

A Pediatric Case Presented with Posterior Reversible Encephalopathy Due to Cystinosis: Case Report

Çocukluk Çağında Sistinozise Bağlı Posterior Reversibl Ensefalopati Sendromu

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ABSTRACT Cystinosis is an inherited autosomal recessive disorder, which the defect involves cystinosis, the membrane transport protein playing role in amino acid cystine metabolism. Posterior reversible encephalopathy syndrome (PRES) is a clinic-radiographic entity of heterogeneous etiologies that are grouped together because of similar findings on neuro-imaging and associated symptom complex of headache, vision loss, altered mentation, and seizures. We describe a 10-year-old male patient with nephropathic cystinosis being treated with peritoneal dialysis was admitted to emergency service after generalized tonic clonic seizures at home. Initial brain diffusion weighted magnetic resonance imaging indicated that particularly bilateral parieto-occipital regions revealed restricted diffusion areas and cytotoxic edema elicited neural parenchymal insult. In our case, hypertensive crisis related to ineffective peritoneal dialysis and brain tissue damage due to cystinosis may be able to provide a basis for PRES. Appropriate and prompt treatment is essential to protect the patients from harmful effects of irreversible brain injury.

Key Words: Cystinosis; posterior leukoencephalopathy syndrome; kidney failure, chronic; child

ÖZET Sistinozis; sistin aminoasit metabolizmasında membran transport protein olarak görev alan sistinosin proteinindeki defekt sonucu oluşan otozomal resesif kalıtılan bir hastalıktır. Posterior reversibl ensefalopati sendromu (PRES); baş ağrısı, görme kaybı, nöbetler ve bilinç değişikliği gibi semptomlara yol açan ve radyolojik olarak benzer bulgulara sahip birtakım farklı etyolojilerin oluşurabileceği klinik-radyografik bir antitedir. Nefropatik sistinozis nedeniyle periton diyalizi yapılan 10 yaşında erkek hasta jeneralize tonik klonik nöbet geçirme şikayeti ile acil serviste değerlendirildi. Difüzyon ağırlıklı manyetik rezonans görüntülemesinde bilateral parieto-okspital bölgede difüzyon kısıtlılığı ve nöral parankimal hasara neden olan sitotoksik ödem görüldü. Etkin yapılamayan periton diyalizi nedeniyle hipertansif kriz ve sistinozise bağlı beyin dokusundaki hasar PRES için zemin hazırlamış olabilir. Ensefalopati ve konvülsiyonla başvuran sistinozisli pediatrik hastalarda PRES ayırıcı tanılar arasında düşünülmelidir. Uygun ve hızlı müdahale, hastaları ortaya çıkabilecek geri dönüşümsüz beyin hasarının zararlı etkilerinden korumada esastır.

Anahtar Kelimeler: Sistinoz; posterior lökoensefalopati sendromu; böbrek yetmezliği, kronik; çocuk

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Cystinosis is an inherited autosomal recessive disorder, which the defect involves cystinosis, the membrane transport protein playing role in amino acid cystine metabolism. Thus, cystine accumulates in lysosomes and elicits the symptoms in childhood like end stage renal disease, secondary Fanconi syndrome (proximal renal tubular acidosis).¹ Neurologic complications consisting of cystinosis encephalopathy, myopathy, stroke like episode with coma, hemiplegia and myopathy are seen later.

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Clinical findings of cystinosis encephalopathy are characterized by altered mental status, symptoms associated with cerebellar and pyramidal system, pseudo bulber palsy, and seizures.² Magnetic resonance imaging (MRI) in patients with cystinosis shows frequently cerebral/cerebellar atrophy with ventriculomegaly.³

Posterior reversible encephalopathy syndrome (PRES) is a clinic-radiographic entity of heterogeneous etiologies that are grouped together because of similar findings on neuro-imaging and associated symptom complex of headache, vision loss, altered mentation, and seizures.⁴ Although usually considered benign and reversible, characteristics of this syndrome in pediatric patients remain obscure. However, not all cases are reversible, and if left untreated, it may be fatal. It can occur in many clinical situations, the most common being hypertensive crisis.⁵

In this article, we would like to report a PRES case in a child with cystinosis.

