Scientific Research Publishing

Open Journal of Pathology, 2023, 13, 217-223
https://www.scirp.org/journal/ojpathology
ISSN Online: 2164-6783
ISSN Print: 2164-6775

A Case of Cerebral Aspergillosis in a Patient with Chronic Lymphoid Leukemia

Aimé Sosthène Ouédraogo[1,2], Franck Auguste Hermann Adémayali Ido[2,3], Ibrahim Savadogo[4], Souleymane Ouattara[3], Rakiswendé Alexis Ouédraogo[2,5], Assita Lamien Sanou[2,6], Olga Mélanie Lompo[2,6]

[1]Pathological Anatomy Service of Bogodogo Teaching University Hospital, Ouagadougou, Burkina Faso
[2]UFR/SDS, Joseph Ki-Zerbo University, Ouagadougou, Burkina Faso
[3]Pathological Anatomy Service of Tingandogo, Ouagadougou, Burkina Faso
[4]Pathological Anatomy Service of Ouahigouya, Ouahigouya, Burkina Faso
[5]Embryology, Cytogenetics and Reproductive Biology of Bogodogo Teaching University Hospital, Ouagadougou, Burkina Faso
[6]Pathological Anatomy Service of Yalgado Ouédraogo, Ouagadougou, Burkina Faso
Email: sostheneaime@yahoo.fr

How to cite this paper: Ouédraogo, A.S., Ido, F.A.H.A., Savadogo, I., Ouattara, S., Ouédraogo, R.A., Sanou, A.L. and Lompo, O.M. (2023) A Case of Cerebral Aspergillosis in a Patient with Chronic Lymphoid Leukemia. *Open Journal of Pathology*, **13**, 217-223.
https://doi.org/10.4236/ojpathology.2023.134022

Received: March 11, 2023
Accepted: October 13, 2023
Published: October 16, 2023

Abstract

Cerebral aspergillosis commonly affects immunocompromised hosts, primarily patients on immunosuppressive therapy and those with acquired or immunodeficient states such as AIDS. We report a case of cerebral aspergillosis in a 39-year-old woman with a history of treated chronic lymphocytic leukemia (CLL). Multiple fragments of fixed tissues with formalin were freshly sent to the laboratory. An extemporaneous examination was performed by spreading. The rest of the sample was embedded in paraffin and studied according to the standard histological method with special stains and an immunohistochemical study. A microscopic observation showed abundant clusters of tangled mycelial filaments, Grocott+. At the edge, a nervous tissue was observed remodeled by an abundant inflammatory infiltrate consisting essentially of small lymphocytes and plasma cells. Additional immunohistochemistry was performed using anti-CD20, anti-CD3, anti-CD5, anti-CD23, anti-Bcl2, anti-Ki67, anti-IgD and anti-Kappa and Lamda antibodies. All taken together there were no further founding in support of a secondary localization of CLL. Cerebral aspergillosis is quite rare and often occurs in a context of immunosuppression. This case indicates the importance of a close collaboration between clinicians and pathologists for optimal patient care.

Keywords

Cerebral Aspergillosis, CLL, Grocott Gomori, Immunohistochemistry

1. Introduction

Cerebral aspergillosis is an opportunistic fungal infection that commonly affects immunocompromised hosts, primarily patients on cytotoxic chemotherapy or immunosuppressive therapy, those receiving long-term corticosteroids and individuals with acquired or immunodeficient states like AIDS [1] [2] [3] [4] [5]. Indeed, fungi of the *Aspergillus* type represent the third cause of fungal opportunistic infections in immunocompromised patients after *Candida* spp. and *Pneumocystis jirovecii* [2] [3] [4]. *Aspergillus* is the most common filamentous in patients with neutrophil line deficiency. It behaves like an opportunistic fungus and is responsible for severe prognostic lesions most often pejorative. The clinical manifestations of invasive aspergillosis are essentially pulmonary or sinus, and sometimes cutaneous. Vascular, cardiac, osteoarticular, ocular, digestive and renal damage have been reported in the literature [1] [2] [3]. They can be isolated or secondary to dissemination of the fungal disease. Its cerebral location is rare [3] [4] [5]; its clinical symptoms are non-specific, and its CT scan appearances can mimic those of a tumor [5] [6] [7]. In the aspergillosis surveillance study conducted in France between 2005 and 2007 in 12 centers, brain localization was found in 5% of patients with invasive aspergillosis [2].

