Cerebral Toxoplasmosis in a patient with chronic lymphocytic leukemia (CLL) treated with obinutuzumab-chlorambucil.

H. Vellemans, A. Sonet, J. Depaus, E. Collinge, B. Devalet, M. André

CHU UCL Namur Mont-Godinne, Yvoir, BELGIUM

Objectives

Toxoplasmosis, usually due to reactivation of a latent infection with toxoplasma gondii, can cause a life-threatening CNS or disseminated infection in immunocompromised patients.

Methods

We describe the case of an old man who developed toxoplasmic encephalitis after a treatment with obinutuzumab-chlorambucil for a CLL.

Results

A 76-year-old man was diagnosed in 2008 with CLL stage Binet A (13q14 deletion). In October 2018, the patient developed auto-immune hemolytic anemia and grade III thrombocytopenia, classifying CLL as stage Binet C. Given the age, obinutuzumab-chlorambucil was started on January 2019. Five of six cycles were administered due to hematological toxicity. The treatment ended in May 2019 with persistent anemia. Seven months later, the patient presented to the emergency for confusion, agitation, Brocca aphasia, diplopia and left mydriasis. Biology showed especially lymphocytopenia. Brain MRI showed at least eight intra-axial supra-tentorial lesions. Three of them were supracentimetric with marked perilesional edema predominant in the left parietal, compatible with secondary lesions (no argument for lymphoma or PML). In 2018, toxoplasma serology was IgG positive. An exhaustive bacteriological assessment was carried out with, among others, search for cryptococcus, herpes simplex and toxoplasma gondii in CSF: negative. Thereby, a brain biopsy was performed and showed florid toxoplasmosis associated with encephalitis. Treatment with high dose trimethoprim-sulfamethoxazole (TMP/SMX) was started. Further, TMP/SMX was stopped because of major hyponatremia and shifted to clindamycin 600 mg four times a day and pyrimethamine 75 mg once daily for a duration of 42 days. An improvement in the patient's neurological condition was gradually observed.

Discussion

Obinutuzumab (type II humanised anti-CD20 recombinant monoclonal antibody) combined with chlorambucil, is indicated for the treatment of previously untreated CLL in elderly unfit patients. A depletion of B lymphocytes caused by the anti-CD20 antibody is to be anticipated during treatment and often predisposing to a variety of infectious complications**.** Cerebral toxoplasmosis is among the most common CNS infections in immunocompromised patients. A recent retrospective French study of 180 PCR-positive toxoplasmosis cases in immunocompromised patients found that 14% of cases occurred in the non-transplant, non-HIV-infected group, especially in patients with hematologic malignancy and connective tissue disease on immunosuppressive medications[1].For the diagnosis of

[1] Robert-Gangneux F and al.2015. Molecular diagnosis of toxoplasmosis in immunocompromised patients: a 3-year multicenter retrospective study. J Clin Microbiol 53:1677–1684

toxoplasma lesions, brain imaging like MRI should be used as initial choice due to its greater sensitivity than CT. A brain biopsy provides a definitive diagnosis of toxoplasmosis in most cases. The cornerstone of treatment is a combination of pyrimethamine, trimethoprim-sulfamethoxazole, sulfadiazine or clindamycin.

Conclusion

With the advent of new monoclonal antibodies and the associated lymphopenia, there is an evolving need for recommendation for prevention and management of opportunistic infection in patients receiving these agents. It is essential to think of opportunistic cerebral infections even at distance from therapy. Brain MRI and prompt brain biopsy can provide rapid diagnosis and adequate treatment of cerebral toxoplasmosis.