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Case report

# Posterior reversible encephalopathy syndrome in IgA vasculitis: Neuroimaging of a 14-year-old child

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ARTICLE INFO

*Article history:*
Received 2 August 2017
Accepted 5 November 2017
Available online 14 November 2017

*Keywords:*
Posterior leukoencephalopathy syndrome
IgA vasculitis
Children
Hypertension
Nephritis

ABSTRACT

IgA vasculitis (IgAV) is a leukocytoclastic vasculitis and characterized by involvement of small vessels in skin, gastrointestinal system, joints, kidneys, and less frequently other organs. It is the commonest vasculitis in childhood and etiology is not completely known. Neurological manifestations of IgAV are very rare and usually seen in patients with severe hypertension or as an uncommon feature such as peripheral neuropathy. Posterior reversible encephalopathy syndrome (PRES) is a clinic-radiologic entity characterized with temporary vasogenic edema developing typically in posterior circulation of the brain and has been reported as a rare manifestation of IgAV. In this paper, a PRES case of 14-year-old male with IgAV is reported and etiopathogenesis was discussed with literature. Diagnosis was made by magnetic resonance imaging because of the existence of neurological symptoms (headache and visual loss) during the course of disease. His radiological findings have resolved with therapy. Although neurological involvement is a rare manifestation in IgAV, we recommend magnetic resonance imaging in such patients for diagnosis and evaluation of complications.



## 1. Introduction

IgA vasculitis (IgAV) is the most frequent vasculitis of childhood with an incidence of 10–20/100 000/year [1]. IgA vasculitis, formerly called Henoch-Schönlein purpura, is an immune complex vasculitis predominantly affecting small vessels. It is characterized by non-thrombocytopenic purpura, arthritis, arthralgia, and renal involvement, stomachache and gastrointestinal hemorrhage. While, as seen less frequently, every organ system can be involved. Although the etiopathogenesis is not understood completely, various factors such as infectious agents, vaccines, medicines, nutrients, and insect bites have been reported that could trigger the pathogenetic mechanism [1,2].

IgAV is usually a self-limited disease lasting an average of 4 weeks [1]. More commonly, renal involvement is a mild disorder with good prognosis and is presenting with only

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https://doi.org/10.1016/j.pjnns.2017.11.006
0028-3843/

hematuria and/or low-grade proteinuria. Nephrotic syndrome or renal function impairment is rarely seen in IgA vasculitis (IgAV) patients [2].

Posterior reversible encephalopathy syndrome (PRES) has been firstly identified by Hinchey et al. in 1996 and ''reversible posterior leukoencephalopathy syndrome'', ''hypertensive encephalopathy'', ''reversible posterior cerebral edema syndrome'' and ''posterior reversible leukoencephalopathy'' are all terms that have been used to define a clinical and radiologic syndrome characterized by headache, alteration of consciousness, seizures, and visual disturbance associated with reversible cerebral vasogenic edema [3–6]. Main underlying causes in children are hypertensive encephalopathy, haemolytic uremic syndrome, treatment with immunosuppressive drugs, acute/chronic renal failure and lupus nephritis [3,5,7].

In this paper, we present a case, in which skin, kidney, gastrointestinal system involvement have been observed. PRES has developed in association with IgAV and diagnosed by neuroimaging. Abnormal radiological findings disappeared on MRI soon after starting treatment.

## 2. Case report

A 14-year-old male with a two weeks history of purpuric rush, arthralgia, nausea and severe abdominache was admitted to our hospital. The previous medical history was unremarkable. Physical examination on arrival revealed blood pressure (BP) 100/60 mmHg, typical palpable purpura on both lower extremities and arthritis findings on both ankles. His weight was 56 kg (50–75 percentiles) and height 160 cm (25–50 percentiles). No fever, pretibial edema or rebaund on abdominal examination were noted. On laboratory investigation; hemoglobin was 13.9 g/dl, leukocyte count 19 330/mm$^3$ and thrombocyte 209 000/mm$^3$. Serum sodium was 138 mEq/L ($N$ = 136–146), potassium 4.8 mEq/L ($N$ = 3.5–5), calcium 8.2 mg/dl ($N$ = 8.8–10.8), blood urea nitrogen (BUN) 48.5 mg/dl ($N$ = 5–18), creatinine 2 mg/dl ($N$ = 0.3–0.7), albumin 2.8 g/dl ($N$ = 3.9–5.3). Serum transaminases, C-reactive protein, erythrocyte sedimentation rate and coagulation parameters were normal. Urine analysis revealed hematuria and moderate proteinuria (26 mg/m$^2$/h). Diagnosis of IgAV and nephritis has been made based on these findings. To rule out other vasculitis, the serum C3 and C4 levels were normal; ANA, anti-dsDNA, p-ANCA, and c-ANCA were also negative. For arthritis, a non-steroid anti-inflammatory agent was given. The impairment in renal function tests improved via liquid treatment in first two days. Stomachache became intensified, and gastrointestinal system hemorrhage developed, so 1 mg/kg/day dose of oral prednisolone treatment was started. In 3rd day of treatment, chest pain and sinus bradycardia developed. Cardiological examinations and echocardiography were normal.

