

Neuromeningeal Cryptococcosis: A Fatal Disease in Tropical Practice

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Abstract

Background: Neuromeningeal cryptococcosis (NMC) frequency has increased since the appearance of HIV/ AIDS infection with high mortality rate. Objective: To assess the clinical and epidemiological features of the NMC in hospital field. Materials and method: It was a retrospective study carried out on patients at 4 public health structures in the largest region of the country from 2009-2011. The mainly criteria were HIV+ conditions and the research of cryptococcus neoformans in CSF by India ink test. The anthropometric, clinical, therapeutic and follow up data were also collected. Results: The study covered 41,327 patients. HIV + patients were 18.52

Index terms— neuromeningeal cryptococcosis, epidemiology, clinical features.

1 Introduction

his paper deals with neuromeningeal location of Cryptococcus neoformans which is the most common in HIV/AIDS infection. It caused fatal meningoencephalitis in low income countries. [1] Its incidence varied from 5 to 10% in developed countries, [2,3] and 15-35% in central Africa. [1,4,5] The prevalence varied from 2.24 to 5.1% in Africa. [6][7][8][9] Clinical data show no specific clinical signs. Laboratory confirmation test is done by highlighting "Cryptococcus neoformans" in CSF by India ink. [8,10,11] In our developing Author ? ? ? ? ¥ §: Campus University Hospital/ university of Lomé/ togo. e-mails: seraphinassogba@yahoo.fr, abalogou@yahoo.fr, damelan03@yahoo.fr encountered in consultation, and the prevalence of HIV/ AIDS. We aimed to study the epidemiological and clinical characteristics of neuromeningeal cryptococcosis.

2 II.

3 Materials and Methods

This retrospective study was conducted in the departments of internal medicine, infectious diseases and neurology, and laboratories of the four major public hospitals of the region (Tokoin university hospital, Campus university hospital, Regional Hospital and District Hospital). These four sites were selected for their important capacity which is a total of 409 beds and the quality of the technical platform of their laboratory. This study focused on the analysis of recorded patients admitted between 1 January 2007 and 31 December 2011, and the positive of Cryptococcus neoformans in CSF. The main variables studied were formed by the epidemiological indicators (age, sex, incidence, frequency), clinical features (clinical signs and associated pathologies), routine analyzes (CSF, search of cryptococcus neoformans by staining the India ink and culture on Sabouraud medium, HIV status and CD4 count), therapeutic and progressive (disease duration before the consultation, hospitalization stay and the outcome). Physician in charge of the patient decided to perform or not CSF analysis, depending on clinical symptoms encountered. CSF study consisted of three phases namely cytology examination, direct staining India ink and the quantitative determination of proteins and glucose. The search of soluble antigens was not available. The determination of CD4 lymphocytes was performed by an automatic CD4counter. HIV

serology was considered positive by the detection in serum of specific antibodies by both tests (ELISA I and II) and confirmatory test by Western Blot. The study of viral load was not available. CT scan was done for all patients, and shown diffuse cerebral edema with leptomeningeal contrast. All patients had provided informed consents and the study were approved by the local Ethics Committees.

4 III.

5 Results

During the study period, 41,327 patients were hospitalized in all four hospitals involved in this study T

6 Global Journal of

The main concern of this paper had been a retrospective study consisted of the analysis of hospital recorded files in four public hospitals in the biggest region of the country. We encountered some difficulties such as patient's financial difficulties and poor access to care, which limited the sample size. In other words, this study is by no means exhaustive and does not allow beforehand to assess the extent of cryptococcal meningitis in the general population in the community or at the national level. The limitation of the study was also that we were unable to assess all patients admitted for brain infection meningitis in the region. Finally, because we only included patients admitted to hospitals, we were unable to collect patients who could not afford hospital care or were more likely to attend basic clinic-type (Level 1) hospitals or traditional healers. These have been the bias in the recruitment of patients encountered in the retrospective studies. These findings may not reflect the real incidence and frequency of that disease. However, the consistency of our results with other studies provides some validity to the data.

