Case Report

Atypical Posterior Reversible Encephalopathy Syndrome (PRES) in a Patient with Polymyalgia Rheumatica and Giant Cell Arteritis

PAOLO FALSETTI[1], CATERINA ACCIAI[2], EDOARDO CONTICINI[1], LUCA CANTARINI[1], BRUNO FREDIANI[1]

[1]Rheumatology Unit, University of Siena, Santa Maria alle Scotte Hospital, Siena, Italy

[2]Neurorehabilitation Unit, S. Donato Hospital, Arezzo, Italy

ABSTRACT: Posterior reversible encephalopathy syndrome (PRES) is a potentially life-threatening condition, composed of focal neurologic symptoms and peculiar magnetic resonance imaging (MRI) findings suggestive for cerebral vasogenic edema. PRES has been predominantly associated with severe hypertension, but a concomitant inflammatory state, common in vasculitis, can contribute to worsening cerebral vasogenic edema towards cytotoxic edema, and it should be promptly treated with glucocorticoids (GC). Atypical cases of PRES should be suspected in cases of focal neurologic symptoms, associated with severe hypertension, and systemic inflammation. We report the first description of a patient with polymyalgia rheumatica and giant cell arteritis who developed PRES after GC discontinuation for arthroscopic surgery.

KEYWORDS: *PRES, Posterior reversible encephalopathy syndrome, Polymyalgia rheumatica, Giant cell arteritis.*

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a relatively new neuroradiological diagnosis. Hinchey described in 1996 a reversible syndrome presenting with an acute headache, consciousness and visive impairment, seizures, related with cerebral gray and white matter abnormalities due to vasogenic edema. The lesions predominantely affect the brain posterior parietal and occipital lobes, with symmetrical and bilateral appearance [1,2].

In a minority of cases PRES is also caused by endothelial injuries, mainly reported in inflammatory states as sepsis, vasculitis and immuno-mediated diseases [3-6]. PRES is associated with significant morbidity and mortality if it is not expeditiously recognized, and in about a third of cases the presentation is atypical and asymmetrical [7].

The first-choice treatment for PRES includes blood pressure reduction and supportive measures, while the use of glucocorticoids (GC) remains debated [1,2].

Polymyalgia rheumatica (PMR) is the most common inflammatory syndrome of elderly and it can be associated with giant cell arteritis (GCA), a large vessel (LV) vasculitis, in about a third of cases [8]

GCA is the most common primary systemic vasculitis, mainly occurring in older subjects and involving large and medium size arteries, especially the branches of the external carotid artery such as temporal artery (cranial-GCA) and supra-aortic branches (LV-GCA) [8].

Early diagnosis and prompt treatment of patients with GCA are important since patients may develop irreversible ischemic damages, as blindness due to ischemic optic neuropathy, or strokes [8,9].

Ultrasound (US) has been used in diagnosis of GCA with high diagnostic accuracy, low invasivity and low costs [10,11].

GCA is characterized by inflammatory infiltration of the artery wall resulting in the "halo sign", which is a hypoechoic uncompressible circumferential thickening of the vessel wall due to edema, as visualized by US [10,11].

We reported the first case, to date, of atypical PRES in a patient with PMR and US-diagnosed cranial-GCA presenting with acute and asymmetric neurologic symptoms, with severe hypertension and inflammatory state, where only high doses of GC could lead to full recovery.

Case Description

A 67-year-old Italian man, with a history of hypertension and PMR in low dose GC therapy, underwents arthroscopic rotator cuff repair with acromioplasty in an orthopedic clinic under general anesthesia and brachial plexus block.

There were no electrocardiographic or laboratory abnormalities on preoperative examination, and his GC therapy was stopped before surgery. On awakening from anesthesia he had self-limiting convulsive generalised

10.12865/CHSJ.47.02.23

seizures, associated with left hemiplegia, hemineglect and homonymous left hemianopsia, mild left hypoesthesia, dysarthria, mild confusion. His blood pressure was high with peak values around 200/100mm Hg. This condition required infusive antihypertensive therapy (Urapidil and Clonidine).

