JVIN Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Convexity Subarachnoid Hemorrhage Secondary to Adalidumab in a Patient with Ulcerative Colitis

Lucrecia Bandeo[1*], **Astrid Rausch**[2], **Miguel Saucedo**[1], **Anibal Chertcoff**[1], **Luciana Leon Cejas**[1], **Claudia Uribe Roca**[1], **Sol Pacha**[1], **Manuel Fernandez Pardal**[1], **Ricardo Reisin**[1], and **Pablo Bonardo**[1]

[1]*Department of Neurology, Hospital Británico de Buenos Aires, Buenos Aires, Argentina*

[2]*Department of Gastroenterology, Hospital Británico de Buenos Aires, Buenos Aires, Argentina*

Abstract

The TNF-α antagonists are the drugs used for the treatment of ulcerative colitis (UC). Nontraumatic convexity subarachnoid hemorrhage is an infrequent nonaneurysmal subtype of subarachnoid bleeding caused mainly by reversible cerebral vasoconstriction syndrome (RCVS), cerebral amyloid angiopathy, and posterior reversible encephalopathy syndrome (PRES).

We present a 26-year-old female patient with a diagnosis of UC taking Adalimumab. She received her last doses the same day she was admitted to our hospital for an acute severe UC exacerbation. Steroids were added to the treatment. Five days after admission she presented a thunderclap headache with photophobia, nausea, and vomiting. An MRI was performed showing left frontal convexity subarachnoid hemorrhage and hyperintense lesions on T2-weighted and FLAIR sequences located in both occipital lobes, left cerebellar hemisphere, and brainstem. Digital angiography was unremarkable. Adalimumab was discontinued but persisted on treatment with steroids. The patient evolved with complete resolution of her symptoms and was discharged with a normal neurological exam. Two months later, she was asymptomatic and her MRI revealed superficial siderosis secondary to cSAH with resolution of white matter hyperintensities.

Convexity subarachnoid hemorrhage in our patient could be secondary to PRES or to RCVS. Analogous MRI findings can be observed in both syndromes, along with similar clinical and angiographic findings. This suggests that both conditions may reflect different manifestations of the same pathology, in which vascular tone and endothelial dysfunction play a major role. To our knowledge, this is the first report of a patient with severe UC and convexity subarachnoid hemorrhage associated with Adalimumab.

Introduction

Ulcerative colitis (UC) is an idiopathic chronic inflammatory disease of the large bowel characterized by a remitting-relapsing clinical course [1]. The Food and Drug Administration approved TNF-α antagonists in 2005 for its use in UC. Since then, they have become a mainstay for its treatment, especially in steroid-dependent or resistant outpatients with moderately to severely active UC, and for in-patients with acute severe steroid-refractory colitis exacerbation [1,2].

Nontraumatic convexity subarachnoid hemorrhage (cSAH) is an infrequent nonaneurysmal subtype of subarachnoid bleeding, localized in one or more cortical sulci of the brain without the involvement of the adjacent parenchyma or extension into the interhemispheric fissures, basal cisterns, or ventricles. Many etiologies have been related to cSAH, with reversible cerebral vasoconstriction syndrome (RCVS), cerebral amyloid angiopathy, and posterior reversible encephalopathy syndrome (PRES) being the most common [3].

We report a patient with acute severe UC that presented a convexity subarachnoid hemorrhage associated with Adalimumab.

Case Report

The patient was a 26-year-old woman with a diagnosis of UC, taking Adalimumab (40 mg every other week) as

Vol. 10, No. 2, pp. 62–64. Published November, 2018.

Address correspondence to: Lucrecia Bandeo.

***Corresponding Author:** Lucrecia Bandeo, Department of Neurology, Hospital Británico de Buenos Aires, Perdriel 74, Buenos Aires 1280, Argentina. Tel.: (54) 11-4304-1081. lucre.bandeo@gmail.com.

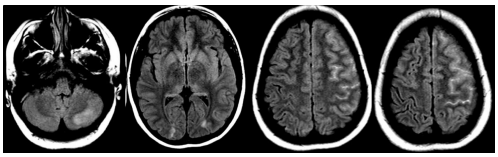

Figure 1. MRI 24 hours after symptoms onset: FLAIR sequence shows hyperintense signals on the left cerebellar hemisphere and in both occipital lobes. cSAH was also observed in left frontal sulci.

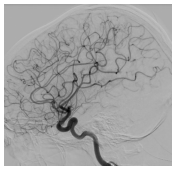

Figure 2. Digital angiography 30 hours after symptoms onset: normal.

the only medication for the last seven months. She received her last doses the same day she was admitted to our hospital for an acute severe UC exacerbation. Steroids were added to the treatment. Five days after admission, she presented a thunderclap headache with photophobia, nausea, and vomiting. Her blood pressure was 150/90 mmHg. Her peripheral blood cell counts were normal and she had no fever or coagulopathy. Brain CT scan was normal. An MRI was performed showing left frontal cSAH and hyperintense lesions on T2-weighted and FLAIR sequences located in both occipital lobes, left cerebellar hemisphere, and brainstem (Figure 1). Diffusion-weighted imaging was normal, and there was no contrast enhancement. Digital angiography was unremarkable (Figure 2). Adalimumab was discontinued but persisted on treatment with steroids. The following five days the patient evolved with complete resolution of her symptoms and was discharged with a normal neurological exam. Two months later, she was asymptomatic and her MRI revealed superficial siderosis secondary to cSAH with resolution of white matter hyperintensities (Figure 3).

