EDORIUM Journals
www.edoriumjournals.com

CLINICAL IMGES PEER REVIEWED | OPEN ACCESS

Rituximab-related posterior reversible encephalopathy syndrome in HUS patient post kidney transplant

Mohamad Habli, Nada Elyoussef, Mounir Khoury, Najat Joubran Fares

ABSTRACT

Abstract is not required for Clinical Images

CLINICAL IMAGES PEER REVIEWED | OPEN ACCESS

Rituximab-related posterior reversible encephalopathy syndrome in HUS patient post kidney transplant

Mohamad Habli, Nada Elyoussef, Mounir Khoury, Najat Joubran Fares

CASE REPORT

A 27-year-old female admitted for evaluation of anemia, thrombocytopenia, low grade fever and elevated creatinine two months after kidney transplantation.

Patient was receiving at home tacrolimus 2 mg bid, mycophenolate mofetil 1 g bid, prednisolone 20 mg daily, valgancyclovir 900 mg, and sulfamethoxazole/ trimethoprim 900/160 mg three times/week. On admission patient was hemodynamically stable with blood pressure 110/70 mmHg, pulse rate 78/min, temperature 37.8°. No history of hypertension or hypertensive crisis. No elevated blood pressure recorded during hospitalization.

Upon admission, patient underwent kidney biopsy that showed features of thrombotic microangiopathy (TMA).

So patient was started on daily sessions of plasma exchange with fresh frozen plasma for five consecutive days without any improvement in platelet count or hemoglobin level and evidence of ongoing hemolysis (very low haptoglobin level, high LDH, low platelets and hemoglobin level).

Anti-CD20 rituximab was suggested as second line therapy for treatment of atypical HUS.

Mohamad Habli[1], Nada Elyoussef[2], Mounir Khoury[2], Najat Joubran Fares[1]

Affiliations: [1]Division of Nephrology, Department of Internal Medicine, Saint George Hospital University of Balamand, Beirut, Lebanon; [2]Division of Neurology, Department of Internal Medicine, Saint George Hospital University of Balamand, Beirut, Lebanon.

Corresponding Author: Mohamad Mostafa Habli, Division of Nephrology, Department of Internal Medicine, Saint George Hospital University of Balamand, Beirut, Lebanon; Email: dr_mh_habli@hotmail.com

Received: 26 October 2015
Published: 01 February 2016

Eight hours following infusion of rituximab, patient started to complain of severe headache, blurred vision with scintillating scotomas, right hemianopsia that progressed to generalized constriction of the visual field with tunnel vision. Patient also developed simple focal seizures with rotation of eyes and head towards the right side. So, urgent MRI scan of brain was done (Figure 1) which showed extensive involvement of the posterior regions of both hemispheres, more prominent in the left posterior circulation, sparing the gray matter and unassociated with mass effect.

There are focal areas of increased signal on T2 FLAIR in the parietal and occipital lobes bilaterally and posteriorly. There are more prominent on the left. A similar subcortical patch of T2 increased signal is also noted in the left temporal lobe. These show faint or no restriction on diffusion. Signs in favor of posterior reversible encephalopathy syndrome (PRES).

Patient was started on antiepileptic drug (valproic acid IV) and pain killer for headache (paracetamol). During the same day patient complained from on and off visual symptoms and recurrent facial fasciculation, but headache subsided.

On the next day, patient developed more severe headache and facial fasciculation and blurred vision persist, so another MRI scan of brain was done (Figure 2).

The examination is compared to previous done on the previous day. There is increase in the extension of the previously described cortical and subcortical hyperintensities of the posterior aspects of the occipital and parietal lobes as well as of the left temporal lobe.

Decision was taken to do plasma exchange in order to remove rituximab as offending drug, because of severe neurological symptoms and worsening of radiological findings. So, on day-2 after rituximab therapy, patient underwent plasmapheresis with albumin. A Few hours following plasma exchange, patient started to have marked improvement in blurred vision and headache subsided. On day-3, patient was free of all neurological symptoms that developed after IV administration of anti-

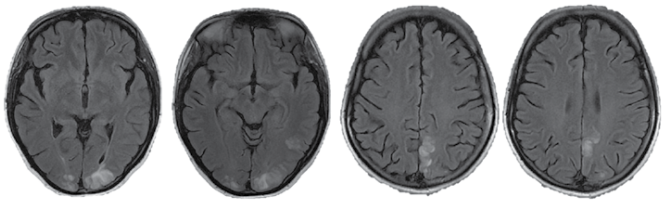

Figure 1: Magnetic resonance imaging of brain T2 FLAIR.

