

Primary Cerebral Lymphoma: About 22 Cases with Literature Review

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Abstract

Primitive cerebral lymphoma (PCL) is a rare entity often poorly known. They are defined as extra nodal tumor interesting the CNS, brain and eye, and this in the absence of systemic lymphoma disease and brain metastases. The favoring factor is established immunosuppression which is explained by an increase in the incidence related to HIV. The basis of treatment is chemotherapy with consolidation radiotherapy. We report the experience of the National Institute of Oncology in Rabat in management of this disease.

Keywords

Primitive Cerebral Lymphoma, Chemotherapy, Radiotherapy

1. Introduction

The primitive cerebral lymphoma (PCL) is a rare entity often unclear; they are defined as lymph node tumors extra interesting CNS, meninges and the eye, and this in the absence of systemic lymphoma disease and brain metastases [1] [2]. They represent 1% - 2% of Non-Hodgkin lymphoma (NHL), 4% of brain tumors and 4% - 6% of extra nodal lymphoma. The encouraging factor is established immunosuppression which is explained by an increased incidence associated with HIV [3]. Treatment is based on consolidation chemotherapy with radiation therapy.

We report the experience of the National Oncology Institute in Rabat in the treatment of this pathology.

Objectives

Meet the epidemiological, clinical, histological, radiological and treatment of this pathology.

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2. Patients and Methods

This is a retrospective study of 22 cases of LCP collected at the National Oncology Institute in the period between 2004 and 2012 were included in this study all patients with positive biopsy of brain injury and in which the overall balance showed no systemic lymphoma disease or brain metastasis.

What were excluded from the study are patients without a positive biopsy, or with systemic lymphoma disease or brain metastasis.

3. Results

The average age of our population was 46 ± 14 years with a male predominance (63%). The average time of consultation was 6 months (1 - 24 mois). The first reason for consultation was the occurrence of headaches rebels and focal deficits. HIV status returned negative in 12 patients, positive in 3 patients and was not performed in 7 patients. All patients underwent a CT and/or MRI imaging magnetic resonance (torque CT and MRI in 11 patients) for the diagnosis of brain tumor. Histologically, all patients underwent stereotactic biopsy, diffuse large B-cell lymphoma was the most LCP (73%). The small cell lymphoma B was found in 4 patients and 2 patients had a type of lymphoma T. The treatment received was a CHOP-based chemotherapy in 18 patients and only 4 of our patients received methotrexate; Adjuvant radiotherapy was performed in 10 patients (30 Gy on total brain with an add on GTV 10 Gy). After a median follow up of 28 months (2 - 89) evolution was marked by the death of 8 patients, 9 are in good control and the other 5 were lost to view.

4. Discussion

PCL is a rare entity, it is 1% to 2% of non-Hodgkin lymphoma and 4% of all brain tumors; although the factor favoring established or immunosuppression, but an increased incidence observed in immunocompetent [3]. Most cases of PCL unrelated to HIV are diagnosed in patients between 45 and 70 years, with a median age at diagnosis around 50 years [4]. In HIV positive people, the average age is lower than 35 years [5].

The clinical symptomatology is polymorphous; in immunocompetent occurring mainly in the diagnosis a focal neurological deficit in 70% of cases, which is associated with alterations in mental status, signs of intracranial hypertension, and to a lesser extent a convulsive state and visual symptoms [6] [7].

The imaging typically include a monofocal or multifocal involvement in 25% of cases and supratentorial in 87% of cases (periventricular, thalamus, corpus callosum, basal ganglia); CT shows a rounded mass lesion taking the nonspecific appearance contrast, however, some elements draw attention to the particular lymphoma edema perished moderate lesion with low mass effect compared to tumor volume, intense contrast enhancement and homogeneous poorly defined edges and above the multiplicity and bilateral lesions; there are diffuse and infiltrative forms corresponding to hypodenses beaches brain parenchymal not taking the contrast, or as cortical opacities gyriformes; on brain MRI, the typical appearance of lymphoma is an expansive process although limited, periventricular, taking the contrast of intense and evenly, providing a look into "snowball" or "cotton". In general, the lesion is hypo or isosignal T2, surrounded by a more or less severe edema [5] [8].

The diagnosis of a PCL is a histological; when there is an eye tumor diagnosis may be cytological.

Stereotactic brain biopsy is the diagnostic method of choice and is essential especially for deep locations [9]-[11].

In 90% - 95% of cases, histological diagnosis is a B cell lymphoma diffuse large cell, high grade [12] malignancy (73% diffuse large B cell lymphoma cells in our series). Wherever possible, we must avoid any corticosteroids before performing brain biopsy that can be negated by a single outlet. However, corticosteroid therapy should be initiated immediately after the completion of the biopsy gesture; it would result in approximately 30% improvement and up to 10% complete response; conversely, if white biopsy, it is permissible to discuss the possibility of lymphoma when patients took corticosteroids [10].