Discussion

Our patient had a cSAH associated with white matter lesions during an acute severe UC exacerbation while she was on treatment with Adalimumab.

It is well known that UC may present a great variety of neurological complications: cerebrovascular infarction, cerebral venous thrombosis, vasculitis, demyelinating

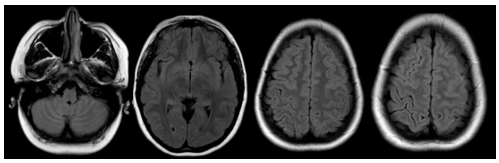

Figure 3. MRI performed two months later: shows superficial siderosis secondary to cSAH and resolution of white matter hyperintensities.

disease, epilepsy, autonomic nervous system dysfunction, cranial mononeuropathies, and neuromuscular diseases like myasthenia gravis, myopathy, and peripheral neuropathy with acute or chronic axonal/demyelinating involvement. Some of these complications are treatment-related and some are not [4,5]. However, PRES, RCVS, or cSAH has not been previously associated with UC itself. There is one report of PRES associated with acute exacerbation of UC without immunosuppressive therapy. The patient was a 25-year-old female diagnosed with UC four years before without regular treatment. She was hospitalized for an acute severe UC exacerbation and was treated with antibiotics (cefazolin, vancomycin, metronidazole), prednisolone, 5-aminosalicylate, and blood transfusions. Her clinical and radiological presentation resembled PRES, interpreted as secondary to blood transfusions or as an atypical presentation of metronidazole-induced encephalopathy [6]. This patient did not receive immunosuppressive treatment, but she received blood transfusions a well-known risk factor for developing PRES.

Our patient was treated with Adalimumab and steroids for an acute exacerbation of UC. Many neurological complications have been reported following therapy with TNF-α antagonists. An increased risk of central nervous system demyelination, peripheral neuropathies, and leukoencephalopathy was described on patients treated with etanercept, infliximab, certolizumab, and adalimumab [7]. Mahévas *et al*. [8] have recently described PRES associated with anti-TNF-α. They reported a 58-year-old female patient diagnosed with spondyloarthritis who was taking Adalimumab. She presented headache, unsteadiness, horizontal diplopia, and vomiting. Her MRI showed white matter lesions compatible with PRES but without cSAH. Two weeks after the drug was discontinuation her MRI was normal. Two more cases of PRES during anti-TNF-α therapy have been reported: a male subject taking etanercept for rheumatoid arthritis and a female taking infliximab for Crohn's disease [8]. Nevertheless, neither of both cases had cSAH.

Convexity subarachnoid hemorraghe in our patient could be secondary to PRES or to RCVS. Analogous

MRI findings can be observed in both syndromes, along with similar clinical and angiographic findings. Interestingly, PRES-like lesions are observed in 38% of patients with RCVS, and likewise, vasoconstriction is observed in 85% of patients with PRES when arteriography is performed. This suggests that both conditions may reflect different manifestations of the same pathology, in which the vascular tone and endothelial dysfunction play a major role [9]. Although digital angiography was normal in our patient, RVCS could not be excluded. In up to one-third of patients with RCVS vasoconstriction may not be visualized during the first week following symptom onset. This could be due to initial segmental vasoconstriction in small and peripheral arterioles before the involvement of medium and large cerebral arteries is evident [10].

To our knowledge, this is the first report of a patient with severe UC and convexity subarachnoid hemorrhage associated with Adalimumab. Physicians should be aware of this serious adverse event since early diagnosis and appropriate treatment could reverse the clinical scenario.

Acknowledgments

None.

References

1. Pugliese D, et al. Anti Tnf-α therapy for ulcerative colitis: current status and prospects for the future. *Expert Rev Clin Immunol* 2017;13(3):223–233.
2. Cohen BL, Sachar DB. Update on antitumor necrosis factor agents and other new drugs for inflammatory bowel disease. *BMJ* 2017;357:j2505.
3. Kumar S, et al. Atraumatic convexal subarachnoid hemorrhage: clinical presentation, imaging patterns, and etiologies. *Neurology* 2010;74(11):893–899.
4. Moris G. Inflammatory bowel disease: an increased risk factor for neurologic complications. *World J Gastroenterol* 2014;20(5):1228–1237.
5. Ferro JM, et al. Neurologic manifestations of inflammatory bowel diseases. *Handb Clin Neurol* 2014;120:595–605.
6. Kikuchi S, et al. Reversible posterior leukoencephalopathy syndrome associated with treatment for acute exacerbation of ulcerative colitis. *Intern Med* 2016;55(5):473–477.
7. Deepeak P, et al. Neurological events with tumor necrosis factor alpha inhibitors reported to the Food and Drug Administration Adverse Event Reporting System. *Aliment Pharmacol Ther* 2013;38(4):388–396.
8. Mahévas T, et al. Posterior reversible encephalopathy syndrome (PRES) in a patient taking adalimumab for spondyloarthritis. *Joint Bone Spine* 2016;83(2):243–244.
9. Fischer M, Schmutzhard E. Posterior reversible encephalopathy syndrome. *J Neurol* 2017;264(8):1608–1616.
10. Miller TR. Joint Bone Spine. Reversible cerebral vasoconstriction syndrome, part 2: diagnostic work-up, imaging evaluation, and differential diagnosis. *Am J Neuroradiol* 2015;36(9):1580–1588.