Cervical lymph node mucormycosis: A case report

Mucormycose cervicale ganglionnaire: A propos d'un cas

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ABSTRACT

Introduction: Mucormycosis is a rare and life-threatening fungal infection that usually affects immunocompromised patients. The most frequent anatomical locations are pulmonary and rhino-orbito-cerebral ones. Others ENT and cervico-facial locations are rare. We propose to present an exceptional case of a cervical lymph node mucormycosis associated with mediastinitis and to study clinical, therapeutic and prognostic aspects.
Observation: It was a 50-year-old woman, with a history of decompensate type 2 diabetes, who presented to ENT emergency with a painful left latero-cervical swelling evolving for 4 days. Further examinations revealed a mucormycosis cervical adenophlegmon complicated by a necrotizing fasciitis of the neck and mediastinitis. Both surgical debridement of necrotic tissue and systemic anti-fungal therapy were prescribed and the patient was admitted in an intensive unit care. The evolution was unfavorable with a cascade of complications: nosocomial surinfection; renal failure as a side effect of the anti-fungal therapy and death in a septic shock.
Conclusion: Mucormycosis is a rare fungal infection with a high morbidity and mortality despite the antifungal treatments progress. It typically involves the rhino-cerebral and pulmonary areas. The involvement of the cervical lymph nodes and the mediastina is rare. The identification of risk factors is necessary to reduce the incidence of mucomycosis and a multidisciplinary approach is essential for prompt diagnosis and management of this disease.
Key words: Mucormycosis, Head and neck, Epidemiology, Diagnosis, Treatment, Prognosis

RÉSUMÉ

Introduction: La mucormycose est une infection fongique rare pouvant être létale qui affecte généralement les patients immunodéprimés. Les localisations les plus fréquentes sont pulmonaires et rhino-orbito-cérébrales. Les autres localisations ORL et Cervico-faciales sont exceptionnelles. Nous présentons un cas rare de mucormycose ganglionnaire cervicale associée à une médiastinite avec étude des aspects cliniques, thérapeutiques et pronostiques.
Observation:
Il s'agit d'une femme de 50 ans, aux antécédents de diabète de type 2 décompensé, qui s'est présentée aux urgences ORL avec une tuméfaction latéro-cervicale gauche douloureuse évoluant depuis 4 jours. Les examens complémentaires ont objectivé un adénophlegmon en rapport avec une mucormycose cervicale, compliqué d'une fasciite nécrosante du cou et d'une médiastinite. La patiente a été admise en unité de soins intensifs. Un débridement chirurgical des tissus nécrotiques et un traitement antifongique systémique ont été prescrits. L'évolution a été défavorable avec une cascade de complications: surinfection nosocomiale, insuffisance rénale comme effet secondaire du traitement antifongique et décès par choc septique.
Conclusion: La mucormycose est une infection fongique rare avec une morbi-mortalité élevée malgré le progrès des traitements antifongiques. Il s'agit typiquement d'une atteinte rhino-cérébrale ou pulmonaire. L'atteinte des ganglions lymphatiques cervicaux et du médiastin est rare. L'identification des facteurs de risque est nécessaire pour réduire l'incidence de la mucomycose et une approche multidisciplinaire est essentielle pour un diagnostic et une prise en charge rapides de cette maladie.
Mots clés: Mucormycose, tête et cou, épidémiologie, diagnostic, traitement, pronostic

INTRODUCTION:

Mucormycosis or phycomicosis, is a rare and life-threatening fungal infection that usually affects immuno-compromised patients [1]. Initially, this disease was descriped in 1885 by Paltauf, it is due to filamentous saprophytic fungi among the order of the "Mucorales" which belongs to the class of Phygomycetes [2]. Different anatomical locations can be seen, the most frequent are pulmonary and rhino-orbito-cerebral ones [3]. Other ENT and cervico-facial locations such as oral

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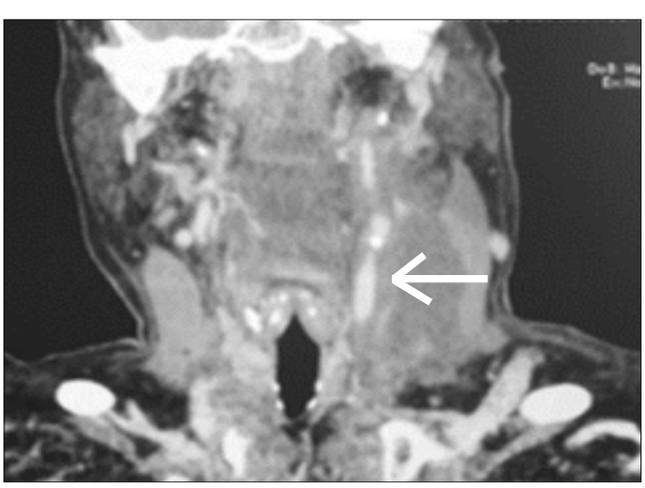
and pharyngeal ones are less usual [4,5]. Furthermore, cervical lymph node mucormycosis is exceptional, to our knowledge there are only two human cases that have been reported [6,7,8].
Our aims were to present an exceptional case of a cervical lymph node mucormycosis associated with mediastinitis and to study clinical, therapeutic and prognostic aspects.