CASE REPORT

A 10-year old male patient with nephropathic cystinosis being treated with peritoneal dialysis (PD) was admitted to emergency service after generalized tonic clonic seizures at home. He complained about persistent vomiting and headache over the past several days. During the neurologic examination, we observed that he had impaired consciousness, papilledema, intentional tremor. In addition, his pupils were isochoric, and direct-indirect light reflexes were normal. Deep tendon reflexes were hyperactive and Babinski sign was absent bilaterally. There were no findings of meningeal irritation nor focal neurologic deficit in physical examination. He had severe hypertension (blood pressure; 180/95 mmHg, above 95 percentile) without pretibial edema. His laboratory tests on admission were as follows: hemoglobin, 9 g/dL; hematocrit %28; white blood cells 12000/ mm³; platelets 249000/mm³; blood urea nitrogen 204 mg/dL; creatinine 5,7 g/dL; sodium 134 meq/L; potassium 5.04 meq/L; Cl 94 meq/L; calcium 9 mg/dL; and phosphore 6.4 mg/dL. His liver function tests, total protein and albumin levels were all in normal ranges. Acute phase markers (C-reactive

protein, erythrocyte sedimentation rate, etc) and viral markers were negative. Cranial compute CT images showed not only increment in density of cortex, but also reduction in density of white matter at bilateral parieto-occipital regions and absence of intracranial hemorrhage or space occupying lesion. Diffusion weighted MRI indicated that particularly bilateral parieto-occipital regions revealed restricted diffusion areas and cytotoxic edema elicited neural parenchymal insult (Figure 1A, B). After starting antihypertensive treatment he was transferred to pediatric service. However, generalized tonic clonic seizures repeated, and antiepileptic drug (AED) treatment with phenytoin, together with sodium nitroprusside infusion was initiated. Electroencephalography (EEG) showed generalized slowing waves without epileptiform activity. Based on his medical history, he was on a continuous ambulatory PD program for 7 months because of end stage renal failure (ESRF) due to nephropathic cystinosis, and taking 1.95 g/m²/day dosed cysteamine. However, we have been informed that the last week dialysis was not done adequately. During his previous follow up, blood pressure measurements were within normal range without antihypertensive drug. He had renal osteodystrophy because of ESRF, and bilateral corneal opacity due to the complication of cystinosis.

During the follow up, his clinical symptoms improved after effective peritoneal dialysis, antihypertensive and antiepileptic drug therapy. He had stabilized within 4 days of admission. The following MRI performed at 7th days of admission demonstrated moderate resolution of the bilateral parieto-occipital lesions on both FLAIR sequence and Diffusion weighted sequence (Figure 1C, 1D). Antiepileptic drug therapy medication was terminated as a consequence of lack of seizure. Ten days after admission, the patient recovered and was discharged without any dznd cysteamine for a year and did not have no similar complaint.

DISCUSSION

Posterior reversible encephalopathy syndrome, that Hinchey et al. firstly identified as a clinical neurologic condition including headache, altered mental