He was tranferred in the same day in the Stroke Unit of local hospital, with suspicion of right hemispheric stroke. Brain computed tomography (CT) excluded cerebral haemorrage. CT-angiography showed not critical stenosis of right vertebral artery. Normal cerebrospinal fluid was obtained with lumbar puncture. The electroencephalogram was negative for electrical seizures. Echocardiography excluded cardiomyopathy, endomyocarditis, valvular heart disease and pericarditis. ECG was negative for arrythmias. Despite the lack of a definite evidence of ischemic stroke he was treated with Clopidogrel 75mg, and Levetiracetam 500mg bid for secondary prevention of seizures. A low dosage of Ramipril mantained blood pressure in the normal range. After 8 days from event, the patients was then transferred in a post-intensive neurorehabilitation unit with dysarthria, dysphagia, left hemiplegia with hypertonia, hemineglect and homonymous left hemianopsia, unable to walk, moderately confused.

He had mild recurrent fever. Laboratory data at admission revealed: C-reactive protein 14mg/L (nv<5), eritrosedimentation rate 46mm/h (nv 2-30), fibrinogen 668mg/dL, (nv 150-450), hemoglobine 11.5g/dL (nv 11.7-16) with normal leucocyte count, normal TSH and complement, cholesterol, omocysteine 12.2 micromol/L (nv 0-15), high levels of triglycerides (550mg/dL, vn <150). All autoimmunity markers resulted negative. Blood and urinary cultures were negative. The patient underwent a MRI with gadolinium with demonstration of edema, predominantly localized in gray and white matter of the occipital and parietal lobes of the brain with asymmetrical appearances (prevalence in the right hemisphere). The lesions were hypointense on T1-weighted and hyperintense on T2-weighted sequences, and they were mostly visible on FLAIR (Fluid-Attenuated Inversion-Recovery) images as cortical and subcortical hyperintensities (Figure 1), without abnormalities on Diffusion Weighted Imaging (DWI). No enhancement was seen following injection of the contrast agent. The radiological findings, together with the presence of severe hypertension at onset, raised the suspicion of PRES [1,2,7].

As hypertension was well controlled with Ramipril, and on the suspicion that a concomitant vasculitis could contribute to mantain brain edema the patient was treated with 8 mg of Desametasone intravenous every day, with slow tapering. Because of the presence of PMR in anamnesis, a GCA was suspected. A high frequency color Doppler ultrasound examination demonstrated "halo sign" at temporal arteries, with not complete compressibility of the vessels (Figure 2).

These data were highly suggestive for cranial GCA [10,11].

Weakness in the left arm and leg improved slowly but continuously, and he was able to walk with mild assistance, without relevant speech, visual or cognitive impairment after two weeks of treatment. The patient was discharged after about one month from event, in good general conditions, after a brain MRI demonstrating complete resolution of the lesions (Figure 3).

A follow-up electroencephalogram produced normal results with no sequelae. The levels of triglycerides restored after GC therapy, suggesting an inflammatory triggering also for this abnormality.

Inflammatory reactants were normalised at discharge and an oral corticosteroid therapy, with slow tapering, was prescribed.

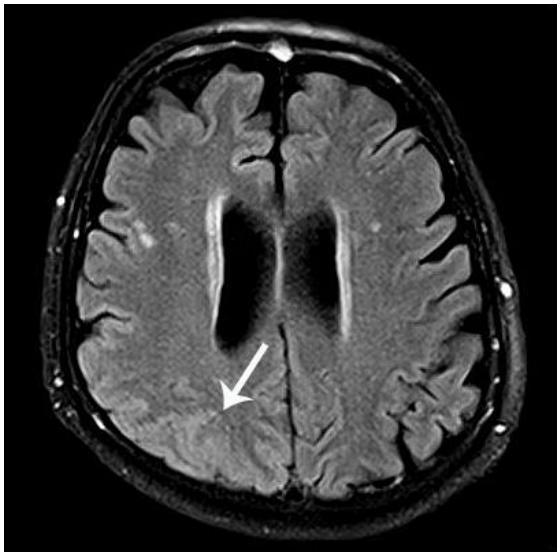

Figure 1. At the time of diagnosis (September, 29), axial Fluid-Attenuated Inversion-Recovery (FLAIR) magnetic resonance (MR) images demonstrated diffuse bilateral areas of hyperintensity because of vasogenic edema in temporo-parietal lobes with cortico-subcortical distribution and predominant right involvement (arrow).