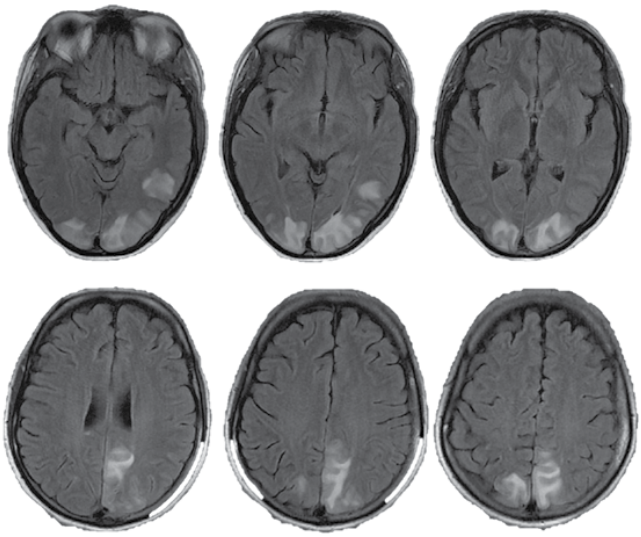

Figure 2: Magnetic resonance imaging of brain T2 FLAIR.

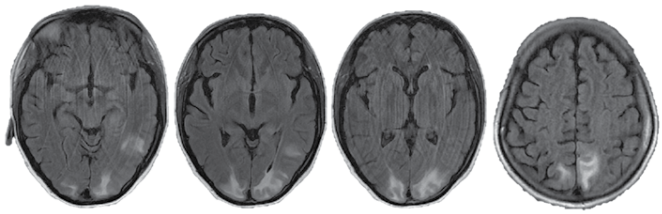

Figure 3: Magnetic resonance imaging of brain T2 FLAIR.

CD 20. No blurred vision or hemianopsia, no headache, and no more simple focal seizures.

Follow-up brain MRI scan was done on day-3 to check if clinical improvement was associated with radiological improvement also.

There has been a significant decrease in the high signal intensity in the cortical and subcortical regions of the parietal and occipital lobes. In particulars the diffusion restriction has also decreased markedly.

DISCUSSION

Although posterior reversible encephalopathy syndrome (PRES) has been recognized after description by Hinchey et al. in the mid-nineties, both its clinical symptoms and underlying causes remain poorly defined.

The diagnosis of PRES includes the presence of neurological symptoms such as seizure, headache, encephalopathy, and visual disturbances, in addition to radiologic findings on brain MRI of focal vasogenic edema [1–7]. The syndrome was described in association with acute hypertension, preeclampsia or eclampsia, renal disease, sepsis, and exposure to immunosuppressive agents [8–14]. It has been less commonly described in the setting of autoimmune disease [15–19].

Radiographic findings in PRES are rarely isolated to the posterior white matter, despite the syndrome's name, and instead often involve the cortex, frontal, occipital lobes, brainstem and basal ganglia [20, 21]. No strong evidence supports a clear relationship between severity of clinical symptoms and specific imaging findings, although some studies correlated greater vasogenic edema in normotensive patients [11] and basal ganglia involvement in patients with preeclampsia or eclampsia [22].

The pathophysiology of PRES remains unclear, but the most widely accepted theory appears to be related to disordered cerebral autoregulation, particularly in the posterior head region. When the upper limit of cerebral

Table 1: laboratory findings upon admission and during hospitalization.1 hemoglobin, 2 laboratory studies upon admission, 3 laboratory studies on day of treatment (before administration of rituximab), 4 to note that patient received one PRBC, 5 laboratory studies on day-1 after administration of rituximab.

Date	WBC(10^3/ mm^3)	Hb1 (g/dl)	platelets(10^3/mm^3)	LDH (U/L)	Haptoglobin (g/l)	Creatinine(g/dl)
Day a2	3.2	7.3	41	781	0.07	2.4
Day b3	5.8	8.84	43	1014	0.11	3.6
Day c5	4	9.1	33	656	0.16	3.8

autoregulation is exceeded, arterioles dilate and cerebral blood flow increases resulting brain hyperperfusion causes extravasation of fluid and blood products into the brain parenchyma [7, 16, 23].

An alternative theory proposes that endothelial dysfunction has also been implicated in the pathogenesis of PRES, especially in cases associated with preeclampsia or cytotoxic drugs [24, 25].

In some clinical settings, renal failure, sepsis, hypomagnesemia, and other metabolic disturbances may be responsible for the associated symptoms and radiologic findings [26–28].