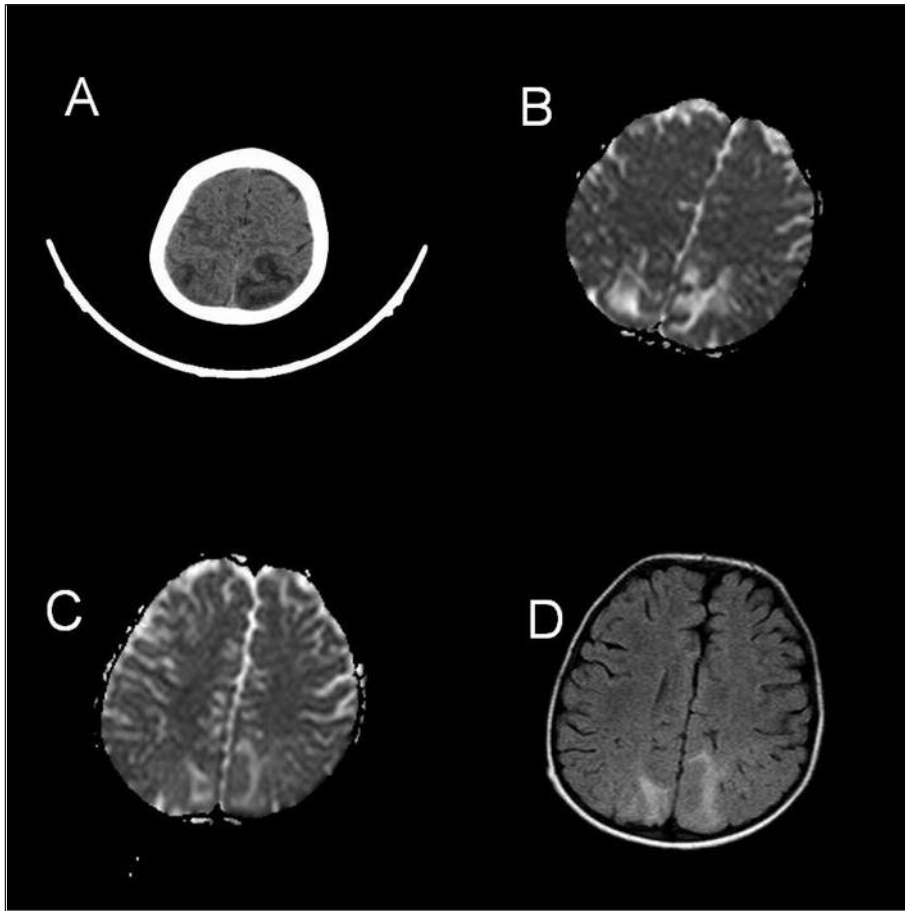


FIGURE 1: Cranial tomography (A) and Diffusion weighted magnetic resonance imaging (B) showing revealed restricted diffusion areas and cytotoxic edema on bilateral parieto-occipital regions during the admission. Diffusion weighted (C) and FLAIR sequence (D) magnetic resonance imaging performed on seventh days of treatment; demonstrated moderate resolution of the bilateral parieto-occipital lesions.

status, visual loss, and seizures in 1996.⁶ Underlying main etiologic factors consist of hypertensive crisis, immunosuppressive conditions, anticancer treatment, hypercalcemia, vasculitis, trombocytopenic syndromes, and renal failure.^{6,7} Commonly cytotoxic edema affecting bilateral parieto-occipital lobes is detected at images on MRI.^{1,8}

Although patients with renal disease and those treated with chemotherapeutic agents or immunosuppressants appear to be at increased risk of developing PRES, the clinical spectrum of associated conditions are ever widening. Keeping in mind the PRES ensures the ESRF patients presenting with seizure and encephalopathy and avoids unnecessary investigation and treatment. Prompt diagnosis and appropriate therapy with anti-hypertensive agents, anti-epileptic drugs, removal of any of-

fending agents and treatment of any associated disorders are essential to prevent progression to irreversible brain injury or even death. Otherwise, the vasogenic brain edema turns into cytotoxic brain edema and consequently causes permanent brain injury and neurological sequelae.⁴

Infection and/or inflammation are some of other etiologic factors in the pathogenesis of PRES. The septic shock response likely reflects systemic toxicity similar to systemic inflammatory response syndrome or multiorgan dysfunction syndrome and bacteremia, or endotoxins/exotoxins are considered as potential triggers.⁹ In literature, only a pediatric case with ESRF receiving PD was established as a PRES case because of sepsis and hypertension.¹⁰ Sepsis was excluded in our case with clinical and laboratory examinations. To the best

of our knowledge, this is the first child case of PRES in a patient with cystinosis when we exclude the well known other etiologic factors. In our case, hypertensive crisis related to ineffective PD and brain tissue damage due to cystinosis may be able to provide a basis for PRES.

Despite symptomatic central nervous system injury caused by Cystinosis tends to increase because of new medical approaches, the primary brain damage due to Cystinosis is uncommon. Berger et al. reported a patient presented with cervical myelitis, who had hyperintense lesions in internal capsule and hemisphere on T2 weighted cranial MR images, some of which increased uptake after injection.¹¹ According to histological analysis, perivascular lymphocyte infiltrate due to cystine crystal deposition and inflammation, vasculitis of small and median sized vessels are seen. We estimate that prolonged life expectancy and in-compliance to treatment of these patients with chronic renal failure due to Cystinosis would lead to increase frequency of the neurologic complications caused by this disorder.

Cystinosis encephalopathy divides into two types . The first type is associated with cerebellar

and pyramidal signs, mental deterioration and finally pseudo-bulbar palsy. The other type of cystinosis encephalopathy includes a stroke-like episode with coma and hemiplegia or milder symptoms. Based on our patient's reversible clinical and radiological findings, we excluded cystinosis encephalopathy while evaluating the differential diagnosis.²

In our case report, we presented Cranial CT and MR images of a pediatric patient with Cystinosis in PRES and saw that Cystinosis did not change these radiologic findings. Posterior reversible encephalopathy syndrome should be considered in differential diagnosis of pediatric patients with cystinosis admitting with convulsion and encephalopathy. Appropriate and prompt treatment is essential to protect the patients from harmful effects of irreversible brain injury.

'In conclusion; We recommend that PRES may mimic cystinosis encephalopathy; including altered mental status, cerebellar and pyramidal system symptoms, seizures in pediatric patients with cystinosis and be kept in mind as a differential diagnosis of Cystinosis encephalopathy'.

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