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Acute glomerulonephritis associated with complicated eczema herpeticum

Ostre kłębuszkowe zapalenie nerek w przebiegu powikłanego wyprysku Kaposiego

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Abstract

Primary acute glomerulonephritis is a disease of the glomeruli with a sudden onset. It is caused by the presence of immune complexes following group A beta-haemolytic streptococcus infection. This is usually due to a streptococcus infection of the throat or, less commonly, of the skin. The main signs of the disease include oedema, hypertension and erythrocyturia. Systemic symptoms can also develop such as malaise, nausea and vomiting. In a severe form of the disease, transudation of fluid to body cavities occurs and renal failure develops requiring dialysis therapy. In this paper, we present an atypical case of a 9-year-old patient with acute glomerulonephritis associated with bacterial superinfection of eczema herpeticum.

Keywords: glomerulonephritis, proteinuria, atopic dermatitis, *Streptococcus pyogenes*

Streszczenie

Pierwotne ostre kłębuszkowe zapalenie nerek jest nagle występującą chorobą kłębuszków nerkowych, związaną z obecnością kompleksów immunologicznych po przebyciu zakażenia paciorkowcem beta-hemolizującym grupy A. Najczęściej ma związek z infekcją paciorkowcową gardła, rzadziej skóry. Do podstawowych objawów chorobowych należą obrzęki, nadciśnienie tętnicze oraz zmiany w moczu pod postacią krwinkomoczu. Mogą również występować objawy ogólne, takie jak złe samopoczucie, nudności czy wymioty. W ciężkiej postaci choroby dochodzi do przesięku do jam ciała oraz niewydolności nerek z koniecznością dializoterapii. Poniżej prezentujemy nietypowy przypadek 9-letniego pacjenta z ostrym kłębuszkowym zapaleniem nerek, do którego doszło w przebiegu nadkażenia bakteryjnego wyprysku Kaposiego.

Słowa kluczowe: kłębuszkowe zapalenie nerek, proteinuria, atopowe zapalenie skóry, *Streptococcus pyogenes*

CASE REPORT

A 9-year-old boy was admitted to hospital due to generalised pyogenic dermatitis. The patient had an approximately 6-month history of skin lesions treated initially as varicella-related. The lesions were of various severity and nature: from urticaria-like rash to exudative eruptions (herpes lesions). Following dermatology consultation, formulations for external use were applied. Upon admission, the patient was afebrile and had a normal arterial pressure. Physical examination revealed a few abnormal findings. A very large number of purulent lesions were found on the skin of the whole body, including the scalp, in the form of bullae and exudative lesions with pus. The skin between the purulent lesions had an uneven surface with red and blue discolouration. In addition, subcutaneous oedema was observed, particularly in the face, lower legs and feet (initially, it was considered to be periwound oedema). On subsequent days, exacerbating oedema was observed and the patient developed ascites. Additional tests revealed a high erythrocyte sedimentation rate (ESR), a moderately increased C-reactive protein (CRP) level, anaemia and leukocytosis with neutrophilia. Furthermore, total protein and albumin levels, which were initially normal, were observed to decrease. Urinalysis revealed leukocyturia, erythrocyturia and mild proteinuria. Initially, these symptoms were considered to be related to the presence of purulent lesions near the external urethral orifice; however, due to increasing hypoproteinaemia and exacerbating oedema and fluid transudation to body cavities (ultrasound examination revealed fluid in the left pleural cavity and in the peritoneal cavity), glomerulonephritis was suspected. A 24-hour urine collection test was performed, which revealed subnephrotic proteinuria. In addition, a blood complement C3 level decrease was observed. Skin lesion discharge culture was positive for *Streptococcus pyogenes*. Anti-streptolysin O (ASO) titre was normal. Based on the whole clinical presentation, acute glomerulonephritis was diagnosed. In addition, anti-neutrophil cytoplasmic antibody (ANCA) test was performed, which was negative; cytoplasmic ANCA (C-ANCA) and perinuclear ANCA (P-ANCA) were also assayed and the result was below 5.0 RU/mL. Due to the suspicion that pyogenic dermatitis developed secondary to atopic dermatitis, total IgE assay was performed and a very high level of IgE was found, which exceeded the upper limit of analytical determination. The whole clinical presentation indicates acute glomerulonephritis associated with bacterial superinfection of eczema herpeticum (atopic dermatitis superinfected with herpes virus).

