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CASE REPORT

Posterior reversible encephalopathy syndrome following sepsis in a Crohn's disease patient: A case report

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Abstract

Posterior reversible encephalopathy syndrome (PRES) is a clinico-ragiological syndrome presenting with neurological symptoms and characteristic radiologic findings. PRES occurs in the setting of various clinical conditions and requires prompt management of the causative factor for a full recovery. This is a case report of a Crohn's disease patient who developed PRES syndrome during a complicated post-operative course. In the presence of multiple causative factors, sepsis was considered as the predominant one. After prompt management, the patient recovered with no permanent neurological damage.

Key words: Crohn's disease; Sepsis; Posterior reversible encephalopathy syndrome; Diagnosis

Core tip: We present the case of a Crohn's disease patient who suffered posterior reversible encephalopathy syndrome in the setting of a troublesome post-operative course. The etiology has not been clarified, since various

contributing factors existed, however sepsis represents the predominant reason. The patient was diagnosed early, since neurological consult was seeked immediately, and after prompt management, he fully recovered without neurological deficits. Our goal is to stress out the importance of clinical suspicion in such cases, as the post-operative course in a Crohn's disease patient can often be perplexed and challenging.

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INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a well-described clinico-radiological entity that has been associated with a variety of clinical conditions. It is characterized by neurological symptoms including seizures, visual abnormalities, altered mental status, headache and focal neurological signs. The clinical presentation is accompanied by characteristic cerebral magnetic resonance imaging (MRI) findings. Cerebral vasogenic edema represents the principal abnormality, but the underlying pathophysiological mechanisms remain controversial, as a number of etiologies have been implicated in the pathogenesis of this syndrome. As suggestive by its name it is reversible in most cases, however, permanent impairment and even death have been reported. Crohn's disease is considered a rare cause of PRES, as only a few cases have been described in the literature. The aim of this report is to underline the importance of clinical suspicion and prompt management in such cases, in order to achieve an optimal outcome.

CASE REPORT

A 29-year-old, Caucasian male, with a long medical history of multiple surgical operations due to ulcerative colitis, was admitted to our hospital after repeated episodes of ileus and weight loss during the last nine months. The patient's previous operations included a subtotal colectomy with end-ileostomy formation and mucus fistula of the rectal stump at the age of seven, followed by rectum removal and an ileal J-pouch with a temporary loop-ileostomy. The patient underwent four reoperations over the following years due to complications and multiple episodes of ileus. Prior to his admission, two endoscopic dilatations were performed in an effort to conservatively treat existing enteral stenosis, with unsatisfactory results.

When admitted to our hospital, the patient was subjected to thorough work up, including abdominal and pelvic CT-scans and MRI-enterography which revealed ileus of the small bowel with dilatation of the ileum and obstruction of the afferent ileal loop above the pouch. Following discussion at our multidisciplinary team (MDT) meeting, a decision was reached to proceed with an exploratory laparotomy. During the operation, laborious lysis of adhesions was performed and 15 cm of jejunum along with a segment of ileum, proximal to the pouch, were removed. On inspection of the resected segments, a fistula was present between the jejunum and ileum along with multiple constricted areas. An end-ileostomy was created. The histopathological examination surprisingly revealed lesions compatible with Crohn's disease.

The postoperative period was cumbersome and complicated. From the ninth postoperative day onwards, the patient developed post-operative ileus. A few days later, due to a sudden episode of fever, blood cultures were ordered, in which *Escherichia coli* (*E. coli*) was isolated and appropriate antibiotics where administered. The patient remained stable until the twenty fifth postoperative day when he suddenly deteriorated. He presented septic profile, with fever, hypotension and tachycardia (T: 35 ℃, arterial blood pressure: 7.9/5.9 kPa, 135 beats/min, 30900/IU WBCs) and underwent urgent laparotomy. During the operation a dilated bowel segment, a sizable retroperitoneal hematoma, and a pelvic abscess were discovered and drained with an adequate number of drainage tubes left in place. After the operation, the patient was unstable and therefore transferred to the intensive care unit (ICU), where he was supported with vasopressors and transfused with pRBCs, platelets and fresh frozen plasma. After a new episode of fever, new sets of blood cultures were sent and *Pseudomonas aeruginosa* was isolated. Meropenem was added to the administered antibiotics, according to cultures sensitivities. The patient's condition progressively improved and he was finally discharged from the ICU eight days later. Despite his improvement, the patient was in need of frequent platelets' transfusion due to profound and persistent thrombocytopenia.