After diagnosis of PCL general examination must be performed consistently with a HIV serology, complete eye examination and lumbar puncture (except in cases of threatening brain injury). The balance was not always thorough in our practice.

The differential diagnosis of primary brain lymphoma depends on the terrain: in immunocompetent be discussed astrocytic tumor if the lesion is isolated, meningioma in case of nodular lesions of the convexity and metastasis, abscess or forms nickname tumor sarcoidosis and multiple sclerosis if lesions are multifocal; in immunocompromised patients (AIDS), the main differential diagnosis is toxoplasmosis [5].

The therapeutic armamentarium includes chemotherapy, radiotherapy and steroids. Surgical excision is not indicated as causes no benefit in terms of survival [9].

One of the characteristics of the LCP is their cortico-sensitivity; corticosteroids induce apoptosis cell lymphomas and can cause significant regression of lesions LCP with clinical and radiological improvement; corticosteroids should be initiated only after a biopsy, because that can make it impossible to obtain a definitive diagnosis. Although the response to corticosteroids is not sustainable, it can mean a more favorable prognosis, with good survival for good responders [9] [13].

PCL are radiosensitive; RTH of the brain in total has been the standard for many years with an improved median survival of 10 - 18 months against 1.5 months without treatment. A retrospective study of 132 patients in Japan between 1990 and 1999, with a WHR of the brain at a dose of 40 Gy showed a median survival of 18 months, 39% survival at 2 years, and survival at 5 years 18% [14]. The radiation problem is its sometimes delayed neurotoxicity type dementia and ataxia. Combined with chemotherapy with methotrexate RTH would be responsible for a severe leukoencephalopathy [10]. RTH remains the standard consolidation therapy in patients less than 60 years.

Unlike systemic lymphoma, the treatment of cerebral lymphomas requires medication well through the blood brain barrier. LCP reference treatment remains intravenous chemotherapy with methotrexate based high doses ($>1 - 3 \text{ g/m}^2$), usually associated with other molecules (cytarabine, etoposide, nitrosoures, vincristine, procarbazine, etc.) [15] in our series of chemotherapy used was CHOP in 82% of cases. Treatment with methotrexate is highly nephrotoxic, requiring intravenous hydration and prolonged monitoring in hospitals; among other side effects of chemotherapy, infectious complications are very common, especially in patients on prolonged corticosteroid or bedridden with cognitive disorders [10]. The chemosensitivity is high, with 45% to 60% complete response after induction chemotherapy [15]. It is considered that the response is complete when the contrast enhancement MRI disappeared while he persists in general Flair hyperintensity sequelae [10] [16]. Despite the good results Patients treated with CMT alone show many relapses hence the importance of adjuvant treatment.

There is a consensus that the combination regimen (chemoradiotherapy) is superior to other modalities [17] [18]. The treatment consists of a high dose of methotrexate based CMT associated with a consolidation by radiotherapy on total brain; This strategy is most commonly used for the treatment of LCP in immunocompetent patients; although this approach has significantly improved results in the management of LCP, it is still subject to a higher incidence of neurotoxicity, particularly in patients older than 60 years [19]-[21].

In our study 10 patients received the combined treatment and 8 of them are still in good control with acceptable neurotoxicity.

It nevertheless remains to elucidate questions to know what optimal dose of radiation? (Tendency to de-escalation), is it yes or no to the boost? Should radiate so complete response after chemotherapy?

However, relapses are very common, occurring on average after six to ten months in the elderly [10]. In 90% of cases, relapse is cerebral, locally or remotely, uni- or multi-focal; in 10% to 20% of cases, it is ocular and systemic that is in 5% to 10% of cases. Several clinical and molecular prognostic factors are recognized: the young, a good initial clinical status, early and complete response to treatment are associated with prolonged survival [10] [22], while the loss of 6q chromosome rearrangements BCL6 is associated with a poor prognosis [10] [23].

The overall prognosis is poor with a median survival of about 30 to 60 months [15], which reaches 15 to 35 months in patients over 60 years. Nevertheless there 20% to 30% of long-term survivors (> 5 years) and healing has become a focus of treatment. In our series we have 2 long survivors with respectively 83 months and 89 months of decline.

5. Conclusion

The PCL is a rare tumor. In the absence of randomized chemoradiotherapy, it remains the standard treatment in patients under 60 years. The challenge remains the management of neurological toxicity and improved patient survival.

Conflict of Interest

The authors report no conflict of interest.

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