International Journal of Medical and Pharmaceutical Case Reports
7(4): 1-5, 2016; Article no.IJMPCR.22409
ISSN: 2394-109X, NLM ID: 101648033

SCIENCEDOMAIN *international*
www.sciencedomain.org

Successful Chemo-radiotherapy of Primary T- anaplastic Central Nervous Lymphoma: A Case Report

Y. Ben Youssef[1], H. Regaieg[1*], B. Achour[1], N. Ben Sayed[1], H. El Omri[1] and A. Khelif[1]

[1]Department of Clinical Hematology, Farhat Hached Hospital, Sousse, Tunisia.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2016/22409
Editor(s):
(1) Rakesh Kumar Tiwari, Chapman University School of Pharmacy, Chapman University Harry and Diane Rinker Health Sciences Campus, Irvine, CA, USA.
Reviewers:
(1) Pasquale Cianci, University of Foggia, Italy.
(2) Heshu Sulaiman Rahman, Universiti Putra Malaysia, Malaysia.
Complete Peer review History: http://www.sciencedomain.org/review-history/15473

Case Study

Received 30th September 2015
Accepted 19th October 2015
Published 24th July 2016

ABSTRACT

Primary central nervous system lymphoma (PCNSL) constitutes a rare group of extra nodal Non - Hodgkin's lymphoma (NHL). Immunodeficiency is the main risk factor phenotype and involvement of the cranial vault is an unusual manifestation of aggressive PCNSL.

We report a case of Primary central nervous system anaplastic lymphoma in an immunocompetent patient.

A 25 year-old man with a history of left hemiplegia, headache, raised intracranial pressure and 8 cm sized cerebral tumor was admitted in Neurosurgery Department of Sahloul Hospital in Sousse, Tunisia in July 2003.

Magnetic resonance imaging (MRI) showed of 3 cm parasagital right heterogeneous cerebral tumor with perilesionnel edema. Biopsy concluded to the diagnosis of meningioma, a resection of the tumor mass was done. Ten months later an occipital cerebral tumor appeared, the biopsy concluded to the diagnosis of large cell anaplastic lymphoma ALK+, CD30+. The patient underwent 4 cycles of chemotherapy ACVBP regimen followed by 2 cycles of high dose Methotrexate and 4 cycles of

**Corresponding author: E-mail: regaieghaifa@yahoo.fr;*

Etoposide- Ifosfamide and consolidation therapy with whole brain radiotherapy with great tolerability, the patient remain in complete remission without late neurological toxicity within a follow-up of 8 years.
This case illustrate the difficulty of pathological diagnosis of PCNSL and the possibility of complete remission with combination of chemotherapy regimens with drugs passing the blood brain barrier and radiotherapy have given the best reported results up to now.

Keywords: Primary CNS lymphoma; chemotherapy; radiotherapy; cranial vault.

1. INTRODUCTION

The incidence of primary central nervous lymphoma (PCNL) is increasing and becoming one of the most important tumors in neuro-oncology [1]. PCNSL represents 2% of all non Hodgkin lymphoma and 5% of all brain tumors [2]. Immunodeficiency increases the risk of PCNL in immunocompetent patients by more than 300%.With radiotherapy we can achieve high response rates and remissions in most patients ,but survival is usually short and don't exceed 12-18 months because of disease recurrence. The addition of systemic chemotherapy particularly intravenous methotrexate had markedly improved disease control and many patients can achieve a durable remission and occasionally cure of their disease [3].

Prognosis of PCNSL is poor and median survival is only 3-5 months in untreated patients, because of the rarity of this entity, we report a case of PCNSL in an immunocompetent man diagnosed in the department of Hematology at Farhat Hached Hospital.

2. CASE REPORT

A 25 year-old immunocompetent man with a history of left hemiplegia, vomiting, a headache, raised intracranial pressure and 8 cm sized cerebral tumor was admitted in July 2003 in neurosurgery department. The remainder of the examination was unremarkable, in particular no lymphadenopathy and no abdominal masses were felt.

Magnetic resonance imaging (MRI) showed of 3 cm parasagital right heterogeneous cerebral tumor with perilesionnel edema (Fig. 1).

Cerebral biopsy concluded to the diagnosis of meningioma, a resection of the tumor mass was done. Ten months later an occipital cerebral tumor reappeared, a second MRI showed a left mass and hypodense signal on axial gadolinium T2 weighted sequence (Figs. 2a and b).