INTRODUCTION

Acute post-streptococcal glomerulonephritis is a disease with a rapid course. It usually develops as a consequence of a respiratory infection, less commonly a skin infection, caused by nephritogenic types of group A beta-haemolytic streptococci[1,2]. Disease manifestations may also be caused by other microbes such as group C and G streptococci, *Streptococcus pneumoniae*, staphylococci, *Salmonella*, *Klebsiella*, viruses [such as echoviruses, *Coxsackie*, rubella, varicella, measles, mumps, Epstein–Barr (EBV), cytomegalovirus (CMV), hepatitis B, human immunodeficiency virus (HIV)], fungi and protozoa[3–6]. The time which elapses from the infection to glomerulonephritis depends on infection severity, method of treatment, infection location and the patient's immune response. In the case of pharyngitis, the period between infection and the onset of symptoms is 5–21 days; in the case of dermatitis, this period is usually 3–4 weeks[2].

PATHOGENESIS

The pathogenesis of glomerulonephritis has not been fully discovered. Immune complexes play a fundamental role: they deposit in the glomeruli causing their damage[2]. There are two theories regarding the site of the complex formation. According to the first theory, a complex composed of a streptococcus antigen, a host's antibody and a complement system component circulating in the blood is filtered, but not removed and, consequently, it accumulates in a glomerulus. According to the second hypothesis, complexes may form *in situ* in the glomeruli. The bacterial antigen binds to the antibody and then to the glomerular basement membrane. As a result, the complement is activated and the basement membrane is damaged[1].

MORPHOLOGICAL PRESENTATION

Histological changes in acute glomerulonephritis are diffuse and generalised. The enlargement of all glomeruli, glomerular capillary endotheliosis, mesangial proliferation and the presence of numerous incoming inflammatory cells (neutrophils, macrophages and, less commonly, lymphocytes and plasma cells) infiltrating the vessels of the glomeruli and the mesangium are characteristic for the disease[4,5,7].

EPIDEMIOLOGY

Acute post-streptococcal glomerulonephritis is more common in children than in adults due to a higher prevalence of respiratory infections associated with streptococci in children[2]. Seasonality of the disease is observed (spring and autumn). Glomerulonephritis is more common in boys with a peak incidence at 5–12 years of age; the disease is rare in children before 3 years of age[8–11]. Acute glomerulonephritis may occur as an epidemic or may be sporadic. In an epidemic, approximately 80% of cases are subclinical in nature. Epidemics are not frequent and occur mainly in underdeveloped countries. Globally, every year approximately 470,000 cases of acute post-streptococcal glomerulonephritis are revealed; 97% of these occur in developing countries. The disease accounts for approximately 5,000 deaths annually, which constitutes 1% of all cases[12].

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CLINICAL PRESENTATION

The course of the disease may vary from asymptomatic to very severe with nephritic syndrome, acute renal failure or nephrotic syndrome. The sporadic form of the disease is less common and is characterised by a more severe course, with concomitant oedema, arterial hypertension, erythrocyturia or haematuria, proteinuria, oliguria and acute renal failure. However, in epidemics, the course of glomerulonephritis is mild, usually with only erythrocyturia revealed on urinalysis. The most common symptoms, which usually occur after 2–3 weeks from streptococcus infection, include abdominal pain, lumbar pain with a weakly positive Goldflam's sign, headaches, nausea, vomiting and malaise. Arterial hypertension, decreased urine secretion and periorbital oedema are also observed; oedema may become generalised. Oedema occurs in approximately 85–90% of patients with acute glomerulonephritis. Oedema is associated with water and fluid retention in the body and with protein loss. These changes can also lead to fluid transudation to body cavities (abdominal and pleural cavities, pericardium). Arterial hypertension and/or circulatory failure are also associated with sodium and water retention, and, according to certain authors, with increased serum endothelin 1 concentration[13]. Arterial hypertension occurs in approximately 80–90% of patients; both systolic and diastolic pressure is elevated. Arterial blood pressure increase may sometimes be sudden and lead to hypertensive encephalopathy, which manifests in 3–5% of patients with strong headaches, vomiting, visual disturbances (cortical blindness), loss of consciousness and seizures[14]. If appropriate hypotensive treatment is used, hypertensive crisis does not leave any neurological deficits. Changes in the colour and volume of passed urine can be observed in the majority of patients. Oliguria and anuria occur as a result of decreased glomerular filtration rate and may lead to acute renal failure with hyperazotaemia, hyperkalaemia and metabolic acidosis. In approximately 30% of patients, urine has a brown colour, which is caused by haematuria, present even up to 2 weeks. After that period, haematuria is reduced to microscopic erythrocyturia, which may persist for 6 months and for as long as 2–3 years in some cases. Under light microscopy, fresh and dysmorphic red blood cells are visible; red blood cell casts may also be present. Under phase-contrast microscopy, dysmorphic red blood cells and acanthocytes are observed. In acute post-streptococcal glomerulonephritis, proteinuria is not a constant sign; if it is observed at all, it usually does not exceed 3 g daily and it is mainly albumins that are lost[2]. In addition, due to the infiltration of glomeruli with multinucleated granulocytes, leukocyturia is observed on urinalysis ("sterile pyuria").