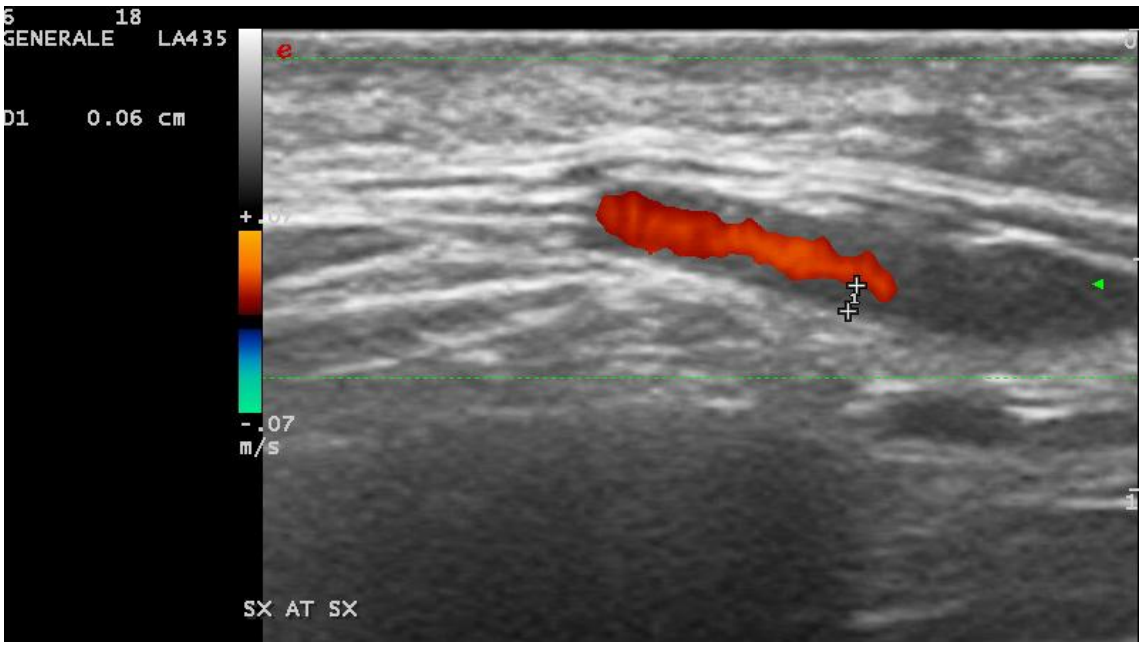

Figure 2. Color Doppler Ultrasound (CDUS) examination with linear multifrequency 6-18 MHz probe. Left temporal artery (common branch) in patient with polymyalgia rheumatica and suspected giant cell arteritis; evidence of wall vessel hypoechoic thickening ("halo sign" suggestive for inflammatory edema) with a significant intima-media thickness (IMT) of 0.6mm.

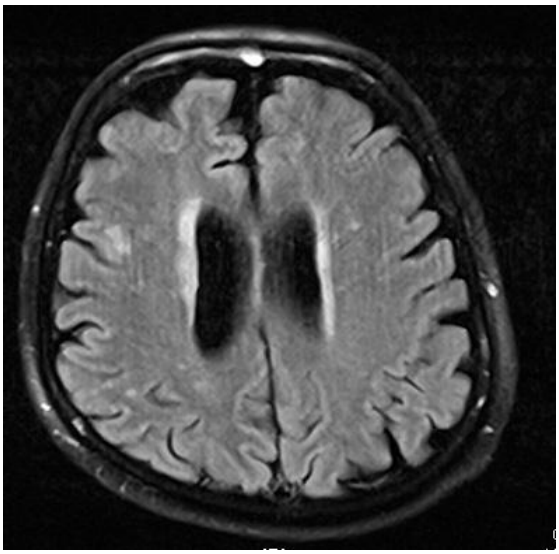

Figure 3. Twenty days later (October, 17), after glucocorticoid therapy, axial Fluid-Attenuated Inversion-Recovery (FLAIR) magnetic resonance (MR) images demonstrated complete regression of signal alteration in both cerebral hemispheres.

Discussion

The pathophysiology of PRES remains to be elucidated. PRES seems to be caused by vascular endothelial dysfunction due to rapid blood pressure variations and excessive production of cytokines from endothelium. The loss of the auto-regulation of posterior cerebral circulation and the leakage of blood brain barrier can cause brain vasogenic edema [1,2].