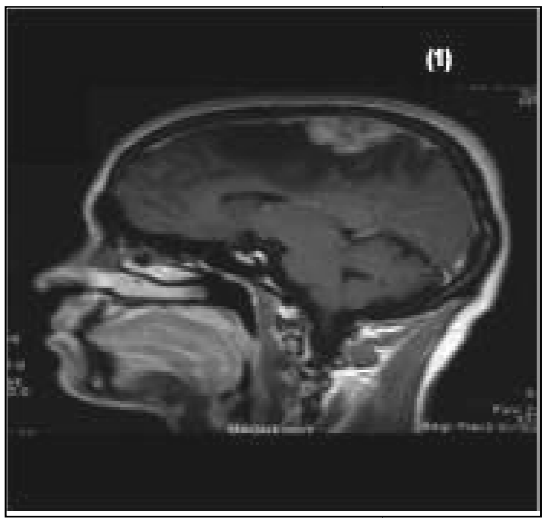

Fig. 1. MRI (sagital) T1-weighted after gadolinium: Before surgery irregular intra axial and parasagital superior right lesion with perilesionel edema

The biopsy of the tumor concluded to the diagnosis of large cell anaplastic lymphoma ALK+, CD30+ (Figs. 3a and b), the bone morrow biopsy was not infiltrated and cerebral spinal fluid was normal.

The patient underwent 4 cycles of chemotherapy ACVBP regimen consisted of (Doxorubicin 75mg/m^2i.v-day 1), Cyclophosphamide 1200 mg/m^2 given i.v-day 1, Vincristine 1.4 mg/m^2 but not more than 2 mg i.v-day 1,5 , Bleomycine 10 mg/m^2i.v- day 1,5, and Prednisolone 60 mg/m^2po days 1-5, intrathecal Methotrexate 15 mg.), the cycles were repeated at 14 days intervals. Than 2 cycles of high dose Methotrexate (5 g/m^2i.v day 1, Acide folinique rescue (50 mg/m^2 i.v. every six hours for 12 doses) and 4 cycles of Etoposide – Ifosfamide and consolidation therapy with brain radiotherapy delivered at a dose of 34 Gray with

an additional 14 Gray boost to contrast enhassing lesions, with great tolerability ,the patient remain in complete remission without late neurological toxicity with a follow-up of 8 years.

3. DISCUSSION

Primary central nervous system lymphoma (PCNSL) is defined as lymphoma localized in the brain, leptomeninges, spinal cord or the ocular soket [4]. This disease represents 1% of all non Hodgkin lymphoma and 4% of central nervous system tumors [5-7].

PCNSL may affect all age group with a peak incidence in the fifth to seven decade in immunocompetent patient [2].

Clinical symptoms are dominated by cognitive dysfunction, psychomotor slowing, personality changes, and disorientation, raised intracranial pressure and focal symptoms [5].

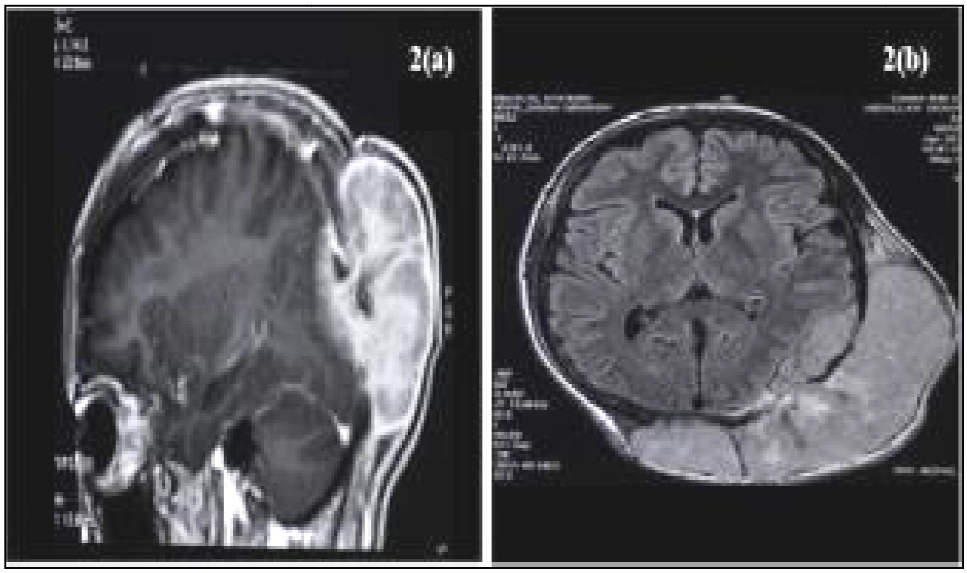

Fig. 2. MRI (axial) T2-weighted (2a), sagital T1- weighted (2b) after gadolinium: Parieto occipital left mass involving the scalp with extra dural and extra cranial extension