OBSERVATION:

She was a 50-year-old woman with histories of decompensate type 2 diabetes (ketoacidosis ten days ago), hypothyroidism under L-Thyroxine 150μg /day, lower urinary tract infection during treatment with ciprofloxacin for 24 hours and left nephrectomy. There was no history of SARS-cov2 infection. She reported an allergy to penicillin which was not documented. She presented to ENT emergency with painful left latero-cervical swelling evolving for 4 days. There was no fever, no dental pain.
On physical examination, the patient was eupneic, the arterial blood pressure was 150/80 mm Hg, the temperature was 37,9°C and the finger blood sugar was 2,2g without ketosis. She had a left upper jugulo-carotid swelling of 4 cm in diameter, firm, tender with redness of the skin. There was no skin necrosis, no subcutaneous crepitations.
Laboratory findings showed an elevated C-reactive protein (342 mg/l) and normal leukocyte count (9940 elts/mm3).
Neck ultrasonography revealed a left lymphadenitis of Ib and II groups associated with infiltration of the sternocleido mastoid (SCM) muscle without collection.
The patient was hospitalized and received probabilistic antibiotic therapy: clarithromycine (500 mg *2/day), parenteral Ofloxacin (400 mg*2/day) and Metronidazole (500 mg*3/ day). She also received insulin therapy and monitoring of diabetes.
Twenty-four hours later, the patient presented an extension of the swelling. A cervico-thoracic CT scan showed a collected left latero-cervical fasciitis extending from the submandibular to the supraclavicular region with infiltration of the upper mediastinal fat without collection (Figure1).



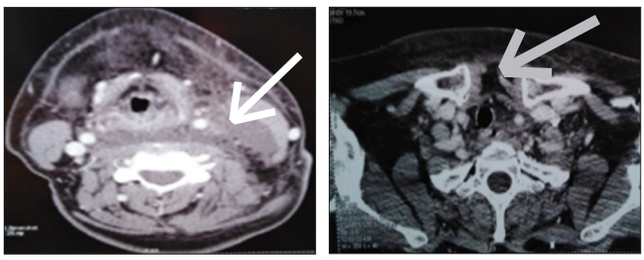


Figure 1: Cervico-thoracic CT scan (axial and coronal sections): A collected left latero-cervical fasciitis extending from the submandibular to the supraclavicular region (white arrow); Infiltration of the upper mediastinal fat without collection (grey arrow).

The patient received Céfotaxime 150 mg/kg/day and we maintained the Ofloxacin and Metronidazole in the same posologies. We did an urgent surgical drainage by a wide left cervical approach of Paul André bringing back thick and whitish pus, we noted a necrotic blackish appearance of the subcutaneous tissues and the SCM muscle (Figure2).

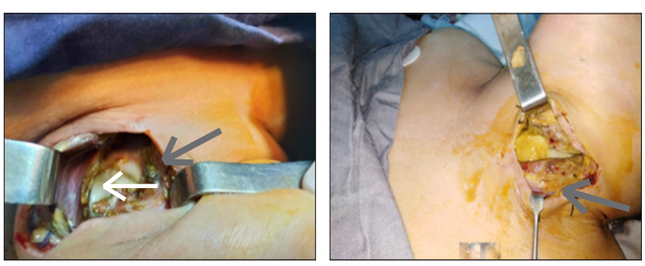


Figure 2: peroperative views: thick and whitish pus (white arrow) Necrotic blackish appearance of the subcutaneous tissues and the SCM muscle (grey arrow).

