Hypertensive encephalopathy secondary to acute post-streptococcal glomerulonephritis

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Abstract

Acute post-streptococcal glomerulonephritis (APSGN) is the leading cause of nephritic syndrome in children and has a broad spectrum of clinical presentation ranging from asymptomatic cases to acute renal failure and encephalopathy. Most cases are sporadic, although the disease may occur in epidemic form, mainly related to poor sanitary conditions. Hypertensive encephalopathy is a severe complication, but there is a good outcome with appropriate treatment.

Case report: We describe the case of a previously healthy 10-year-old male with a history of pharyngitis 1 week before his arrival to the emergency room. He presented with altered consciousness, partial seizures, hypertension and hematuria. Cranial computed tomography was performed and showed no edema, mass or hemorrhage; antistreptolysin O serum titers were elevated. He was treated according to hypertensive encephalopathy due to APSGN, with a favorable outcome. Differential diagnosis should include cerebral vascular diseases, intracranial tumors, central nervous system infections and toxic metabolic disturbances.

Conclusions: APSGN should be suspected in any child with history of pharyngitis and sudden onset of hypertensive encephalopathy.

Key words: glomerulonephritis, hypertensive encephalopathy, seizures, streptococcal infections, antistreptolysin O.

Introduction

Acute post-streptococcal glomerulonephritis (APSGN) presents as a nephritic syndrome with edema, hypertension and hematuria.[1] Patients show diverse clinical profiles such as asymptomatic, mild syndrome or significant complications such as cardiac insufficiency, acute renal failure or encephalopathy.[2] Hypertension is found in up to 90% of patients and 10% may have neurological symptoms, but only few present hypertensive encephalopathy (HTE). The disease is more frequent in children with recent pharyngitis or pyoderma. The prevalence of APSGN is not known precisely because patients may present a subclinical disease in 19%-50% of cases.[2] The incidence of this disease has decreased in developed countries in recent years.[3] Streptococcal infections have been associated with overcrowding and poor sanitary conditions, which may lead to epidemic or family outbreaks in certain groups.[4]

HTE is an acute organic brain syndrome (OBS)[5] and is a consequence of brain hyperperfusion when the upper limit of the brain's auto-regulated vascular activity has been exceeded, leading to brain edema, petechial hemorrhages and micro-infarctions.[6] It is more likely to appear in normotensive patients who experience a sudden increase in arterial tension, as occurs in children with acute glomerulonephritis. The clinical presentation includes acute lethargy, confusion, cephalea, visual

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impairment (including blindness) and seizures. Seizures may be the main symptom that occurs as a focal crisis, a generalized crisis or a focal crisis with secondary tonic/clonic generalization.[5] Severe hypertension is a rare but well-documented complication in children.[7] The prognosis is good in general; however, without proper management, it can develop into permanent brain damage, brain hemorrhage, coma and death.[5,6]

We describe the case of a 10-year-old male with APSGN and an unusual severe complication with favorable evolution.

Case Report

We report the case of a 10-year-old male who was previously healthy and presented fever and cephalea of 1-week duration. The patient was attended at the general medical clinic where he was diagnosed with pharyngitis and prescribed amoxicillin (unknown dosage). When he arrived at the Hospital Emergency Room, he presented sensory system alteration, no response to external stimuli (verbal or tactile), spontaneous eye opening, right nystagmus with gaze deviation and symmetrical pupils with normal photomotor reflex. Hypersalivation was also observed with discreet clonic movements in the left arm and a general increase in muscular tone. At that time the patient had a heart rate of 120 beats/min, respiration rate of 20 breaths/min, blood pressure of 154/101 mmHg and oxygen saturation (SaO_2) of 70%. Supplementary oxygen was applied as well as IV diazepam (0.3 mg/kg), which reduced movements and gaze deviation and normalized muscular tone; SaO_2 improved to 99% and heart rate decreased to 72 beats/min with blood pressure between 145/99 and 152/109 mmHg (these were >95 percentile for age, sex, and size).[8] Examination of the eye fundus revealed neither papilledema nor hemorrhage; cardiovascular parameters and physical examination were normal except for a discreet pretibial edema (sign of fovea positive). There were no signs of meningitis. Computed tomography (CT) revealed no edema, hemorrhages, ischemia, or hypodense or space-occupying lesions. Urinalysis from a tea-colored sample showed density (1025), pH 5.0, abundant erythrocytes, 10 leukocytes/field, blood casts negative, and other parameters were normal. Hemogram showed leukocyte count in 20.5×10^3 /mm^3 with 90% segmented, 6% lymphocytes, 2% bands; hemoglobin: 12.6 g/dL; blood urea nitrogen (BUN): 15.8 mg/dL and creatinine 0.6 mg/dL; electrolytes were normal. Chest x-ray revealed cardiomegaly (level I), hilar congestion, and clear costophrenic angles. The patient received IV furosemide (2 mg/kg) every 6 h and hydralazine (0.1 mg/kg) every 6 h to control blood pressure. He was admitted to the hospital with diagnosis of HTE secondary to acute glomerulonephritis. He weighed 34 kg (50th-75th percentile for age) and was 131 cm in height (10th percentile for age) at the time of admission.