Rituximab (anti-CD 20 monoclonal antibody) has increasingly been used for the treatment of hematological malignancies and autoimmune diseases [29]. Rituximab is used in the treatment of patients with non-Hodgkin's lymphoma in addition to its use in conditions such as lupus nephritis, glomerular disease refractory to conventional treatment, and sarcoidosis. There have been a lot of reports detailing cases of patients developing PRES after receiving rituximab [30, 31]. Similar to our case, patients in these reports developed symptoms early, even within a few hours of receiving rituximab, and symptoms lasted for a day or two before disappearing without leaving any neurological deficit.

The PRES was also reported in patients with thrombotic thrombocytopenic purpura (TTP) as a predominant radiological finding [32–34]. In these reports, authors evaluated neuroimaging studies performed over a 10-year period. Of the patients who had acute abnormalities on brain magnetic resonance imaging, PRES was found in about half of the cases. PRES findings on brain MRI scan were not related to drug administration or initiation of therapy.

In our case, the typical onset of classical neurological symptoms after administration of rituximab and their resolution in less than 48 hours favors the theory of rituximab-associated PRES rather than association with thrombotic microangiopathy (TMA).

CONCLUSION

Posterior reversible encephalopathy syndrome (PRES) is a clinical radiographic syndrome of heterogeneous etiologies that are grouped together because of similar findings on neuroimaging studies. The syndrome is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain.

The posterior reversible encephalopathy syndrome is most commonly encountered in association with acute hypertension, preeclampsia or eclampsia and sepsis. Anti-CD20 related PRES is a rare entity, reported in patients with lymphoma and neuromyelitis optica. Rituximab is increasingly used in the treatment of some glomerular diseases refractory to conventional treatment. So nephrologists should be aware of this major side effect when using this drug.

Keywords: Encephalopathy syndrome, Kidney transplant, Plasma exchange, Posterior reversible encephalopathy syndrome (PRES), Rituximab

How to cite this article

Habli M, Elyoussef N, Khoury M, Fares NJ. Habli. Rituximab-related Posterior reversible encephalopathy syndrome in HUS patient post kidney transplant. Int J Case Rep Images 2016;7(2):135–139.

doi:10.5348/ijcri-201603-CL-10096

****

Author Contributions

Mohamad Habli – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Nada Elyoussef – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Mounir Khoury – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Najat Joubran Fares – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

REFERENCES

1. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. N Engl J Med 2009 Oct 22;361(17):1676–87.
2. Nürnberger J, Philipp T, Witzke O, et al. Eculizumab for atypical hemolytic-uremic syndrome. N Engl J Med 2009 Jan 29;360(5):542–4.