Thus, a cervical debridement was done and emergency mycological and bacteriological examinations of tissue fragments were carried out. We have not done histological examination. As for mediastinitis, according to thoracic surgery specialists, there was no indication of thoracic drainage.
The mycologic direct examination revealed Mucormycosis which was later confirmed by culture. Bacteriologic sample was negative.
Parenteral Amphoterecin B was initiated at 1mg/kg/day on the 3rd day of hospitalization. The patient was admitted in an intensive care unit with monitoring of the hemodynamic, respiratory, renal function and finger blood sugar. Local care under general anesthesia with surgical debridement of necrotic tissue were performed daily. She also benefited of hyperbaric oxygen therapy (3 sessions). Initially, we had noted an improvement of the local condition with disappearance of necrosis, decrease in pus and tissues revitalization. A biological improvement was also noticed with a decrease in CRP level (255 mg/l), normal leukocyte count (7090 elts/mm3) and normal renal function. On the 9th day of hospitalization (6th day of Amphotéricine B), the patient presented an acute respiratory discomfort with orthopnea. A cervico-thoracic CT scan was urgently performed and revealed an

aggravation of the mediastinitis with unlimited collection of the 3 compartments of the mediastinum and pleuro-pericardial effusions, however there was no collection in the neck. The patient had a lateral thoracotomy and thoracic drainage. Mycological examination of thoracic sample was negative; however, bacteriological sample showed an enterococcus feacium which is a multidrug resistant enterococcus.

The antibiotic therapy was adapted to the antibiogram and the renal function: Vancomycin and Tazocillin were prescribed. Amphotericin B and local cervical care were maintained.

The evolution was unfavorable with a cascade of complications: cervical surinfection with enterococcus feacium and recurrence of the collection (figure 3); multiple organ failure and death in a septic shock after one month of hospitalization.

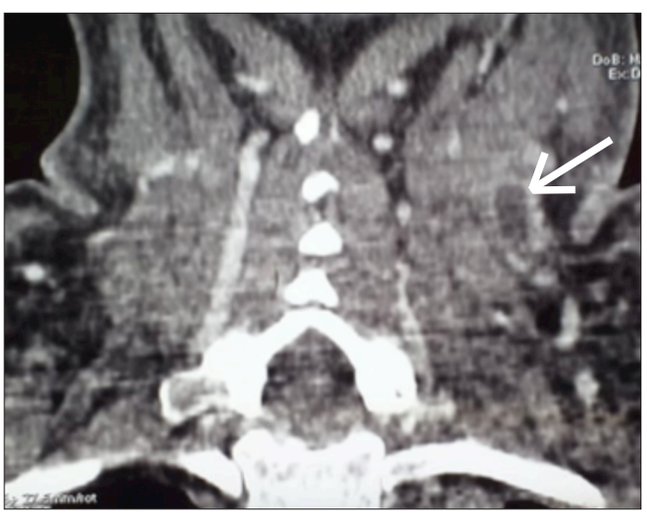


Figure 3: Cervico-thoracic CT scan (coronal section): recurrence of cervical collection

DISCUSSION:

Mucormycosis is a rare disease [2], much less common than other invasive fungal infections caused by aspergillosis [2,9]. It represents up to 13% of all fungal infections [10]. Its incidence varies between continents and it is more frequent in Europe and Asia [3]. It is caused by ubiquitous fungi that belong to the order Mucorales, 38 of which have been associated with human infections. Rhizopus arrhizus is the most common agent causing mucormycosis across the globe [2]. The infection is acquired by inhalation, ingestion or direct fungal contact to open wounds. Animal excreta, soils, certains foods such as fruits and vegetables, compost piles can be potential sources of contamination [3,11,12]. Therefore, farmers are particulary exposed to mucormycosis [11].

Mucomycosis mainly occurs in immunocompromised individuals. Major predisposing factors are diabetes with or without ketoacidosis and neutropenia which is found in malignant hemopathies, in patients taking long-term immunosuppressive drugs. However, immunocompetent patients can be affected, when the spores of the fungus are inoculated in the skin, after a trauma or a burn [2]. Our patient had decompensated type 2 diabetes with acidoketosis that occurred 10 days before the mucormycosis.

The pathogenesis involves a lack of chemotaxis as well as a defect of phagocytosis due to neutropenia. In addition, hyperglycemia alters phagocytic function [1,6,8,9]. All these factors promote multiplication of mucoral agents that have vascular tropism, leading to thrombosis formation and ischemic necrosis of the tissues. The propagation is then locoregional or lymphatic [13]. Based on the anatomical sites of involvement, 6 clinical syndromes are described: rhino-orbito-cerebral which is the most common and deadliest form that usually presents as invasive fungal sinusitis, pulmonary, cutaneous, gastrointestinal, disseminated forms and others uncommon presentations (infection of bones, heart, ear, parotid gland, uterus, urinary bladder and lymph nodes) [3, 8].