In 7th day of prednisolone treatment, subconjuctival hemorrhage and severe headache then after sudden visual loss have developed. His level of consciousness was normal but mild pretibial edema has been occurred. In neurological examination, there was no neck stiffness or positive signs of meningeal irritation; motor and sensorial examination were normal, deep tendon reflexes were normoactive. Pupil reflexes were normal but visual acuity was deteriorated. Fundus examination has revealed mild attenuation of optic disk borders, bilaterally. His blood pressure was 150/90 mmHg, so an angiotensin converting enzyme inhibitor (ramipril) was given for hypertension. In brain CT, hypodense visuals were observed in subcortical region of bilateral parietooccipital and cerebellar hemisphere lobes. Cranial MRI was taken for lesion exclusion, and demonstrated hyperintense regions that observed in T2 and FLAIR sequences in corpus collosum splenium, subcortical regions in parieto-occipital lobes and bilateral cerebellar hemispheres (Fig. 1a and b). There were restrictions in diffusion MRI, and hyperintense visual in apparent diffusion coefficient (ADC) images. These findings indicated a diagnosis of PRES developing as a result of IgAV (Fig. 2a and b).

Due to the diagnosis of PRES, intravenous methylprednisolone with dose of 30 mg/kg/day was started. Impairment of vision resolved immediately after treatment, and proteinuria with hypoalbuminemia was gradually improved. Steroid and antihypertensive therapy were given after discharge. Follow-up MRI after two months was revealed complete resolution of previous findings. Renal function tests and urine analysis were also normal in follow-up period. In control MRI examination

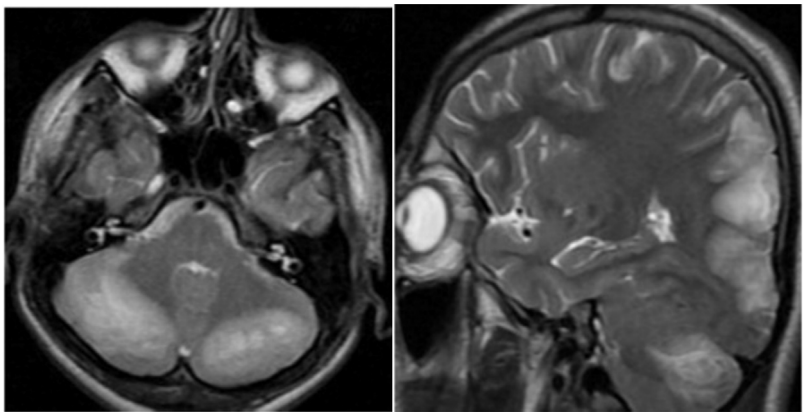

**Fig. 1 – (a and b) Axial and sagittal magnetic resonance fluid attenuated inversion recovery images demonstrate bilateral increased signal within the cortex and subcortical white matter of the parietal and occipital lobes. Lesions also are seen in bilateral cerebellar hemispheres.**

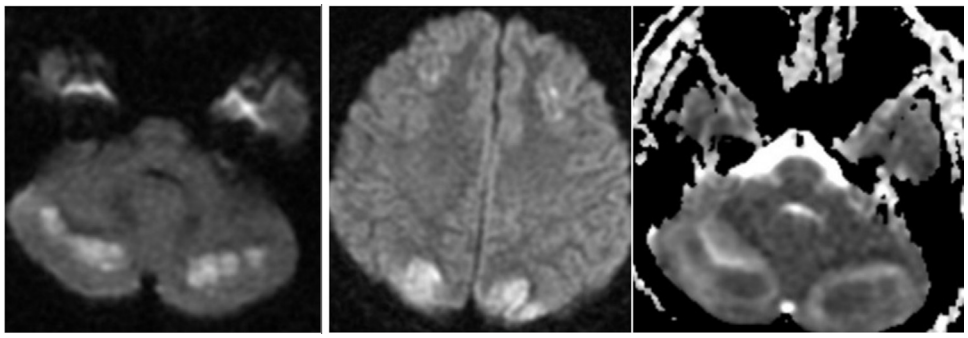

**Fig. 2 – (a–c) Axial diffusion-weighted images revealed restricted diffusivity within these areas of signal change and hyperintense signals on apparent diffusion coefficient images.**

after 4 weeks, a significant improvement was observed and after 2 months, it has been seen that lesions were disappeared (Fig. 3a and b).