We report a case of cerebral aspergillosis occurring in a patient with a history of treated chronic lymphocytic leukemia (CLL).

2. Clinical Information

A 39-year-old patient with a history of CLL treated with chlorambucil, allopurinol and corticosteroid therapy consulted for headaches and decreased visual acuity, associated with an infectious syndrome. The patient retroviral serology was negative, and a cerebral computed tomography was performed. The CT scan showed a right frontal cerebral lesion raising suspicion of a lymphomatous localization.

A surgical biopsy was performed.

3. Description of the Present Case

3.1. Macroscopy

A few tissue fragments measuring between 0.3 and 0.6 cm were freshly sent to the laboratory. They were fibrous in appearance and white in color.

3.2. Extemporaneous Examination

Millimetric fragments were removed and smeared on a slide (crushed) then stained with hematein-eosin. A cerebral parenchyma of slightly increased cell density was observed on the microscope, with numerous lymphocytes of perivascular topography, thus making it possible to propose the diagnosis of cerebral localization of leukemia (**Figure 1**).

The rest of the fragments are fixed in 10% buffered formalin and then examined according to the standard histological method.

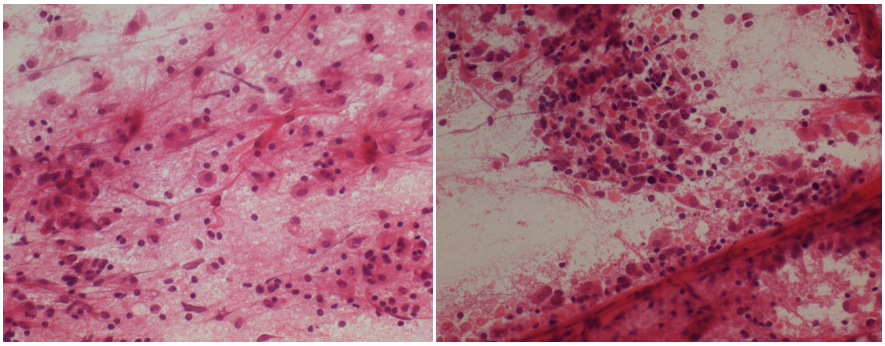
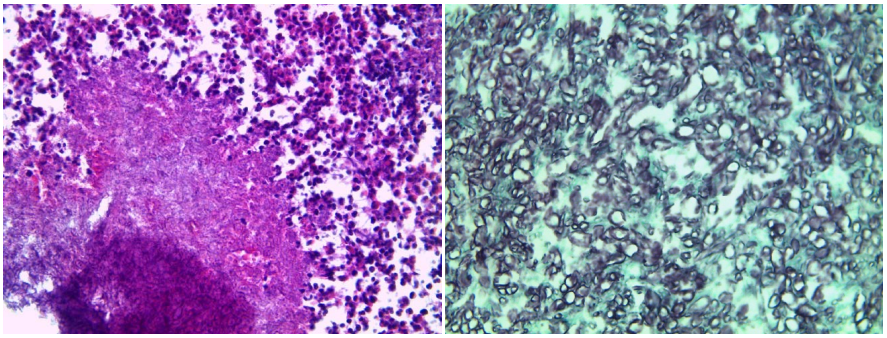


Figure 1. Smear stained with hematein-eosin 400×. Cerebral tissue infiltrated by lymphocytes of perivascular topography.



