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Case Report

A Rare Presentation of Infantile Nephrotic Syndrome Secondary to CMV Infection in 10-Month-Old Infant: A Case Report

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Abstract

Infantile Nephrotic Syndrome (INS) is a rare medical condition in which nephrotic syndrome manifests itself within the first year of life. Primary INS is caused mostly by genetic abnormalities affecting renal filtration proteins, but secondary INS can result from underlying medical disorders or infections. Here, we provide a convincing case report of a 10-month-old girl who developed INS as a result of infection with Cytomegalovirus (CMV). The patient had a fever, cough, and generalized body swelling when he arrived. Nephrotic syndrome-confirming results were found during a clinical evaluation. IgM antibodies from a laboratory investigation supported CMV infection. Antiviral therapy and supportive measures were part of the treatment. This case emphasizes the importance of considering viral infections, such as CMV, as a potential etiology of INS in infants. Additionally, it also highlights the necessity of thorough analyses and specialized management approaches to improve results in these complex instances.

Keywords: Infantile nephrotic syndrome; Cytomegalovirus; Antiviral therapy; Hepatitis B virus; Human immunodeficiency virus

Introduction

A nephrotic syndrome that manifests within the first year of life is identified as "Infantile Nephrotic Syndrome" (INS) [1]. It may be primary or occur secondary to an underlying medical condition or infection. Primary infantile nephrotic syndrome is caused by genetic mutations that affect the functioning of proteins involved in the filtering of blood in the kidneys, whereas the secondary INS is a rare condition, usually associated with infections, e.g., syphilis, Cytomegalovirus (CMV), Toxoplasmosis, Rubella, Hepatitis B Virus (HBV), and Human Immunodeficiency Virus (HIV) infections, as well as metabolic disorders such as cystinosis and galactosemia. Nephrotic syndrome caused by Cytomegalovirus (CMV) usually manifests within the first 3 months of life, and child and adult presentations are rare [2]. In this case report, we describe a 10-month-old infant who presented with the complaints of fever, cough, and generalized body swelling and was subsequently diagnosed with INS secondary to CMV infection.

Case Presentation

A 10-month-old girl was admitted to Dr Ruth Pfau Civil hospital, a tertiary-care teaching hospital in Karachi, with a history of fever and cough for the last 7 days and generalized body swelling for the last 4 days. The patient was in her usual state of health 1 week back, as reported by her parents. Since then, she developed a low-grade fever which was undocumented, episodic, without any rigors or chills, and was only alleviated by antipyretics. The fever was associated with a non-productive cough, with no history of distress and cyanosis. The swelling was initially on the face which later became generalized. Mother denied any history of oliguria/polyuria including rashes and bleeding.

The infant was born by Spontaneous Vaginal Delivery (SVD), after completing a full-term pregnancy in a private hospital at Karachi. Birth weight of the infant was not reported and there was no history of difficult labour. The infant was solely kept on mother's feed during the first month, after then for the next 6 months she was given lactogen with an equal dilution. Shortly after 6 months complementary feeding was also started but still the baby was given only 70% of the required calories per day. Immunization was up to date in accordance with EPI guidelines.

Clinical exam

At presentation, the infant looked sick with generalized edema and had neither dysmorphism nor any apparent features of respiratory distress. Her heart rate was 162 beats/min with a respiratory rate of 60 breaths/min. Her recorded blood pressure was 90/50 mm Hg (50^{th} and 90^{th} percentile) and random blood sugar was 120 mg/dl. Her measured height was 63 cm (5^{th} centile) and weight 7.3 kg with occipitofrontalis circumference of 42.5 cm ($<5^{th}$ centile) and mid-upper arm circumference 12 cm.

The infant had distended abdomen, soft on palpation, with a palpable liver of 3 cm below right costal margin with a total span of 9 cm, left lobe was not palpable. Spleen was palpable as well. The rest of cardiovascular, respiratory and CNS signs were unremarkable. She was a microcephalic with no dysmorphic features.

