Case Report

J Ped. Nephrology 2019;7(1)
http://journals.sbmu.ac.ir/jpn

Atypical Presentation of Cytomegalovirus-Related Infantile Nephrotic Syndrome

How to Cite This Article: Fallahzadeh MA, Fallahzadeh F, Vahhab E, Fallahzadeh MH. Atypical Presentation of Cytomegalovirus-Related Infantile Nephrotic Syndrome. J Ped. Nephrology 2019;7(1).

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Received: Dec-2018
Revised: Dec-2018
Accepted: Jan-2019

Nephrotic syndrome is the most common glomerular disease in children. Most cases are idiopathic and the first episode is rarely related to cytomegalovirus infection, particularly after 3 months of age. We present a 7-month-old infant who developed atypical presentation of nephrotic syndrome secondary to cytomegalovirus infection. The patient was referred to undergo orchiopexy due to right-sided undescended testis. Following the surgery, he developed fever, gastroenteritis and renal failure. A few days later, generalized edema and proteinuria were detected. Due to positive test results for cytomegalovirus, ganciclovir was administered. Remission of nephrotic syndrome was obtained within the first two weeks of the treatment. No relapse of nephrotic syndrome was detected during 12 months of follow up. We may conclude that in unexplained infantile nephrotic syndrome, CMV should be considered as one of the possible etiologies.

Keywords: Nephrotic Syndrome; Cytomegalovirus; Infant; Ganciclovir; Edema; Proteinuria; Gastroenteritis.

Running Title: CMV-Related Infantile Nephrotic Syndrome

Introduction

Nephrotic syndrome (NS) is the most common glomerular disease in children [1]. Pediatric NS is usually idiopathic [2] and uncommon in the first year of life [3]. When it is diagnosed within the first 3 months of age, it is considered to be congenital nephrotic syndrome (CNS). Most cases of CNS have a genetic basis. If the initial presentation of NS is between 4 and 12 months of age, it is called infantile nephrotic syndrome (INS) [2]. INS is a rare disease and cytomegalovirus (CMV) infection as the direct cause in immunocompetent hosts is rarely reported [4,5].

In this report, we present a case of CMV-related INS with an atypical hospital course and a dramatic response to antiviral therapy.

Case Report

A seven-month-old boy was referred to have an operation for right-sided undescended testis. After the surgery, he had persistent fluid leakage at the site of orchiopexy. It was followed by diarrhea, vomiting and fever. Although blood urea nitrogen (BUN) and serum creatinine (Cr) were normal at the time of the operation, they increased to 82

mg/dl and 2 mg/dl, respectively. The patient had normal urinalysis at this time. These events were followed by episodes of urinary retention and serum electrolyte imbalances: Sodium = 118 mEq/L and Potassium = 6 mEq/L. Subsequently, he developed generalized edema, oliguria, ascites, nephrotic range proteinuria, hypoalbuminemia, microscopic hematuria, anemia and hyperlipidemia. Other laboratory evaluations were as follows: Erythrocyte sedimentation rate =75 mm/hour, Lactate Dehydrogenase = 18 IU/L, Creatine phophokinase = 48 IU/L, White blood cell count =13600/mm3, fragmented RBC= 1% and platelet count= 929000/mm3. Prothrombin time, partial thromboplastin time, C3, C4, serum cortisol and antinuclear antibody were normal and urine culture was negative. Likewise, stool evaluations were unremarkable. However, urinalysis revealed 3+ protein, 3+ blood and 3+ glucose with urine protein/creatinine ratio of 6.72 (mg/mg) at this point.

Chest x-ray and echocardiography were normal. Renal ultrasound was normal; however, significant ascites, right sided inguinal hernia and hydrocele were reported in ultrasound imaging. Subsequently, due to difficulty in urination voiding cystourethrography was done and revealed the bladder rupture. Therefore, herniorrhaphy and bladder repair were done and they were followed by normal urinary pattern.

After making the diagnosis of NS, routine evaluations for the possible causes of NS were done. The only positive finding was polymerase chain reaction for CMV in serum and urine. At this stage, BUN, serum Cr and electrolytes were normal. Thus, ganciclovir was started for the patient and it was followed by gradual normalization of proteinuria, and disappearance of edema and ascites within 2 weeks. After three weeks, ganciclovir was discontinued. There was no recurrence of CMV infection or NS within 12 months of follow-up.

Discussion

Our patient had INS secondary to CMV infection with diarrhea and acute renal failure as the initial presenting signs. His impressive response to ganciclovir supports a causal relationship between INS and CMV infection.

Clinical manifestations of CMV infection are variable. Most cases are asymptomatic, some develop mononucleosis syndrome and some present with symptoms of specific internal organ involvement [6]. CMV infection in childhood can be associated with multiple glomerular diseases especially in immunocompromised hosts [7].

There are few similar reported cases of NS secondary to CMV infection with complete remission following antiviral therapy [3,8]. According to a report from Brazil, evidence of recent CMV infection was observed in 4.1% of children with NS. The authors concluded that there may be a relationship between CMV infection and NS [9]. Also, a case of CMV-associated collapsing glomerulopathy responsive to combined ganciclovir and glucocorticoid therapy was reported in 2000 [10]. In a more recent study, a 34-year old man was reported with cytomegalovirus-induced collapsing focal segmental glomeruloscleros which was responsive to ganciclovir [11].

Although gastroenteritis due to direct CMV infection in the immuncompetent host is very unusual, few such cases are reported [12-14]. We did not examine the stool for CMV as the cause of gastroenteritis. However, considering all the findings, we can presume that the gastroenteritis could be related to the viral process. Nevertheless, bladder rupture in this patient was probably not related to CMV infection. As previously reported, it can be explained as a complication of orchiopexy [15].

Conclusion

CMV infection should be considered as one of the possible etiologies of INS, even in the immunocompetent infant, especially if it is preceded by gastroenteritis.

Financial Support

No support in the form of grants, equipment, or drugs

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