(a) (b)

Figure 2. (a) Standard histological examination (hematein-eosin staining, 400×). Diffuse inflammatory infiltrate consisting of lymphocytes, plasma cells and eosinophils. Abundant focus of necrosis. (b) Grocott Gomori stain 400×: filaments and *Aspergillus* heads stained in black.

3.3. Extemporaneous Control

3.3.1. Standard Coloration

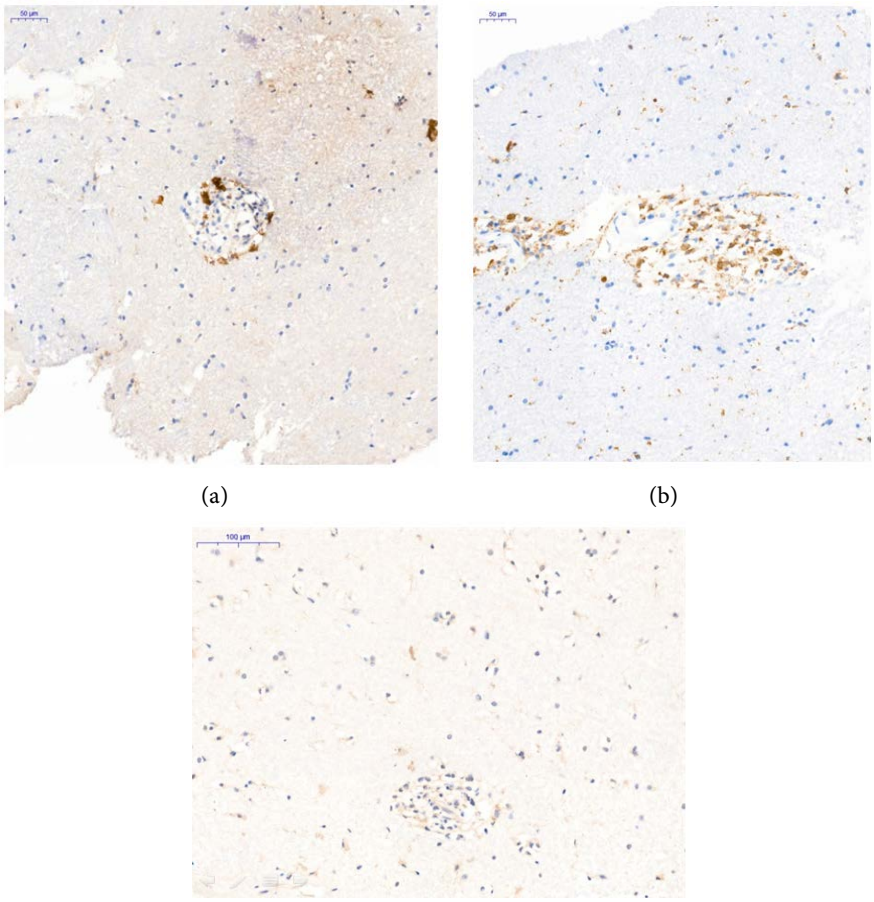
The cerebral parenchyma is remodeled by an abundant inflammatory infiltrate consisting essentially of small lymphocytes and plasma cells without clear granulomatous organization. Polymorphonuclear eosinophils and some neutrophils were observed. A patch of necrosis and numerous clusters of entangled mycelial filaments were also present (**Figure 2(a)**). Thus, the diagnosis of aspergillosis was then proposed.

3.3.2. Grocott Gomori Coloration

These mycelial filaments were stained black with Grocott Gomori (**Figure 2(b)**), confirming the diagnosis of cerebral aspergillosis.