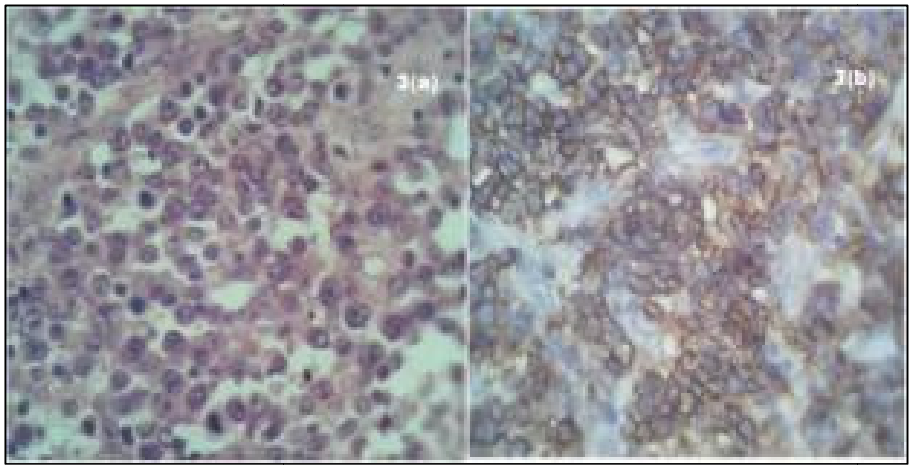

Fig. 3a. A specimen of cerebral mass showing large round cells with nuclear polymorphisms, mitoses and large vessels (HE, original magnification x200)
Fig. 3b. Positive staining immunochemistry for CD30 (original magnification x200)

Brain stem and cerebellar signs as well as cranial nerve dysfunction are present in 10-40% of cases [6-8].

The most common sites of involvement are the frontal lobes, followed by the basal ganglia and thalamus, involvement of the cranial vault is an unusual manifestation, only fifteen patients with non-HIV related cranial vault lymphoma have been reported in the literature, its appearance can mimic those of metastatic carcinoma, osteomyelitis, or meningioma [9]. PCNSL can also spread across the corpus collasum, giving a typical butterfly pattern.Ependymal spread is often seen, particularly in HIV associated lymphoma [8,10].

The diagnosis of PCNSL must always be confirmed histologically, this must be done by stereotactic biopsy. About 90% of PCNSL are DLBCLs as evidenced by their expression of the B cell markers CD19, CD20, and CD79a, they express monoclonal surface or cytoplasmic immunoglobulin, most commonly Ig Mk. The rest being either low grade, Burkitt or T cell lymphomas which have preponderance for the supratentorial space, T cell lymphoma arise more frequently in the cerebellum [4].

PCNL is classified according to the Ann Arbor staging system as stage IE, however this classification does not relay information of the prognostic relevance [4].

Contrast enhanced magnetic resonance imaging scan are the imaging modality of choice; although computed tomography is also informative. Magnetic resonance imaging of the spin is only warranted in the presence of localizing symptoms [11].

Cerebro spinal fluid (CSF) examination should be done it includes cell count, cytology and flow cytometry protein, glucose and immunoglobulin heavy –chain gene rearrangement studies [2].

An ophthalmological examination, including slit lamp evaluation, computed tomography of the chest, abdomen and pelvic and bone marrow biopsy should be carried out. Blood tests should include HIV and serum lactate dehydrogenase. A testicular ultrasound should be considered in man [12].

Standardized guidelines for the baseline evaluation and response assessment have been published by the international PCNSL collaborative group [11].

Surgery is restricted to diagnostic biopsy. PCNSL is a highly radiosensitive and chemo sensitive infiltrative tumor. Despite a high rate of response radiotherapy alone provides limited survival benefit in PCNSL patients, with a median OS duration of 10-18 months and a 5 years survival rate less than 5% [11].

The main reasons for arguably the poorest clinical outcome of all forms of extranodal non-Hodgkin's lymphoma are to be found in the resistance of PCNSL to local and systemic therapy, and in the limited tolerance of the human organism to the toxic side effects of chemo-and radiotherapy directed specifically at the CNS. While the first factor leads to incomplete responses and frequent relapse, the second problem renders the implementation and completion of effective therapy difficult [4].