Search for cryptococcal antigens soluble in blood and CSF were not made for technical shortcomings, which would have allowed us to approach the real frequency of further disease. Some studies, however, showed that the use of both tests the India ink and the search of soluble antigens did not reveal a significant difference in observed frequency. [5,9,12] The average age was 36 years (range from 28 to 45 years). It is comparable to that reported in Morocco, Mali and Zambia which were respectively 32 years, 34 years (18-60 years) and 33 years (15 to 65). [13][14][15] The age of the young population slice is superimposed on the most affected by HIV /AIDS in our communities and is also the target of death. [13, ??6] We found a male predominance (M/F:1.67), as in most studies, [6,9,15] while HIV is feminized. Only 3.82% of patients (1578 /41327) underwent CSF examination and research of cryptococcus neoformans by the India ink was performed in 18.54% of cases. This rate of lumbar puncture seems as low as noticed Mbuagbaw et al. [6] This low rate may be due to limited technical tray and non-specific clinical signs of cryptococcal meningitis. Hospital frequency of CNM was 0.02% for all patients and 0.10% in HIV + patients. The incidence of cryptococcosis in Africa varies greatly by region, from 1.7% in Gabon to 94.6% in Ivory Coast. [5,11,12, ???,18] The number of cases per year is highly variable from year to year and in the same region. The hospital incidence is 1.6 cases / year. This incidence is similar to that reported from Senegal, 2.9 cases/year [19] and below than the average from South Africa with 10.48 cases / year (range 1.6 to 230 cases / year). [13,14,20] The variable incidence rate are related to the ecological environment favorable or not, and the prevalence of HIV / AIDS in the studied region. The symptoms and signs most frequently encountered were fever (75%), headaches (62.50%) and impaired consciousness (50%), as reported by several studies. [7,10,15,21,22] These nonspecific signs may explain the low frequency and the lack of attention to asymptomatic neuromeningeal cryptococcosis in our regions. The search of cryptococcus in CSF depends on the physician appreciation concerning the patient clinical presentation.

Cryptococcus clinical presentation is really vague and no specific signs but in HIV condition the mainly symptoms were marked by fever, severe headaches and confusion or sometimes loss of consciousness. In case of tuberculosis, the evolution is sub acute and fever is fewer than 38.5°C follow by loss of body weight and rarely loss of consciousness. CSF is clear in both cases. CT scan imaging shows a diffuse edema in case of cryptococcus and granuloma as an abscess with large edema in case of bacterial or parasitary infection. The differential diagnosis is made by cytology examination of the granuloma.

Up on analyzing aspects, CSF was clear, it came up with 6/8 and troubles in two cases. The cell count was normal. The low glucose and high protein averages level in CSF were respectively 0.36 g / l and 3.43 g / l. Data from the literature confirm this fall in HIV. CSF was analyzed in 1758 with 978 samples from HIV+ subjects. The incidence was highly variable from one year to the next with an average of 1.6 cases. The research of Cryptococcus was performed in 19.40% (341 cases). It was positive in 8 cases or 2.34%. The sex ratio was 1.67 (5/3) with an average age of 36 years and extreme of 28 to 45 years. Hospital prevalence of CNM was 0.02% and 0.10% in HIV+ patients. Fever (6/8), headaches (5/8) and impaired consciousness (4/8) were the most frequently encountered clinical signs. The oropharyngeal candidiasis (37.50%) were the main associated pathology. CSF was normal according to macroscopic and cytobacteriological criteria in 3/8cases and clear appearance in 6/8cases. Cytology was almost normal in all cases with 0 and 5 cells/mm³. The culture was negative after 5 days for all patients. The average glucose and protein level was respectively 0.36 g / l (range 0.10 to 0.57 g / l) and 3.43 g / l (range 2.44 to 4.45g/ l). The CD4 + lymphocytes count ranged between 21 and 87 cells / mm³ with an average of 37.4. The white blood cells count was normal in 3/4 cases and anemia with decreased hematocrit was present in all cases. All patients were treated with oral fluconazole or through a nasogastric tube in the event of loss of

consciousness or swallowing. The injectable form was difficult to access. The mean duration of symptoms prior to consultation was 5.5 days with a range of 1-14 days. The average length of stay was 12.25 days with a range of 4 to 37 days. The outcome of hospitalization was marked by death for 5 patients and positive for 2 patients. Table ??I reports the clinical, biological and evolutionary description of cases of CNM observed during the study period.