3.4. Immunohistochimical Study

On standard staining, there were sits with a high lymphocyte population, which did not make it possible to formally eliminate a secondary localization of CLL. The paraffin blocks were sent to a pathological anatomy and cytology laboratory in France for immunohistochemical examination (**Figure 3**). This examination found a labeling of some T lymphocytes by the anti-CD3 antibodies; polytypic



(a) (b)

(c)

Figure 3. Immunohistochemical images. (a) Anti-CD3 antibodies: labeling of T lymphocytes; (b) Anti-Kappa antibodies: labeling of plasma cells; (c) Anti-CD23 antibodies: Absence of labeling.

labeling of plasma cells by anti-Kappa and Lamda antibodies; an absence of labeling by anti-CD5, CD20, Bcl2, CD23 and Ki67 antibodies. There was no further founding in support of a secondary localization of CLL, allowing only the diagnosis of cerebral aspergillosis.

3.5. Treatment

The patient received antifungal treatment. The evolution was marked by a worsening of the infectious syndrome followed by death.

4. Discussion

Aspergillosis is a fungal infection of ubiquitous localization, which can be invasive. Its cerebral localization is one of the most severe localizations of invasive aspergillosis. There are no data on the prevalence of aspergillosis in Burkina Faso. Cerebral aspergillosis occurs in 14% to 42% of patients with invasive aspergillosis according to retrospective series [3] [4] but its incidence increases to 59% in autopsy studies [8] [9]. In the aspergillosis surveillance study conducted in

France between 2005 and 2007 in 12 centers, cerebral localization was found in 5% of patients with invasive aspergillosis [3]. No cases have been officially reported in BURKINA FASO.

Certain pathologies or immunosuppressive therapy can promote the development of cerebral aspergillosis. This was the case in the studies by Lortholary O. and Alexandra S. [2] [3], where cerebral aspergillosis most often affects patients in severe immunosuppression (mainly neutropenic patients, followed for malignant hemopathy or patients with a transplant). In our observation, CLL, as well as its treatment, are factors that most likely favor the occurrence of cerebral aspergillosis. However, cerebral aspergillosis on CLL is reported only in rare Western clinical observations [3] [4] [7]. In the series of 81 patients reported by Schwartz *et al.* in 2005 [4], 37% of patients received an allograft, 18.5% were followed for non-allografted malignant hemopathies (including 11 acute leukemias one myelodysplastic syndrome, and one lymphoma), and 14% had a solid organ transplant. In the study, 7% of patients had other acquired immunosuppressive factors, such as corticosteroids (6.2%) or human immunodeficiency virus (HIV) infection (1.2%). HIV serology in our patient was negative. Corticosteroids are part of the therapeutic arsenal of CLL and could be considered as one of the contributing factors in our patient.

Cerebral aspergillosis can appear following hematogenous dissemination from lung or sinus lesions [7] [8] [9]. Pulmonary aspergillosis results from the inhalation of *Aspergillus* spores. *Aspergillus* can also reach the central nervous system by contiguity, from a focus at the base of the skull (paranasal sinuses, orbit, or ear). This is the mechanism implicated in most cases described in patients with the moderate immunosuppressive condition, such as diabetes [5] [7] [9]. Finally, cases of cerebral aspergillosis from inoculation were reported following an invasive medical procedure or the use of intravenous drugs [8]. In our observation, the mechanism of occurrence of cerebral aspergillosis could not be elucidated. The patient did not show any symptoms from a different localization. A thoracic and/or abdominopelvic computed tomography in search of the primary focus could not be performed due to the absence of health insurance. The cost of care remains solely the responsibility of the patient and/or his family in Burkina Faso.

The diagnosis was not proposed based on the extemporaneous examination. It is rather an extemporaneous cytology by apposition of millimetric fragments (smear). If its specificity and sensitivity are high, earning its universal use, it remains a rapid examination with some limitations, as it targets a small section of a lesion.