## 3. Discussion

The pathogenesis of IgAV is not completely understood. It is a leukocytoclastic vasculitis which is a consequence of subendothelial storage of IgA (only $IgA_1$ subclass) immune complexes in small arteries and capillaries. Therefore, IgAV was commonly seen after various viral and bacterial infections [1,2]. But, generally the exact etiology was remaining undetected in most cases, as in our patient.

Renal manifestations in IgAV are reported to be 10–50% and include, microscopic hematuria and/or proteinuria in most cases, nephritis or nephrotic syndrome (20%) and end-stage renal disease [2]. Garzoni et al. reported that severe renal involvement was the most common (29 of 54 patients) concomitant feature in IgAV patients with neurological dysfunction which indicating close correlation between severity of renal disease and neurological features [8].

Neurological dysfunctions with or without severe hypertension have been documented in IgAV. Headache is reported as the commonest and other central and/or peripheral nervous system manifestations include seizures, peripheral neuropathies, chorea, ataxia, aphasia, blindness, coma, EEG abnormalities, intracerebral hemorrhage and infarcts [2,8]. The incidence is unknown but they have been reported in 1–8% of all IgAV patients [2,8]. In addition, a few PRES cases have also been identified with IgAV [3,9–12]. It has been suggested that, immune complex deposition could lead arteriolar inflammation in the cerebral circulation [12]. On the other hand, renal failure, hypertension, electrolyte imbalance or other concurrent conditions could also contribute pathogenesis of neurological involvement [12].

PRES is a clinic-radiologic entity developing with vasogenic edema characterized by generally bilateral hyperintense signals in T2 and FLAIR images on posterior parietal and occipital lobes [3]. The hyperfusion theory is the most commonly approved pathogenetic mechanism. Briefly, causes of PRES (e.g. sudden increase of blood pressure) can induce breakdown in cerebral autoregulation, and as a result, leakage of fluid into the brain parenchyma has been occurred [3]. Due to the slight control of sympathetic system in posterior

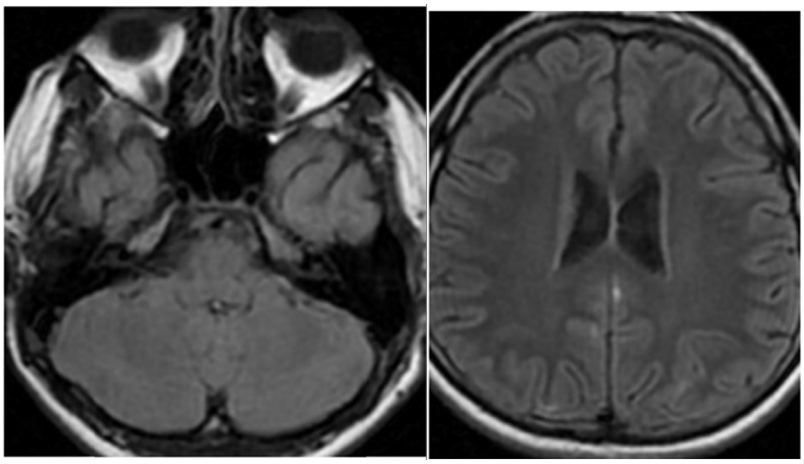

**Fig. 3 – (a and b) Axial magnetic resonance fluid attenuated inversion recovery images performed 2 months after admission show resolution of cerebral lesions.**

**Table 1 – Clinical and radiologic features of patients from literature with PRES in association with IgAV.**

| Age/gender | MRI findings and their localizations | Neurological manifestations | BP (mmHg) | Lab (urine analysis and RFT) | References |
|---|---|---|---|---|---|
| 7/F | Bilateral HWML in the occipital and posterior parietal | GTCC, LOV | 190/100 | Normal | Fuchigami et al. [10] |
| 11/F | Bilateral HWML in the occipitoparietal and left frontal premotor area MRA: normal. | GTCC, LOV, headache, confusion | 115/82 | Normal | Dasarathi et al. [11] |
| 10/M | Bilateral HWML in the occipital and posterior parietal | Convulsions | 130/90 | Normal | Özçakar et al. [7] |
| 13/F | Bilateral HS in the cerebellum, HWML in the occipital, and basal ganglia | GTCC, headache | 180/120 | Grade V HSP nephritis | Sasayama et al. [9] |
| 10/M | Bilateral HS in the parieto-occipital cortical and white matter | LOV, headache | Normal | Hyponatremia (126 mmol/L) | Woolfenden et al. [12] |
| 11/M | Focal lesion in the white and gray matter of the left occipital | GTCC | 150/85 | Normal | Pavlou et al. [14] |
| 8/M | Multifocal bilateral HS within the brain parenchyma | Status epilepticus | 170/115 | Normal | Khandhar et al. [15] |