Investigations

A first line complete blood picture showed anisocytosis, poikilocytosis with hypochromic, microcytic cells excluding any blast cells or target cells. The patient had hemoglobin of 6.9 g/dl, white blood cell count of 5.0 × 10E9/L, platelets count 401 × 10E9/L, mean

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cell volume of 65 fL, ANC of 37500.

A spot urine protein: creatinine ratio was 5 g, serum albumin 2.2 g/dl, serum cholesterol of 210 mg/dl, and 3+protein in urine, additional lab investigations including urine DR, LFTs and RFTs are provided in Table 1.

The TORCH profile of patient demonstrated serum CMV antibody IgM positive (1.64), normal is less than 0.9. The patient's serum iron was 33 mcg/dl and ferritin 331 ng/dl. Ultrasound abdomen showed a normal liver measuring 6.9 cm with homogenous parenchymal patterns. The extrahepatic biliary ducts were not dilated, and the portal vein was normal. The gallbladder wall was thick with no calculus or intra luminal masses and there was no pericholecystic fluid. The pancreas was partially visualized due to overlying gases. Spleen was of normal size measuring 7.2 cm with homogeneous parenchymal pattern. Splenic vein was not dilated.

Both kidneys were of normal size and corticomedullary distinction is intact with no calculus or focal mass. The proximal ureters were not dilated. In the abdominal region a moderate ascites was seen, without any lymphadenopathy.

Treatment

The patient was placed on a nothing-by-mouth (NPO) order and received oxygen therapy via nasal prongs at a rate of 2 l per minute. She was administered a once-daily intravenous injection of ceftriaxone, 550 mg, and received 0.9% saline solution with 50% maintenance. Additionally, she was advised to start a 4-week course of deltacortril tablets at a dosage of 2 mg/kg, with follow-up appointments. Following consultation with another doctor, ganciclovir injections were initiated and Liver Function Tests (LFTs) and Renal Function Tests (RFTs) were monitored. After 15 days of ganciclovir treatment, a urine dipstick test revealed 1+ protein and a specific gravity of 1.020, laboratory findings are provided in Table 2. The patient's LFTs showed a bilirubin level of 4 mg/dL and an SGPT (ALT) level of 82 U/L. The infant was treated with IV ganciclovir for 6 weeks. All symptoms resolved within 2 weeks of commencing treatment, and she fully recovered within 4 weeks. Additionally, she received a Packed Cell Volume (PCV) transfusion to address associated anemia. At the 4-month follow-up, she remained well and didn't develop any complication.

Discussion

The given case demonstrated classical features of Infantile Nephrotic Syndrome (INS) secondary to CMV infection and associated Iron deficiency Anaemia. The serum CMV IgM antibody test was performed and was positive, suggesting recent/acute infection.

Table 2: Laboratory findings.

Parameter	At Admission	After 15 days of Ganciclovir
Hb (g/dl)	6.9	8.2
WBC × 10E9/L	5	8.4
Platelet × 10E9/L	401	254
MCV (fL)	65	-
ANC (/mL)	37500	-
BUN (mg/dl)	5	-
Cr (mg/dl)	0.2	-
Na (mmol/L)	139	-
K (mmol/L)	4.4	-
Cl (mEq/L)	106	-
HCO3 (mEq/L)	26	-
CRP (mg/dl)	7.5	-
Bilirubin (mg/dl)	3.5	4
Sgpt (U/L)	99	82
Alp (U/L)	316	335
Albumin (g/L)	2.2	-
INR	1.6	-
Uric Acid (mg/dl)	2.2	-
Serum Cholesterol (mg/dl)	210	-
Urine Ph	6	7
Specific gravity	1.015	1.02
Protein (mg/dl)	3+	1+
Urine Protein Creatinine Ratio	5	-
Serum Iron (mcg/dl)	33	-
Ferritin (mcg/L)	331	-
Torch Profile	CMV IgM positive	-