The addition of high dose Methotrexate based chemotherapy to radiotherapy results in a substantially longer survival time than with radiotherapy alone (median survival time: 2-4 years, 5 years survival rate: 20-40%) [11].

In contrast, adding standard chemotherapy for systemic lymphoma, such as Cyclophosphamide, Doxorubicin, vincristine, and Prednisolone (the CHOP regimen) to radiotherapy did not appear to result in longer survival than with radiotherapy alone [12,13].

High-dose chemotherapy followed by autologous stem-cell rescue has been utilized in CNSL as primary and salvage therapy. The main advantage of this strategy is the possibility to increase the dose of some cytotoxic agents so that potentially more active or curative dose levels and adequate CSF penetration are achieved, the second advantage is that the absence of marrow involvement offers the additional advantage of allowing for uncontaminated peripheral stem cell harvests [4].

4. CONCLUSION

This case demonstrates that PCNSL must be kept in mind in the differential diagnosis of primary lesions in the vault. Chemotherapy followed by involved field irradiation, appears to be an adapted therapy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Shibamoto Y, Tsuchida E, Seki K, Oya N, Hasegawa M, Toda Y, et al. Primary central nervous system lymphoma in Japan 1995-1999: Changes from the preceding 10 years. Cancer Res Clin Oncol. 2004;130:351-356.
   DOI: 10.1007/s00432-004-0547-x
2. Blay J-Y, Ongolo-Zogo P, Sebban C, Carrie C, Thiesse P, Brion P. Primary cerebral lymphomas: Unsolved issues regarding first-line treatment, follow up, late neurological toxicity and treatment of relapses. Annals of Oncology. 2000;11(suppl. 1):S39-S44.
   Available:http://annonc.oxfordjournals.org/
3. DeAngelis LM. Primary CNS lymphoma: Treatment with combined chemotherapy and radiotherapy. J. Neuro-Oncology. 1999;43:249-257.
4. Fetsher S, Sshmielau J, Bairey O. Successfull high-dose chemotherapy of secondary central nervous anaplastic T-cell Non-Hodgkin's lymphoma in a patient with a 50-year history of relapsing malignant lymphomas. Cancer Therapy. 2007;5:525-530.
5. Uwe Schlegel, Ingo GH. Schmidt-Wolf, Martina Deckert. Primary CNS lymphoma: Clinical presentation, pathological classification, molecular pathogenesis and treatment. Journal of Neurological Sciences. 2000;181:1-12.
6. Herrlinger U, Schabeth M, Bitzer M, Petersen D, Krauseneck P. Primary central nervous system lymphoma: From clinical presentation to diagnosis. J Neuro-Oncol. 1999;43:219-26.
7. Braus DF, Schwechheimer K, Mu¨ller-Hermelink HK, Schwarzkop Volk B, Mundinger F, et al. Primary cerebral malignant non Hodgkin's lymphoma: A retrospective clinical study. J Neurol. 1992; 239:117-24.
8. Gallop-Evans E. Primary central nervous lymphoma. Clinical Oncology. 2012;24: 329-338.
9. Fadoukhair Z, Layla I, Amzerin M, Elkhanoussi B, Sbitti Y, Boutayeb S, M'rabti H, Benjaafar N, Errihani H. Successful management of primary non Hodgkins lymphoma of the cranialvault. Pan African Medical Journal. 2011;8:50. Available:http://www.panafrican-med-journal.com/content/article/8/50/full
10. Tang YZ, Booth TC, Bhogal P, Malhotra A, Wilhelm T. Imaging of primary central nervous system lymphoma. Clin Radiol. 2011;66(8):768-777
11. Del Rio MS, Rousseau A, Soussain C, Ricard D, Hoang-Xuan K. Primary CNS lymphoma in immunocompetent patients. The Oncologist. 2009;14:526-539.
    DOI: 10.1634/theoncologist.2008
12. Bessell EM, Hoang-Xuan K, Ferreri AJM, Reni M. Primary central nervous system lymphoma-Biological aspects and controversies in management. Eur J Cancer. 2007;43:1141-1152.
13. Ekenel M, et al. Primary central nervous lymphoma: The role of consolidation treatment after a complete response to high dose methotrexate-based chemotherapy. Cancer. 2008;113: 1025-1031.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/15473