circulation, lesions are observed dominantly in posterior regions [3,13]. Endothelial dysfunction due to infectious, cytotoxic and immune causes is other possible mechanism [3,5].

In PRES, the signal intensity of lesion is either lower or normal on diffusion-weighted images (DWI), in contrast to cytotoxic edema (high signal in DWI) which is an indicator of acute cerebral infarct. In addition, signal intensity observed on ADC (apparent diffusion coefficient) maps which eliminating the signal effect of T2, is increased while it is low in cytotoxic edema. Although, vasogenic and cytotoxic edemas could seen together and also vasogenic edema can progress to cytotoxic edema, in general, PRES thought to be occurred due to vasogenic edema [3–5,13]. Another difference was that PRES resolves completely after treatment, rather than seen in cytotoxic edema. These features are used to distinguish PRES from ischemic processes such as bilateral posterior lob infarcts and others including cerebral venous thrombosis, viral encephalitis, mitochondrial encephalopathy, hypoglycemia and hyponatremia [3–5].

Hinchey et al. (only adults) and Endo et al. (only children) were reviewed PRES cases due to various causes and reported involving both cortical and subcortical of parieto-occipital, frontal, temporal and cerebellar involvement rate as 93% vs 89.1%, 40% vs 17.4%, 60% vs 17.4% and 6% vs 21.7%, respectively [3,6]. We could identify 7 pediatric case with PRES in association with IgAV in literature. The localizations of lesions are summarized in Table 1. These data present only PRES cases, not vasculitis.

In our case, BP was in normal ranges on admission but it has been increased to 150/90 mmHg level when neurological signs have occurred. According to normograms by age and height in Turkish children, he had a systolic BP above 99th percentile (143 mmHg) and a diastolic BP between 90 and 95th percentile (85–95 mmHg) [16]. Thus, he considered as a slightly hypertensive patient. Most of the children had severe hypertension in previous reports of PRES cases with IgAV. While, Woolfenden et al. and Dasarathi et al. have found radiologic features of PRES without hypertension [11,12]. However, it was difficult to establish the exact cause of PRES in our case, because of positive fundus examination, absence of convulsion or focal neurological deficit, presence of proteinuria and impaired renal functions, the vasogenic pattern of edema and reversible features in neuroimaging by treatment, we determined that our findings as consistent with hypertension. Diagnosis and differentiation of PRES and secondary cerebral vasculitis in IgAV, said to be difficult due to collective attribution of hypertensive or uremic encephalopathy, metabolic disorders, electrolyte imbalance, impairment in auto-regulatory mechanism of cerebral circulation or side effects of steroid therapy [5,10,12,15]. To rule out possible cerebral vasculitis, we did not perform magnetic resonance angiography due to rapid clinical improvement after treatment.

Few data exists concerning treatment of neurologic complications in IgAV. Garzoni et al. suggested that management might include control of hypertension, convulsions and repair of disordered hemostasis with preferably use of steroids and cyclophosphamide for cerebral vasculitis [8]. Early diagnosis of PRES is important, otherwise the clinic situation may advance to ischemia, massive infarct, and even death.

In conclusion, PRES and other severe neurological manifestations can be seen in association with IgAV, the most common vasculitis in childhood. When clinical and radiologic collaboration and follow-up of the disease achieved, PRES can be diagnosed in most cases. Since, delay in the diagnosis and treatment can lead severe damage to CNS and even mortality, this rare complication must be kept in mind in daily practice. Neuroimaging investigations which including diffusion imaging and angiography can give crucial contribution to clinicians for prompt diagnosis. Detailed clinical information and other data of patient will also help the radiologists in evaluating PRES and other entities that can manifest similar findings in neuroimaging.

## Ethical approval

Ethical approval is not necessary for a case report in Regional Education and Research Hospital, Van, Turkey.

## Conflict of interest

None declared.

## Acknowledgement and financial support

None declared.

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