Meanwhile, enterocutaneous fistulae had been established, following the route of draining tubes. Ten days later the patient was transferred again to the ICU due to hemorrhage from the stoma, which was treated conservatively; he returned to the ward after two days on tygecycline, fluconazole and methylprednisolone.

Five days later, the patient suddenly developed initially a right sided focal seizure with eye gaze deviation to the right for several minutes and a post critic gaze deviation to the left. This seizure was followed by a left sided one, a few minutes later, and continued for approximately an hour. During these episodes there was no impairment of consciousness, the patient was well oriented and cooperative, but complained of complete

vision loss. His vital signs where within normal ranges apart from his blood pressure which was 22/13 kPa and presented no neurological deficit. Blood tests revealed normal glucose and electrolyte levels. The patient underwent an urgent cerebral CT scan which showed hypodense areas in cortical and subcortical white matter of the occipital lobe. The antibiotics regimen was discontinued and the patient was treated with levetiracetam 500 mg bid and thiamine, instructions dictated by a specialized neurologist. The next day the patient was free of seizures but the visual impairment was scarcely improved as he could only recognize light. Head MRI revealed increased T2 and Flair signal intensity in cortical and subcortical white matter of bilateral parietal and occipital lobes with a slight contrast enhancement and restricted diffusion areas.

The magnetic resonance angiography was normal. The patient's condition improved over the next days and his vision was gradually restored. Thirty days later, the presence of infectious source was excluded and an MDT meeting was held. The patient was then commenced on infliximab and continued to receive levetiracetam. The enterocutaneous fistulae were still productive but did not cause electrolyte disorders. The patient was discharged after seventy-six days of hospitalization.

Six months later, the follow up MRI was completely normal, revealing no high intensity areas. Today the patient is in good condition, trying to improve his nutritional status; the enterocutaneous fistulae have dried up. His vision is completely restored and no other neurological manifestations have presented.

DISCUSSION

PRES was first described by Hinchey *et al*[1] in 1996. PRES is commonly presented with headache, altered mental status or consciousness impairment, visual disturbances and seizures in more than 90% of cases; status epilepticus is not uncommon[1,2]. Although reversible, permanent neurological impairment and death have also been reported[3].

The pathophysiology of PRES includes abnormal alterations in cerebrum perfusion that lead to vasogenic edema[4]. The lesions are usually located in the posterior parietal and occipital lobes, such as in our case, possibly due to reduced number of sympathetic nerve fibers in this region, followed by the frontal lobe, the temporal lobe and the cerebellum[5]. Two totally different theories tend to prevail over others. The first one involves an increase in cerebral blood flow as a result of an increase in mean arterial pressure (MAP). This hyperperfusion causes a failure of the blood brain barrier, with subsequent injury of the endothelium which finally leads to vasogenic edema[6]. However, this theory fails to explain the pathogenesis of 20%-40% of PRES patients with normal blood pressure values[7]. The other theory involves hypoperfusion of the cerebrum as a result of the damage of the blood brain barrier caused mainly by immune system activation or toxic agents in the setting of conditions such as eclampsia/preeclampsia, cyclosporine toxicity and sepsis/septic shock and may be related or not to severe hypertension[4]. The disruption of the endothelium leads to vasogenic edema. In our case, sepsis seems to be the most important factor that led to PRES. Patient presented acute hypertension during his hospitalization which is described in 67% to 80% of cases of PRES syndrome. However hypertension cannot be considered as a predominant factor in this case, considering that MAP was only slightly elevated (16 kPa) above the range that can be counterbalanced by auto regulation mechanisms. The acute onset of the symptoms, mentioned above and the presence of predisposing factors along with the exclusion of other causative factors of encephalopathy are highly suggestive of PRES. The rapid clinical and radiological improvement after the initiation of targeted therapy with levetiracetam, agrees with the diagnosis of PRES. A variety of factors causing PRES have been reported in the literature, such as toxic agents and immunosuppressive drugs, acute severe hypertension, preeclampsia/eclampsia, renal disease, transplantation, autoimmune disease and sepsis[2,3]. Our patient was exposed to several of the putative causative factors. He suffered from Crohn's disease for over two decades; Crohn's disease itself has been reported as a causative factor in 6% of the cases[5]. To the best of our knowledge there are a few reports of PRES development in Crohn's disease patients[8-11]. However, most of them have implicated immunosuppressant drugs as the main cause. Undoubtedly, sepsis played a key role in our case, as PRES occurred twenty-five days after severe infection. This is in line with the findings published by Bartynski *et al*[12], who described an interval of 15-30 d between sepsis and PRES development. Unlike most cases, with positive blood cultures for Gram-positive bacteria[13], in our patient there was a bloodstream infection attributed to *E. coli* and *Pseudomonas aeruginosa*. In addition, our patient had been on corticosteroid therapy for a week before the onset of symptoms and received numerous blood transfusions during his hospitalization. Hypertension, as a result of corticosteroid therapy, has also been reported to lead to PRES[9] in several cases, while blood transfusion is considered an uncommon causative factor[14].