3. Legendre CM, Licht C, Muus P, et al. Terminal complement inhibitor eculizumab in atypical hemolytic-uremic syndrome. N Engl J Med 2013 Jun 6;368(23):2169–81.
4. Caramazza D, Quintini G, Abbene I, et al. Rituximab for managing relapsing or refractory patients with idiopathic thrombotic thrombocytopenic purpura--haemolytic uraemic syndrome. Blood Transfus 2010 Jul;8(3):203–10.
5. Yassa SK, Blessios G, Marinides G, Venuto RC. Anti-CD20 monoclonal antibody (Rituximab) for life-threatening hemolytic-uremic syndrome. Clin Transplant 2005 Jun;19(3):423–6.
6. Lionet A, Provôt F, Glowacki F, Frémeaux-Bacchi V, Hazzan M. A case of adult atypical haemolytic uraemic syndrome related to anti-factor H autoantibodies successfully treated by plasma exchange, corticosteroids and rituximab. NDT Plus 2009 Dec;2(6):458–60.
7. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. Mayo Clin Proc 2010 May;85(5):427–32.
8. Hauser RA, Lacey DM, Knight MR. Hypertensive encephalopathy. Magnetic resonance imaging demonstration of reversible cortical and white matter lesions. Arch Neurol 1988 Oct;45(10):1078–83.
9. Schwaighofer BW, Hesselink JR, Healy ME. MR demonstration of reversible brain abnormalities in eclampsia. J Comput Assist Tomogr 1989 Mar-Apr;13(2):310–2.
10. Raroque HG Jr, Orrison WW, Rosenberg GA. Neurologic involvement in toxemia of pregnancy: reversible MRI lesions. Neurology 1990 Jan;40(1):167–9.
11. Bartynski WS, Boardman JF, Zeigler ZR, Shadduck RK, Lister J. Posterior reversible encephalopathy syndrome in infection, sepsis, and shock. AJNR Am J Neuroradiol 2006 Nov-Dec;27(10):2179–90.
12. Furukawa M, Terae S, Chu BC, Kaneko K, Kamada H, Miyasaka K. MRI in seven cases of tacrolimus (FK-506) encephalopathy: utility of FLAIR and diffusion-weighted imaging. Neuroradiology 2001 Aug;43(8):615–21.
13. Small SL, Fukui MB, Bramblett GT, Eidelman BH. Immunosuppression-induced leukoencephalopathy from tacrolimus (FK506). Ann Neurol 1996 Oct;40(4):575–80.
14. Appignani BA, Bhadelia RA, Blacklow SC, Wang AK, Roland SF, Freeman RB Jr. Neuroimaging findings in patients on immunosuppressive therapy: experience with tacrolimus toxicity. AJR Am J Roentgenol 1996 Mar;166(3):683–8.
15. Kur JK, Esdaile JM. Posterior reversible encephalopathy syndrome--an underrecognized manifestation of systemic lupus erythematosus. J Rheumatol 2006 Nov;33(11):2178–83.
16. Primavera A, Audenino D, Mavilio N, Cocito L. Reversible posterior leucoencephalopathy syndrome in systemic lupus and vasculitis. Ann Rheum Dis 2001 May;60(5):534–7.
17. Pozo-Rosich P, Villoslada P, Canton A, Simo R, Rovira A, Montalban X. Reversible white matter alterations in encephalopathy associated with autoimmune thyroid disease. J Neurol 2002 Aug;249(8):1063–5.
18. Tateishi Y, Iguchi Y, Kimura K, Aoki J, Uemura J, Shibazaki K. A case of autoimmune thyroid disease presenting posterior reversible encephalopathy syndrome. J Neurol Sci 2008 Aug 15;271(1-2):203–6.
19. Bohnen NI, Parnell KJ, Harper CM. Reversible MRI findings in a patient with Hashimoto's encephalopathy. Neurology 1997 Jul;49(1):246–7.
20. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR Am J Neuroradiol 2007 Aug;28(7):1320–7.
21. Lee VH, Wijdicks EF, Manno EM, Rabinstein AA. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol 2008 Feb;65(2):205–10.
22. Mueller-Mang C, Mang T, Pirker A, Klein K, Prchla C, Prayer D. Posterior reversible encephalopathy syndrome: do predisposing risk factors make a difference in MRI appearance? Neuroradiology 2009 Jun;51(6):373–83.
23. Schwartz RB, Jones KM, Kalina P, et al. Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases. AJR Am J Roentgenol 1992 Aug;159(2):379–83.
24. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. Am J Obstet Gynecol 1998 Nov;179(5):1359–75.
25. Aird WC. The role of the endothelium in severe sepsis and multiple organ dysfunction syndrome. Blood 2003 May 15;101(10):3765–77.
26. Trommer BL, Homer D, Mikhael MA. Cerebral vasospasm and eclampsia. Stroke 1988 Mar;19(3):326–9.
27. Ito T, Sakai T, Inagawa S, Utsu M, Bun T. MR angiography of cerebral vasospasm in preeclampsia. AJNR Am J Neuroradiol 1995 Jun-Jul;16(6):1344–6.
28. Lin JT, Wang SJ, Fuh JL, Hsiao LT, Lirng JF, Chen PM. Prolonged reversible vasospasm in cyclosporin A-induced encephalopathy. AJNR Am J Neuroradiol 2003 Jan;24(1):102–4.
29. Boye J, Elter T, Engert A. An overview of the current clinical use of the anti-CD20 monoclonal antibody rituximab. Ann Oncol 2003 Apr;14(4):520–35.
30. Berger JR, Neltner J, Smith C, Cambi F. Posterior reversible encephalopathy syndrome masquerading as progressive multifocal leukoencephalopathy in rituximab treated neuromyelitis optica. Mult Scler Relat Disord 2014 Nov;3(6):728–31.
31. Siddiqi AI. Rituximab as a possible cause of posterior reversible encephalopathy syndrome. Australas Med J 2011;4(9):513–5.
32. Hawley JS, Ney JP, Swanberg MM. Thrombotic thrombocytopenic purpura-induced posterior leukoencephalopathy in a patient without significant renal or hypertensive complications. J Postgrad Med 2004 Jul-Sep;50(3):197–9.
33. Burrus TM, Mandrekar J, Wijdicks EF, Rabinstein AA. Renal failure and posterior reversible encephalopathy syndrome in patients with thrombotic thrombocytopenic purpura. Arch Neurol 2010 Jul;67(7):831–4.

34. Burrus TM, Wijdicks EF, Rabinstein AA. Brain lesions are most often reversible in acute thrombotic thrombocytopenic purpura. Neurology 2009 Jul 7;73(1):66–70.

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.

Most Favored Author program

Join this program and publish any number of articles free of charge for one to five years.

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US