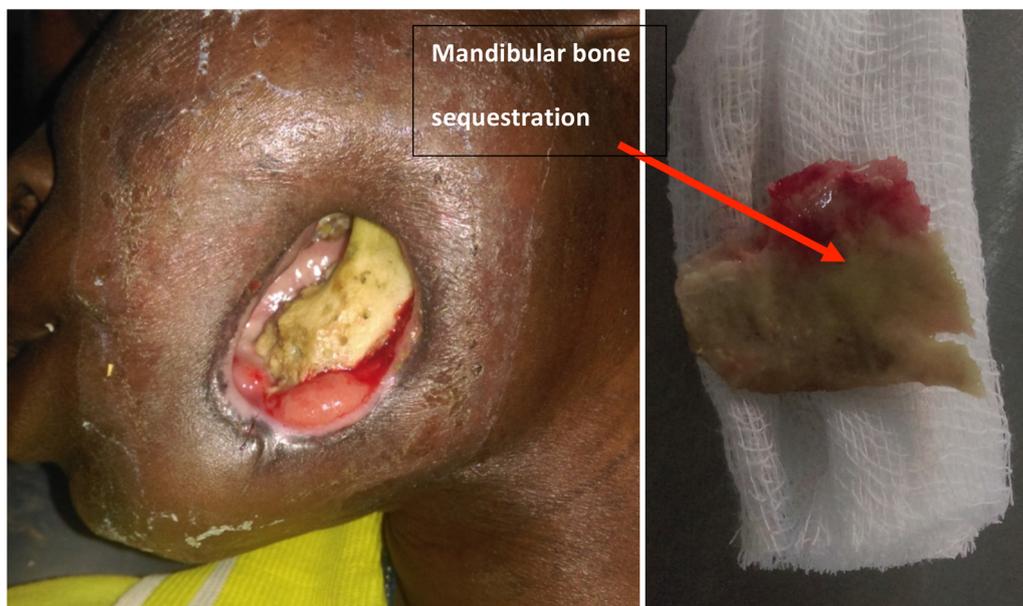


Fig. 4. Wound appearance on the 30th day of hospitalization, demonstrating an orostoma and a mandibular bone sequestration.

oro-pharyngeal and respiratory ones [12]. However, these infections are part of the contributing factors for noma occurrence. The bacteria involved in the occurrence and evolution of noma include *Fusobacterium necrophorum* and *Prevotella intermedia* [2]. In our patient, poverty and lack of peripheral health facilities delayed the diagnosis and early management of CLL. This delay favored the development of infections that can be described as contributing factors for noma occurrence [3].

Immunosuppression and infection can be considered predominant factors in noma occurrence, and this correlation is supported by European, Asian, and African studies [10,11,19–21].

CLL treatment based on chlorambucil initiated in our patient is the most widely used treatment in sub-Saharan Africa [13–15,22]. In Burkina Faso, Koulidiati *et al.* have used this in 60% of the CLL cases [22]. In Togo, Kueviakoe *et al.* have shown the effectiveness of chlorambucil in treating CLL in the context of limited medical resources [15]. In France, it has long been used as monotherapy in CLL treatment [12]. Concomitant with this chemotherapy, a nutritional recovery was instituted, which allowed improvements of the general state and biological parameters of the patient, until the discontinuation of therapy due to lack of financial resources.

The survival rate of CLL varies with regions depending on the availability of medical resources. These resources allow for the early diagnosis and treatment of CLL. In developed countries, the survival period is 5 years on an average [12,23]. In sub-Saharan Africa, it is only 6 months on an average due to late diagnosis of the disease, most often after occurrence of a complication [22]. The death of our patient 15 days after

treatment cessation also emphasizes the damaging impact of the patient's low-income status in sub-Saharan Africa on her survival. The average cost of care was 31,000 CFA francs per week or about 47 €. Financial support from her eldest son aged 21 years (a final-year student), donations, and borrowed money from local merchants were not obtained in time. In developing countries, this can be extended to include all long-term conditions. Only a global overhaul of social assistance system in these countries could make it possible to compensate for these situations wherein patients die because of financial issues and not because of the absence of medical facilities.

Conclusion

The etiology of noma remains largely unknown. Contributing factors have, however, been identified (malnutrition, poor hygiene including poor oral care, immunodepression, history of malaria, or measles). The present case demonstrates a possible association between noma and CLL. We hypothesize that CLL-induced immunosuppression and subsequent infections were responsible for the occurrence of noma in our patient. Further studies involving larger samples would statistically determine the rate of noma in adults with or without CLL. A comparison of these rates would allow for determining whether CLL should be considered as a new contributing factor for noma occurrence.

