Primary central nervous system lymphoma in an adolescent with lupus nephritis

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March 22, 2022

Abstract

Patients with systemic lupus erythematous (SLE) are at higher risk of malignant lymphomas, particularly non-Hodgkin lymphoma. Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin lymphoma. In adults, about twenty cases have been reported. Malignancy in pediatric-onset patients with SLE has been less extensively studied.

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Patients with systemic lupus erythematous (SLE) are at higher risk of malignant lymphomas, particularly non-Hodgkin lymphoma. Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin lymphoma. In adults, about twenty cases have been reported. Malignancy in pediatric-onset patients with SLE has been less extensively studied. Herein, we report the first case of PCNS lymphoma in an adolescent diagnosed with lupus nephritis treated with Mycophenolate Mofetil.

Case report

We report the case of a 16 year old girl diagnosed with proliferative and membranous lupus nephritis 4 years ago. She had also history of PRESS syndrome at the time of diagnosis of SLE. She was treated with 6 pulses of Cyclophosphamide with a total dose of 3 g and 3 pulses of Methylpredisolone as induction therapy followed by Mycophenolate Mofetil 1,5 g daily and Hydoxychloroquine 200 mg for the maintain therapy. A partial remission was obtained after 1 year of treatment. An impairment of kidney function was observed after 3 years of follow up and renal biopsy showed severe tubulointerstitial lesions. On February 2020, she was

admitted to our department with symptoms of vomiting, weight loss and strabismus. Physical examination showed normal blood pressure, right hemiparesis, non-deficient quadripyramidal syndrome and strabismus of the right eye. Laboratory tests revealed blood count cell of 11880/mm, hemoglobin: 9,8g/ dl, platelets: 340000/mm, C-reactive protein was negative. Magnetic resonance imaging (MRI) of the brain demonstrated infiltrative hyperintense mass expanding genu and trunk of corpus callosum (Fig.1a). A stereotactic biopsy diagnosed diffuse large B-cell lymphoma (Fig.1.b). MMF was discontinued. She was started on chemotherapy and she underwent whole radiotherapy.

Discussion

In contrast to adults, malignancy in pediatric-onset patients with SLE has been less extensively studied. In the study of Bernatsky, 14 invasive cancers were found; among these cases, there was no case of primary central nervous system lymphoma [1]. PCNSL is a rare form of extranodal non-Hodgkin lymphoma [2,3]. Its association with SLE was described for the first time by Lipsmeyer in 1972 [4]. Recent studies suggest a relatively high prevalence of auto immune diseases among primary CNS patients [5]. In a scandinavian study, 29% of primary CNS lymphoma patients had an underlying auto immune disease [6]. In the study of Kaulen, the systemic lupus erythematous (SLE) is the most auto immune disease associated with this lymphoma. The relationship between lymphoma and SLE has not been clearly elucidated. It might be a long term exposure to immunosuppressants or persistence of high disease activity [7]. Immunosuppressive agents might lead to lymphoma by direct mutagenesis or by disturbing immune surveillance [2]. In a case based review, 18 English papers of PCNSL in patients with SLE were descried [8]. Their ages varied from 20 to 60 years. Eleven cases were treated with Mycophenolate Mofetil and the others were treated by other immunosuppressive therapy or Prednisolone only. The duration between the diagnosis of SLE and PCNSL varied from 1 to 30 years [7]. Our patient was diagnosed with lupus nephritis since 4 years and was treated by Predisolone, Cyclophosphamide and Mycophenolate Mofetil. The link between Mycophenolate Mofetil and PCNSL has been studied in recent decades. It seems that the development of PCNSL in SLE patients may occur as a result of impaired immune surveillance and compromised T-cell activity resulting from the immunosuppressant leading to persistence of EBV. It was reported that decrease in the activity of cytotoxic CD8T cells by producing interferon gamma for suppression EBV reactivation, triggers the induction of EBV infected β cells and/or high expression of viral gene in some patients with SLE [9].To our knowledge, our case is the first pediatric case of diffuse large cell CNS lymphoma associated with lupus nephritis after treatment with Mycophenolate Mofetil for 4 years. However, in our patient, PCNSL seems to be multifactorial: High activity disease and the use of two immunosuppressive treatments which are Cyclophosphamide and Mycophenolate Mofetil.

In conclusion, clinicians should consider PCNSL in child with SLE presenting with neurological symptoms and the diagnosis must be confirmed by brain biopsy.

Acknowledgements: Published with written consent of the patient

Conflict of interest : The authors declare that they have no competing interest

Author contributions: Drs Ouns Naija, Farah Krifi contributed to the first draft of the manuscript. Drs Ouns Naija, Farah Krifi, Yossra Hammi and Dr Meriem Jrad contributed to the literature search, analysis and interpretation of the data. Tahar Gargah and Ines Chelly gave final approval. All authors read and approved the final manuscript.

Patient consent: Obtained

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