It is reported that certain anatomical locations are associated with particular diseases, indeed pulmonary mucormycosis is more frequent in hematological malignancy patients, rhino-orbito-cerebral mucormycosis is usually associated with diabetes, disseminated form is related to profound immunosuppression [2].

As regards head and neck mucormycosis, sinonasal, orbital and cerebral locations are the most frequent and the most severe [11]. The unusual ENT presentations reported in the series were as follows: a bony palate mucormycosis, acute otomastoiditis [11], a Ludwick's angina [5], a parapharyngeal abscess complicated by a mycotic aneurysm of the internal carotid artery [11]. To our knowledge and upon literature search, there are only two human cases of lymph node mucormycosis [6, 7]. The first described case [6] presented with facial mucormycosis in its cutaneous form with extension to soft tissues and secondary lymph node involvement. The second patient [7] had acute myeloid leukaemia and had, simultaneously, developed a pneumopathy and cervical lymphadenitis. As for our patient, it was a cervical adenophlegmon complicated by necrotizing fasciitis of the neck and mediastinitis without other associated localizations.

Radiological imaging cannot establish but suggests the diagnosis of mucormycosis [14].

As regards others uncommon ENT mucormycosis, the CT scan does not generally show specific aspects, but the presence of arterial thrombosis is strongly suggestive as was the case of parapharyngeal abscess complicated by thrombosis of the internal carotid artery [11,15]. Our patient had not suggestive radiologic signs of mucomycosis. The diagnosis was rather evoked in front of intraoperative necrotic aspect.

Diagnostic confirmation is based either on histopathology or mycological examination as was the case with our patient [2]. Direct microscopy of fresh material is an inexpensive and useful method to rapidly give a presumptive diagnosis and to define

clear surgical margins for invasive fungal infection intraoperatively. Direct Microscopy and histopathology examination are strongly recommended by experts of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium (ECMM/MSG ERC) [16]. Culture of specimens is essential for the diagnosis since it allows identification to the genus and species level. The major concern about culture, however, is its low sensitivity, as it can be falsely negative in up to 50% of mucormycosis cases [17].

Histopathology shows typically non-pigmented, wide (5–20 m), thin-walled, ribbon-like hyphae with no or few septations and right-angle branching. Furthermore, histopathology is a very important diagnostic tool since it distinguishes the presence of the fungus as pathogen in the specimen from a culture contaminant by identifying blood vessel invasion [2].

Nowadays, the molecular methods have improved and gained acceptance for confirmation of the infection. Mucorales PCR can be performed on tissue biopsy or on blood sample. They are able to diagnose mucormycosis in immunocompromised patients earlier than the conventional mycological methods. Although Serum PCR sensitivity is lower than in tissues, it is highly specific [2, 16].

The standard treatment of mucormycosis is both surgical debridement of necrotic tissue and systemic anti-fungal therapy. Liposomal amphotericin B is considered as the first-line molecule since it has been proven to be less toxic than systemic amphotericin B [8]. The dosage is between 5 and 10 mg/kg/day. The total duration of antifungal treatment varies with evolution, but at least advised for 12 weeks [1,13,16,18]. Due to the unavailability of the liposomal form, our patient received systemic amphoterecin B and developed acute renal failure which led to discontinuation of treatment after 24 days. Posaconazole and Isavuconazole are recommended in case of failure of liposomal amphotericin B treatment. Infact, they are better tolerated with fewer side effects [16]. These molecules were unavailable for our patient. Hyperbaric oxygen therapy has proven to be effective as an adjuvant treatment, indeed, it has fungi static effect and helps revascularization of the necrotic and ischemic tissues [19]. Other adjuvant cytokine treatments such as granulocyte-macrophage colony-stimulating factor and interferon gamma are under assessment [18].

The survival rate of mucormycosis patients has been improved by new antifungal agents. However, the overall mortality rate of mucormycosis patients remains high (between 30 and 80%) due to delay and difficulties in diagnosis [8, 11].

CONCLUSION:

Mucormycosis is an aggressive life-threatening fungal infection that occurs mostly in immunocompromised patients. Our case was original and interesting to study because of its exceptional location. Although there was no delay in diagnosis, the decompensate diabetes, the side effects of the systemic antifungal therapy and the nosocomial infection constituted the limits of the therapeutic management of our patient and worsened the prognosis. Urgent multidisciplinary approach is essential for prompt management of mucormycosis. Prevention and incidence reduction of this serious disease involves controlling the contributing factors.

Compliance with ethical standards

Conflict of interest:

The authors stated that there is no conflict of interest.

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