V.

7 Conclusion

Neuromeningeal cryptococcosis is under diagnosed because of its deceptive symptomatology and lack of technical facilities. It affects a young population, severely immune compromised HIV male with limited income. Then it is a real diagnostic and therapeutic challenge for this disease which remains bonded to a high mortality rate in our region. predominance of low glucose / high protein level. [6] Depending on the degree of immunosuppression observed, the average CD4 count was 37.4 with a range of 21-87 cells/mm³. The opportunistic nature of cryptococcosis was already known before the era of HIV/AIDS. A severe deficiency in cell-mediated immunity (CD4 count <100 cel/mm³) is often involved. [23] However, there are studies describing cases of CNM in immunocompetent patients without apparent risk factors. [24,25] The mean duration of symptoms prior to consultation was 5.5 days range 1 to 14 days but it was reported longer (22 to 27.24 days) in the literature. [12] The hospital stay ranged from 4 to 37 days with an average of 12.25 days. Our patients therefore consulted earlier than the other groups. The therapeutic management is done with fluconazole and amphotericin B. Fluconazole is the drug of choice used solely in almost all cases ??,26] or associated with Flucytosin (5-FC). [26,27] Amphotericin B injection as flucytosine are difficult to access and use in our regions. [15,22] Treatment with fluconazole early undertake help patient to survive. The second condition is the early admission and quiet diagnostic. These are some difficulties encountered in the treatment of NMC.

The mortality rate was 62.5% (5/8). In sub-Saharan Africa, the mortality rate varies from 28.5 to 71.1% with an average of 45.9%. The survival median ranged between 10 and 26 days (range 1-164 days) according to several authors. [9,13, ??6] NMC remains a fatal disease in our region in HIV setting.

Tables ??able 1 :



Figure 1:

2

		Number (n) of beds	Patients (n)	HIV+ (n)	CSF tested (n)			
	TOKOIN	281			27605	6174		1253
	-UTH *							
	CAMPUS-	77			7560	743		366
	UTH							
	DHB ?	36			4872	508		97
	RHL ?	15			1290	228		42
	Total	409			41327	7653		1758
N° Sociodemographic data			Clinical features		CSF analysis		CD4 count (cel/mm ³)	Evolution (days)
1							Deceased after 3 days	
	42 years	Symptoms lasting over 3 days ;			Clear		after 5 days	
	Female	headaches, fever, nausea, vomit,			5 elements		40	
	Saler	unconsciousness, general body state altered			Glu 1 =0,13g/l			
					Prot =1,44g/l	2		
2	45 years	Symptoms lasting over 2 days ;			Trouble		21	Deceased
	Male	headaches, fever, convulsions or			4 elements		after 4 days	
	Solder	seizures			Glu 1 =0,15g/l			
	Married				Prot =2,65g/l	2		
3	28 ears	Symptoms lasting over 5 days;			Clear		Deceased after 6 days	
	Female	general		wellbeing altered,	0 elements		12	
	Household	digestive			Glu 1 =0,20g/l			
	wife							
	Married	Candidosis,		chronic	diarrhea	Prot =1,64g/l	2	
		tuberculous						
4	33 years	Symptoms		lasting over 1 day ;	Trouble		Improved after	

[Note: Legend: *UTH: University teaching hospital; ?DHB: District hospital of Bè; ?RHL: regional hospital of Lomé]

Figure 2: Table 2 :

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7 CONCLUSION

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