MRI is the main imaging modality used for the diagnosis of PRES. Regions of high signal in T2-weighted images indicate cerebral vasogenic edema. In our case, multiple regions in bilateral parietal and occipital lobes showed abnormal signal intensity[6]. Computed tomography seems to be of less diagnostic value, with normal findings or nonspecific imaging of hypodense regions in most of the cases[15]. A normal MRI scan, six months after the incidence indicated the reversibility of the syndrome and confirmed the diagnosis in our

patient. Treatment should be initiated as soon as possible. Stabilization of the hemodynamic status and the management of the underlying causative factors are the cornerstones of the treatment of PRES. The patency of the airway should be the first priority, especially during seizure activity. Anticonvulsant agents, such as benzodiazepines or levetiracetam, should be initiated for seizure control. Progressive reduction of blood pressure, when needed, is also recommended[2]. Thiamine was given to our patient due to malnutrition.

The presence of multiple causative factors in this case, complicated the orientation towards a leading factor; however sepsis along with hypertension seemed to play a key role in the development of PRES syndrome in this patient.

PRES is a clinico-radiological entity that may be associated with a variety of clinical conditions, including Crohn's disease. In the presented case, PRES was most probably caused by the severe sepsis the patient sustained. However, whatever the reason is, PRES may confer additional morbidity with putative detrimental effects, especially in patients such as in the presented case, thus mandating a high level of awareness for the prompt identification and management of this entity.

COMMENTS

Case characteristics

A 29-year-old male patient with a history of Crohn's disease presented focal epileptic seizures and vision impairment in the setting of a troublesome post-operative course.

Clinical diagnosis

Focal seizures alternating from right to left side accompanied with complete loss of vision.

Differential diagnosis

Infective encephalitis or meningitis, hypoglycemia, venus sinus thrombosis.

Laboratory diagnosis

All laboratory values were within normal limits.

Imaging diagnosis

Magnetic resonance imaging revealed increased T2 and Flair signal intensity in cortical and subcortical white matter of bilateral parietal and occipital lobes with a slight contrast enhancement and restricted diffusion areas.

Pathological diagnosis

Posterior reversible encephalopathy syndrome (PRES).

Treatment

Administration of levetiracetam and thiamine.

Related reports

PRES is a clinical syndrome that manifests in the setting of several conditions, such as acute hypertension, autoimmune disease, toxic agents, immunosuppressive drugs and sepsis. Crohn's disease has been reported as a rare causative factor. In a clinical setting where several factors exist, it is difficult to determine which one is responsible and target therapeutic action.

Term explanation

PRES is a clinical entity with neurological symptoms and characteristic radiologic imaging. The pathophysiological mechanisms that lead to PRES are yet to be established.

Experiences and lessons

Immediate diagnosis and prompt management are necessary in PRES, in order to avoid permanent neurological impairment. Even when the causative factor cannot be identified with certainty, supportive therapy and amelioration of patient's status lead to a favourable outcome.

Peer-review

An interesting case of importance to clinicians treating inflammatory bowel disease.

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