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Nephrotic Syndrome in Kawasaki Disease

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Introduction

Kawasaki disease (KD), or mucocutaneuous lymph node syndrome, was first reported by Dr Tomisaku Kawasaki of Japan in 1967. Currently, KD is known to have a worldwide distribution as a common disease predominantly affecting children younger than 5 years. KD is the most common cause of multisystem vasculitis in children. The vessels most commonly damaged are the coronary arteries, making KD the number one cause of acquired heart disease in childhood.

Case Report

A 4.5-year-old previously healthy female child presented with fever (104°F) for past 7 days, with nonpurulent bulbar conjunctivitis, mucositis, unilateral cervical lymphadenopathy, edema of the acral parts of the limbs, and excessive irritability. She also had a 5 cm liver, diffuse maculopapular rash, chromonychia, and greenish stool. The child was sick looking, febrile, irritable, and without any sign of heart failure. A pulse rate of 139/minute, blood pressure of 102/74 mm Hg, and a room air saturation of 100% was all that we found. Chest was bilaterally clear and no murmur in the heart could be discerned. Blood tests revealed leukocytosis (14 300/mm^3) with a neutrophilic preponderance, elevated erythrocyte sedimentation rate 95 in first hour, high C-reactive protein (43.2 mg/L), and normal serum creatinine (0.3 mg/dL), acute anemia (7.6 g/dL), and thrombocytopenia (94 000/mm^3). Serum sodium of 129 mmol/L, potassium 4.3 mmol/L, total protein 4.4 g/dL, and albumin 1.8 g/dL with 14 to 16 pus cells/high-power field in urine, and significant proteinuria (++) were noted. Chest X-ray was normal, and urine and blood cultures were sterile. The child was diagnosed as a case of KD and intravenous immunoglobulin transfusion was started with a dose of 2 g/kg in a single dose. Aspirin was also added along with immunoglobulin. Fever subsided within 24 hours of starting intravenous immunoglobulin transfusion, but the edema of the hand and foot increased over time and the child also developed ascites with anasarca within the next 48 hours. Serum albumin was found to be significantly decreased (1.3 g/dL) and the ultrasonography of abdomen showed ascites with a normal-sized kidney, with normal echogenicity, and a normal corticomedullary differentiation. Serum triglyceride was high (197 mg/dL) and urine protein was (++++), with a urinary protein creatinine ratio of 107. Serum C3 and C4 levels were normal and infection serology (human immunodeficiency virus, hepatitis B surface antigen, hepatitis C virus) was negative. Echocardiography revealed multiple valvular involvement with trivial tricuspid and mitral regurgitation. So it was diagnosed as a case of nephrotic syndrome in KS. But the patient was not put on steroids and was kept on observation. The edema gradually subsided and the urine became negative for protein ~~in~~ 9 days of immunoglobulin transfusion. The patient was discharged after 13 days of hospital admission, and in follow-up echo, the heart was found to be normal and there was no relapse of nephrotic syndrome in next 1 year.

Discussion

All the cases previously reported had some kind of complications. ~~The~~ 4-month-old Japanese girl[1] had steroid-resistant nephrotic syndrome and her renal biopsy demonstrated a diffuse mesangial proliferative glomerulonephritis with microcystic tubular dilatation. She ultimately died of chronic renal failure at the age of 11 months. In 1989, the first case reported by Lee et al[2] was a 3-month-old infant with KD presenting with ~~nephritic~~ syndrome during the acute phase of the illness, which improved under steroid therapy. However, the patient died from acute myocardial infarction due to coronary aneurysm. Krug et al[3] reported 3 cases of KD, where 1 child developed acute renal failure and the other presented with features of hemodynamic shock. But our case had all the typical features of KD, ~~but~~ did not

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develop any other complication but nephrotic syndrome and responded rapidly to treatment with intravenous immunoglobulin.

Kawasaki disease is a self-limiting systemic inflammatory disease that occurs predominantly in children younger than 5 years.Clinical manifestations of KD include prolonged fever (1-2 weeks, mean 10-11 days), conjunctival injection, oral lesions, polymorphous skin rashes, extremity changes, and cervical lymphadenopathy, all of which comprise diagnostic criteria. In addition, arthritis, aseptic meningitis, anterior uveitis, gall bladder hydrops, urethritis, and lung involvement can be seen. Some more severely affected patients show cardiac complications, particularly coronary artery lesions, such as aneurysms and ectasias, which develop in approximately one quarter of untreated children and 5% to 10% of intravenous immunoglobulin–treated children. These diverse systemic inflammations (mainly vasculitis) may be caused by inflammatory mediators with circulating immune cells (neutrophils, lymphocytes, natural killer cells, and monocytes), and there may be various immune cell infiltrations in all affected pathologic lesions from affected lymph nodes to skin rashes. Particularly, a larger number of T cells (more CD8 cells than CD4 cells), large mononuclear cells, macrophages, and plasma cells, with a smaller number of neutrophils, are observed in various organ tissues of fatal cases of acute KD.[4]

Primary idiopathic nephrotic syndrome is a frequent source of morbidity in children. In a minority of cases, mutations in podocyte genes[5] explain proteinuria. Pathogenesis, however, is unknown for the major group of patients who do not present molecular defects, in which case a general problem has been proposed linked to T cell immunity.[6] Multiple independent observations point to the involvement of free radicals of oxygen (reactive oxygen species) in proteinuria deriving from an altered regulation by regulatory T cells of polymorphonuclear neutrophil burst. In fact, reactive oxygen species production by polymorphonuclear neutrophil in children with idiopathic ~~nephritic~~ syndrome is increased 10-fold and correlates with proteinuria.[7] Oxidants are toxic for the kidney in humans and in animals, and when oxidant production overcomes the intra- and extracellular defenses, it leads to renal damage.[8]

So we can conclude that nephrotic syndrome can be one of the renal manifestations of KD and it can be hypothesized that a common immune-mediated damage is responsible for both[9,10] these manifestations. We have also observed that treatment of KD with intravenous immunoglobulin is sufficient, and the associated nephrotic syndrome resolves spontaneously without the need of any steroid therapy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.[AQ: 3]

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