According to another theory, a direct endothelial injury, as present in autoimmune diseases and septic states, can be a potential etiological factor [3].

However, in most cases, PRES is caused by vasogenic and not cytotoxic edema and the first choice treatment includes reduction of blood pressure and supportive measures [1,2].

In our case neurological symptoms did not resolve with a complete control of hypertension, while they progressively ameliorated with GC therapy. Hypertension and an intense proinflammatory response, probably triggered by the orthopedic surgery and suspension of low GC chronic therapy, could be the culprits for the development of PRES in this patient.

Our observations suggest the hypothesis that also in this case hypertension is to be considered the first step of PRES pathogenesis, while, in a second step, endothelial activation and dysfunction, promoted by inflammation, could have played a crucial role in maintaining vasogenic edema and promoting cytotoxic edema [3].

Altogether, we present the first case of PRES associated to PMR/GCA reported to date although another large vessel vasculitis as Takayasu arteritis has previously been correlated with development of PRES [4].

10.12865/CHSJ.47.02.23

Conclusions

We are hereby suggesting to consider PRES in the differential diagnosis of a neurological deterioration associated with hypertension and inflammation. Even if there is no specific treatment for this condition, an antihypertensive treatment is mandatory, but GC should be added when systemic inflammation is demonstrated.

Acknowledgments

The authors received no grants or fees for writing this article.

Conflict of interests

The authors declare that they have no competing interest.

References

1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, Pessin MS, Lamy C, Mas JL, Caplan LR. A reversible posterior leukoencephalopathy syndrome. N Engl J Med, 1996, 334(8):494-500.
2. Pereira PR, Pinho J, Rodrigues M, Rocha J, Sousa F, Amorim J, Ribeiro M, Rocha J, Ferreira C. Clinical, imagiological and etiological spectrum of posterior reversible encephalopathy syndrome. Arq Neuropsiquiatr, 2015, 73(1):36-40.
3. Marra A, Vargas M, Striano P, Del Guercio L, Buonanno P, Servillo G. Posterior reversible encephalopathy syndrome: The endothelial hypotheses. Medical Hypotheses, 2014, 82:619-622.
4. Camara-Lemarroy CR, Lara-Campos JG, Perez-Contreras E, Rodríguez-Gutiérrez R, Galarza-Delgado DA. Takayasu's arteritis and posterior reversible encephalopathy syndrome: a case-based review. Clin Rheumatol, 2013, 32:409-415.
5. Lioger B, Diot E, Ebbo M, et al. Posterior reversible encephalopathy syndrome and systemic vasculitis: report of six cases. Clin Exp Rheumatol, 2016, 34:S7-11.
6. Khanjar I, Abdulmomen I, Yahia YM, Al-Allaf AW. Posterior Reversible Encephalopathy Syndrome (PRES) in Rheumatic Autoimmune Disease. Eur J Case Rep Intern Med, 2018, 5(6):000866.
7. McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, Teksam M. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. AJR Am J Roentgenol, 2007, 189(4):904-912.
8. Mackie SL, Pease CT. Diagnosis and management of giant cell arteritis and polymyalgia rheumatica: challenges, controversies and practical tips. Postgrad Med J, 2013, 89(1051):284-292.
9. Conticini E, Sota J, Falsetti P, Baldi C, Bardelli M, Bellisai F, Tosi GM, Frediani B, Cantarini L. The Role of Multimodality Imaging in Monitoring Disease Activity and Therapeutic Response to Tocilizumab in Giant Cell Arteritis. Mediators Inflamm, 2020, 27;2020:3203241.
10. Schäfer VS, Jin L, Schmidt WA. Imaging for Diagnosis, Monitoring, and Outcome Prediction of Large Vessel Vasculitides. Curr Rheumatol Rep, 2020, 22(11):76.
11. Schmidt WA. Ultrasound in the diagnosis and management of giant cell arteritis. Rheumatology (Oxford), 2018, 57(suppl_2):ii22-ii31.

Corresponding Author: Paolo Falsetti, Rheumatology Unit, University of Siena, Siena, Italy, Rheumatology Unit, University of Siena, Le Scotte Hospital, Viale Bracci 53100 Siena, Italy, e-mail: paolo.falsetti@virgilio.it