ADDITIONAL TESTS

Blood tests may also reveal abnormal findings. Tests on complement components and total haemolytic activity of complement (CH50), ASO, anti-DNase and IgG are very helpful in diagnostic investigation. Hypocomplementaemia and a decreased properdin level are evidence for a C3 level reduction and total haemolytic complement activity (CH50) decrease. This is accompanied by C5 and properdin levels reduction. These changes may persist for 6–8 weeks. The diagnosis of streptococcal origin of the disease is confirmed by an increased ASO titre, which is elevated in over 80% of children with pharyngitis and in 30–50% with dermatitis[1]. At the time when signs and symptoms of acute post-streptococcal glomerulonephritis occur, ASO titre usually exceeds 200 IU/mL and gradually increases to reach a peak after 4–6 weeks. That level persists for a few weeks and subsequently decreases and returns to normal after a few months. Streptococcal origin of the disease can also be demonstrated by checking the levels of anti-deoxyribonuclease B (anti-DNase B), anti-hyaluronidase or antibodies against nicotinamide adenine dinucleotidase (anti-NADase). In children with a history of dermatitis, the determination of anti-DNase and anti-hyaluronidase levels is more useful than an ASO test[6]. Abnormal antibody levels are also sometimes found: the serum IgG level increases in over half of patients with acute post-streptococcal glomerulonephritis; in approximately 30% of patients, the IgA level also increases.

On ultrasound, kidney enlargement, loss of corticomedullary pattern and kidney hyperechogenicity may be observed. In the diagnostic investigation of acute glomerulonephritis, chest radiography is also recommended since enlarged cardiac silhouette and the presence of fluid in the pleural cavity are observed in some patients. Electrocardiography can show changes associated with hyperkalaemia and hypocalcaemia[15]. If the clinical course of the disease is typical, kidney biopsy is not necessary. It is only performed if prolonged renal failure, severe proteinuria and hypocomplementaemia are observed. In the case of a prolonged complement C3 decrease, biopsy is indicated for diagnosis verification. Other indications for kidney biopsy include concomitant extrarenal signs such as arthritis, haemoptysis or vasculitis.

TREATMENT

The treatment of acute glomerulonephritis involves eliminating the signs and symptoms and the cause of the disease; consequently, both symptomatic and causal treatment (targeted antibiotic therapy) are used. Urine secretion, body mass and arterial pressure should be monitored. In addition, serum creatinin and potassium should be assayed. Unconditional bed rest is recommended until oedema, hypertension and haematuria subside. Dietary management involves reduced fluid and salt intake; if a tendency for hyperkalaemia is present, potassium intake reduction is also recommended[1]. Eliminating hypervolaemia and hypertension plays a very important

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role in the treatment of acute glomerulonephritis. Furosemide at 1–4 mg/kg of body mass in 2–4 doses is used[1]. As well as administering loop diuretics, the treatment of hypertension involves the use of calcium channel blockers. Due to their possibility of causing hyperkalaemia, ACE inhibitors are not recommended in the treatment of hypertension associated with acute glomerulonephritis. Acute renal failure with treatment-unresponsive severe hyperhydration, hyperkalaemia and arterial hypertension is an indication for dialysis therapy. Since acute glomerulonephritis occurs usually as a result of streptococcal infection, antibiotic therapy should also be applied in order to eradicate the streptococcus. It is recommended that phenoxymethylpenicillin be administered orally at 50–100,000 U/kg zof body mass daily in 3–4 doses, up to 3 g daily for 10 days in children[2]. Benzathine penicillin can also be used. If the patient is allergic to penicillin, macrolide antibiotics are used. After such treatment, in approximately 95% of patients bacteriological tests do not show the presence of nephritogenic streptococci. There are reports that other antibiotics such as cephalosporins or semi-synthetic penicillins administered for a shorter time than 10 days may also be used with as good an efficacy as penicillin[1].

PROGNOSIS

Prognosis in children with acute glomerulonephritis is usually good, provided that the condition is quickly diagnosed and appropriate treatment is applied. In the majority of cases, kidney function returns to normal after approximately 2 weeks. Isolated erythrocyturia is the longest-persisting sign. In some cases, microalbuminuria or mesangial proliferation may be found on biopsy even 10 years after the end of treatment. Reduction of functional kidney reserve has also been observed on oral protein tolerance test 10 years after the acute period of the disease. It is estimated that recurrence may be found in 0.7–7% of cases[14]. Usually after recovery antibodies against streptococcal M protein stay in the body, which provides long-term immunity.

Conflict of interest

The authors do not report any financial or personal affiliations to persons or organisations that could adversely affect the content of or claim to have rights to this publication.

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