The diagnosis of aspergillosis is biological (by direct examination or mycological culture) and pathological [1] [2] [3]. Pathological study reveals septate "*aspergillus*-like" or non-septate mycelial filaments. PAS and Grocott Gomori staining allow to confirm their *aspergillus* nature [7] [8]. In our case, the diagnosis of cerebral aspergillosis was proposed from the definitive histological examination after including all the tissue material sent to the laboratory and the hematein-eosin staining. The Grocott Gomori staining confirmed the diagnosis.

If the standard histological examination allowed for the diagnosis of aspergillosis, this is not the case for the diagnosis of CLL. This diagnosis requires a complementary immunohistochemical analysis using anti: CD20, CD3, CD5, CD23, IgD, Kappa, and Lamda antibodies. As Burkina Faso does not have all the antibodies, the remaining examination was carried out by a pathological anatomy laboratory in France, which made it possible to eliminate the diagnosis of CLL.

5. Conclusion

There is a small number of cerebral aspergillosis of treated CLL in the literature, particularly in Burkina Faso. However, significant cases of cerebral aspergillosis have been reported by various authors in patients with a declined immune system. If the diagnosis of aspergillosis remains accessible to standard histology, confirming or infirming of CLL requires immunohistochemistry, a technique which is little accessible in Burkina Faso for our analysis. This case is a reminder of the collegiality of anatomo-clinical diagnosis.

Conflicts of Interest

The authors report no conflict of interest.

References

[1] Hadhria, R., Zemoura, L., Berniera, M., Denouxa, Y., Djibre, M. and Baglina, A.C. (2009) Myocardite Aspergillaire. *Annales de Pathologie*, **29**, 428-430. https://doi.org/10.1016/j.annpat.2009.10.004

[2] Alexandra, S. (2017) Étude rétrospective multicentrique nationale des aspergilloses cérébrales en France. *Médecine Humaine et Pathologie*.

[3] Lortholary, O., Gangneux, J.-P., Sitbon, K., Lebeau, B., de Monbrison, F., Le Strat, Y., *et al*. (2011) Epidemiological Trends in Invasive Aspergillosis in France: The SAIF Network (2005-2007). *Clinical Microbiology and Infection*, **17**, 1882-1889. https://doi.org/10.1111/j.1469-0691.2011.03548.x

[4] Schwartz, S., Ruhnke, M., Ribaud, P., Corey, L., Driscoll, T., Cornely, O.A., *et al*. (2005) Improved Outcome in Central Nervous System Aspergillosis, Using Voriconazole Treatment. *Blood*, **106**, 2641-2645. https://doi.org/10.1182/blood-2005-02-0733

[5] Pagano, L., Ricci, P., Montillo, M., Cenacchi, A., Nosari, A., Tonso, A., *et al*. (1996) Localization of Aspergillosis to the Central Nervous System among Patients with Acute Leukemia: Report of 14 Cases. *Clinical Infectious Diseases*, **23**, 628-630. https://doi.org/10.1093/clinids/23.3.628

[6] Santosh, V., Mahadevan, A., Yasha, T.C., *et al*. (2010) Infectious Lesions Mimicking Central Nervous System Neoplasms. *Seminars in Diagnostic Pathology*, **27**, 122-135. https://doi.org/10.1053/j.semdp.2010.04.004

[7] Yachnis, A.T. and Rivera-Zengotita, M.L. (2014) Aspergillosis. In: *Neuropathology, a Volume in the High-Yield Pathology Series*. Elsevier/Saunders, Philadelphia, 212-213.

[8] Bauserman, S.C. and Gill Naul, L. (2003) Bacterial, Fungal, and Parasitic Diseases of the CNS. In: *Principles and Practice of Neuropathology*, 2nd Edition, Oxford Uni-

versity Press, New York, 45-77.

[9] Louati, I. and Mrissa, R. (2009) Aspergillose cérébrale chez le sujet immunocompétent. A propos de trois cas. *Revue Neurologique*, **11**, 957-961. https://doi.org/10.1016/j.neurol.2009.02.008