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

References

1. Touré S, Siriki S, El-Radi, Assi K. Approche chirurgico-prothétique des séquelles d'un cas de noma intéressant l'hémiface. *Odonto-Stomato-Tropicale* 1991;14:27–32.
2. Zwetyenga N, See LA, Szebel J, Beuste TEM, Aragou M, Oeuvrard C, Martin D, Empananza A. Le Noma. *Rev Stomatol Chir Maxillofac Chir Orale* 2015;116:261–279.
3. Ashok N, Tarakji B, Darwish S, Rodrigues JC, Altamimi MA. A review on Noma: a recent update. *Glob J Health Sci* 2015;8:53–59.
4. Enwonwu CO, Falkler WA, Philips RS. Noma (Cancrum Oris). *Lancet* 2006;368:147–156.
5. Tonna JE, Lewin MR, Mensh B. A case and review of Noma. *PLoS Negl Trop Dis* 2010;4:e869.
6. Diombana ML, Coulibaly KD, Alhousseini Ag M. Epidémiologie du noma dans le service de stomatologie et de chirurgie maxillo-faciale de l'hôpital de Kati : 61 Cas. *Mali Med* 2004; 19:28–33.
7. Organisation Mondiale de la Santé. Rapport sur la santé bucco-dentaire dans le monde 2003, Genève, Suisse. WHO/NMH/NPH/ORH/03.2. Accessible le 11 septembre 2018 sur http://www.who.int/oral_health/media/fr/orh_report03_fr.pdf
8. Evrard L, Laroque G, Glineur R, Daelemans P. Noma: clinical and evolutive aspect. *Acta Stomatolog Belgica* 1996;93:17–20.
9. Huyghe A, Francois P, Mombelli A, Tangomo M, Girard M, Baratti-Mayer D, Bolivar I, Pittet D, Schrenzel J; Geneva Study Group on Noma. Microarray analysis of microbiota of gingival lesions in noma patients. *PLoS Negl Trop Dis* 2013;7:e2453.
10. Ki-Zerbo GA, Guigma Y. Noma et infection à VIH : A propos d'une observation au centre hospitalier national de Bobo-Dioulasso (Burkina Faso). *Odonto-Stomatologie Tropicale* 2001;96:26–29.
11. Millogo M, Konsem T, Ouedraogo D, Ouoba K, Zwetyenga N. VIH et noma au Burkina Faso. *Rev Stomatol Chir Maxillofac* 2012; 113:433–436.
12. Pamoukdjian F, Levy V, Al-Nalwakil C, Cymbalista F, Sebbane G. 2015 La leucémie lymphoïde chronique du sujet âgé au carrefour des avancées thérapeutiques innovantes et de l'oncogériatrie! *Repères en Gériatrie* 2015;17:180–183.
13. Mounkaila B, Touré IA, Gragnic G, Mounkaila I. Hémopathies malignes à Niamey à propos de 90 observations sur 6 ans. *Méd Afr Noire* 1996;43:472–475.
14. Malam-Abdou B, Brah S, Djibrilla A, Andia A, Chefou M, Mahaman-Sani MA, Beydou S, Daou M, Adehossi EO. Leucémie Lymphoïde Chronique au Niger : une étude de 99 cas au Service d'Onco-Hématologie de l'Hôpital National de Niamey. *HealthSci Dis* 2018; 19:93–96.
15. Kueviakoe IM, Agbetiafa K, Padaro E, Layibo Y, Vovor A, Segbena AY. Traitement de la leucémie lymphoïde chronique (LLC) au Togo. *J Rech Sci Univ Lomé* 2012;14:129–133.
16. Limongelli WA, Clark MS, Williams AC. Nomalike lesion in a patient with chronic lymphocytic leukemia. Review of the literature and report of a case. *Oral Surg Oral Med Oral Pathol* 1976;41:40–51.
17. O'Hana D, Baudet-Pommel M, Barthélémy I, Devoize L. Ulcérations buccales révélatrices d'une leucémie aiguë myéloïde de type 4. *Med Buccale Chir Buccale* 2010;21:37–41.
18. Nafil H, Tazi I, Mahmal L. Cancer de la prostate et leucémie lymphoïde chronique. *Afr J Urol* 2013;19:35–38.
19. Majmundar K, Heller AJ. A rare case report about Noma or Cancrum Oris occurring in a neutropenic patient. *Otolaryngol Head Neck Surg* 2004;131:112.
20. Konsem T, Millogo M, Gare J, Ouedraogo D, Ouoba K. Noma et maladie de Burkitt, une association exceptionnelle à propos de trois observations vues au centre hospitalier universitaire Yalgado Ouedraogo (Burkina Faso). *Bull Soc Pathol Exot* 2014;107: 146–150.
21. Chiandussi S, Luzzati R, Tirelli G, Di Lenarda R, Biasotto M. Cancrum oris in developed countries. *Aging Clin Exp Res* 2009;21: 475–477.
22. Koulidiati J, Ouedraogo DD, Tineo H, Bationo B, Kafando E, Drabo YJ. Hémopathies malignes de l'adulte à Ouagadougou (Burkina Faso): aspects épidémiologiques, diagnostiques et thérapeutiques. *Rev Cames Sante* 2015;3:10–16.
23. Tsimberidou AM, Wen S, McLaughlin P, O'Brien S, Wierda WG, Lerner S, Strom S, Freireich EJ, Medeiros LJ, Kantarjian HM, Keating MJ. Other malignancies in chronic lymphocytic leukemia/small lymphocytic lymphoma. *J Clin Oncol* 2009;27:904–910.