During his hospital stay, blood pressure was controlled (95/60 mmHg) using the same treatment, but hydralazine was suspended because of dizziness, and furosemide was administered orally from the second day on. Other analyses carried out during hospitalization revealed proteinuria: 7.1 mg/m^2/h (normal <4 mg/m^2/h; nephritic >40 mg/m^2/h); serum albumin: 3.5 g/dL (normal 3.2-5 g/dL); C-reactive protein: negative; antistreptolysin O: 1270-1350 IU/mL (normal <200 IU/mL); complement C3: 38 mg/dL (normal 80-180 mg/dL); pharyngeal culture: negative. These data were conclusive to diagnose APSGN. The patient received IM benzathine penicillin (1.2×10^6 UI) and evolved favorably with appropriate diuresis and without additional neurological problems. The patient was discharged after 3 days and prescribed furosemide for 1 week (2 mg/kg every 8 h). In the clinical follow-up after 1 month, the patient showed normal blood pressure and was asymptomatic with normal C3 levels.

Discussion

Acute post-streptococcal glomerulonephritis is the leading cause of nephritic syndrome during childhood.[1] It is a clinical entity with variable presentation, from patients being asymptomatic or with complications. The most common complications are congestive heart failure, acute renal failure and HTE.[2] Some authors report HTE is present in 7% of cases,[4] although neurological symptoms such as cephalea, nausea, vomiting and consciousness alterations may be found in up to 10% of patients.[5] In severe cases, these symptoms may lead to seizures. In Costa Rica, encephalopathy has been reported in <1% patient series.[9,10] In general, this complication is reversible when blood pressure is controlled and leads no sequelae.

The case reported is interesting because the seizure was subtle with discreet focal/clonic movements and consciousness alteration that could be considered as a status epilepticus because of its duration until the patient's arrival at the Emergency Room. Some authors have reported that the seizure types associated

with HTE are tonic/clonic, focal, generalized or focal with secondary generalization,[5] which is in contrast to our case. During the patient's care at the Emergency Room it was necessary to perform imaging studies in order to document possible brain damage. Differential diagnosis should consider vascular complications such as intracranial hemorrhage, subarachnoidal hemorrhage or brain infarction as well as brain tumors and central nervous system infections (meningitis, encephalitis, brain abscess). Other causes may be toxic/metabolic (uremia, hypoglycemia, electrolytic alterations); however, the history of this patient did not lead to this group of problems. Diagnosis of glomerulonephritis was clear once CT scan was obtained with the additional revelation of hematuria. It has been reported that diagnosis of glomerulonephritis sometimes is difficult[11] or delayed; in the case discussed here the clinical presentation was HTE and only after hematuria was detected, we could be certain that glomerulonephritis was the cause of hypertension.[12]

In recent years, the reversible posterior leukoencephalopathy syndrome (RPLS) has been described as a phenomenon characterized by white-matter edema on parietal and occipital lobes.[13,14] CT scan reveals bilateral hypodensity of cerebral white matter in parietal and occipital lobes, generally symmetrical in an area beyond the posterior cerebral artery, which helps to differentiate it from localized vascular lesions or strokes. Magnetic resonance helps to better identify lesions of compromised lobes. Conventional resonance studies are used for hypointense lesions (T_1) or hyperintense lesions (T_2) on cerebral white matter that sometimes also affect the gray matter. RPLS is associated with HTE in children but also appears in eclampsia, in hypertension associated with immunosuppressive therapy and in patients with renal failure.[14] Visual impairment is frequently found in patients with RPLS, but this was not reported in our case. We also did not find the usual RPLS characteristics during CT scan and, because of the favorable evolution of our patient, MRI was not performed.

In patients with streptococci infection and history of neurological compromise, we should consider the pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). These patients present obsessive/compulsive disorders, tics or choreoathetotic movements during a streptococcal infection.[3,15] However, in the case presented here, there were no such manifestations. It is important to consider this during differential diagnosis of acute neurological disorders.

On the other hand, some authors report that APSGN diagnosis is defined by its suggestive clinical profile: sudden manifestation, edema, hypertension, macroscopic or microscopic hematuria associated with red blood cell casts and non-nephritic proteinuria, evidence of streptococcal infection, reduced C3 serum levels and spontaneous improvement of renal disease and complications.[2] It is recommended to take cultures from pharynx or from active skin lesions in order to document streptococcal infection; however, the organism is isolated in variable percentages as reported by different authors, even in patients who have not previously received antibiotics. In the case reported here, it was not possible to isolate the organism from pharyngeal culture and, therefore, the high levels of antistreptolysin O presented conclusive evidence of streptococcal infection.[3] Other antibodies help to determine the infection, such as antideoxyribonuclease-B that, together with antistreptolysin O, provides the ability to identify the infection with 100% accuracy.[4] Other serological tests include the determination of antibodies such as antihyaluronidase and antistreptokinase. Renal biopsy is not currently performed in children with APSGN because the clinical feature is sufficient to diagnose the disease. Renal biopsy is recommended only if there is rapid deterioration of renal function, complement levels remain low >8 weeks or there are clinical data that suggest another etiology (e.g. Schönlein-Henoch purpura, lupus glomerulonephritis, membranous or membranoproliferative glomerulonephritis).[3]

In conclusion, some authors report that diagnosis of APSGN should be considered with high suspicion in children with upper airway infection followed by sudden encephalopathy and hypertension. For example, a case was reported where urinalysis was normal, which required a more complex and expensive diagnostic approach including renal biopsy, in a potentially reversible clinical entity.[16]

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