HB: Hemoglobin; WBC: White Blood Cell Count; MCV: Mean Cell Volume; ANC: Absolute Neutrophil Count; BUN: Blood Urea Nitrogen; Cr: Creatinine; CRP: C-reactive Protein; SGPT: Serum Glutamate Pyruvate Transaminase; ALP: Alkaline Phosphatase; INR: International Normalized Ratio

The patient had microcephaly with no other evident CNS signs and dysmorphism but was requested to undergo a CT scan of the brain to rule out possible calcifications. Nonetheless, she had microcytic anemia and required a Packed Cell Volume (PCV) transfusion. The patient received IV ganciclovir under supervision for 6 weeks. The antiviral therapy was followed by a noticeable improvement in the patient's lab profile, indicating that perinatal CMV exposure may have caused the presenting symptoms and signs of congenital nephrotic syndrome.

The constellation of symptoms and findings in this case suggested a systemic disease with multi-organ involvement. The initial differential diagnosis included infectious causes such as viral or bacterial infections, as well as systemic inflammatory conditions or genetic disorders, or blood pathology such as infantile leukemia.

Table 1: Initial Investigations.

CBC	HB	WBC	PLT	MCV	N	L	ANC		
	6.9	50	401	65	75	18	37500		
Biochemistry labs	BUN	Cr	Na	K	Cl	HCO_3	CRP		
	5	0.2	139	4.4	106	26	7.5		
LFTS	SB	Db	SGPT	ALP	ALB	APPT	PT	INR	UA
	3.5	2.3	99	316	2.2	37	16	1.6	2.2
Urine DR	Proteins	pH	Sp. Gravity						
	+ ve	6	1.015						
miscellaneous	Serum Iron		Ferritin	HPLC	UPCR	CMV Ab			
	33		331	Normal*	5	1.66			

CBC: Complete Blood Count; HB: Hemoglobin; WBC: White Blood Cells; PLT: Platelets; MCV: Mean Corpuscular Volume; BUN: Blood Urea Nitrogen, Cr: Creatinine; Na: Sodium; K: Potassium; Cl: Chloride; HCO_3: Bicarbonate ions; SGPT: Serum Glutamic Pyruvic Transaminase; UA: Uric Acid; DR: Detailed Report; Sp.: Specific; HPLC: High Performance Liquid Chromatography; UPCR: Urine Protein Creatinine Ratio; Ab: antibodies; *Normal means no Haemoglobinopathy is present

Table 3: Case reports of infantile nephrotic syndrome owing to CMV infection.

Source	Year	Country	Age/Sex	Diagnosis	Treatment	Outcome
Giani et al. [3]	1996	Italy	5 m/F	Serum and Urine CMV IgM	IV ganciclovir	Recovered
				Kidney Biopsy		no relapse in 12 months
Berbel et al. [4]	2003	Spain	5 m/M	Serum CMV IgM	Oral ganciclovir	Recovered
				Kidney Biopsy		no relapse in 17 months
Stańczyk et al. [5]	2015	Poland	9 m/M	Urine CMV PCR 6200 copies/μL	IV ganciclovir followed by oral valganciclovir	Recovered
						no relapse in 12 months
Hogan et al. [6]	2015	France	5 m/M	Blood CMV PCR 123,000 copies/mL	IV ganciclovir followed by oral valganciclovir	Recovered
						no relapse in 30 months
Kaur et al. [7]	2020	India	7 m/F	Blood CMV PCR 7700 copies/μL	IV ganciclovir followed by oral valganciclovir	Recovered
						no relapse in 18 months
Present Case	2023	Pakistan	10 m/F	Serum CMV IgM	IV ganciclovir	Recovered

The history of fever, cough, and generalized edema for several days raised suspicion of a viral infection, as CMV is known to cause fever, hepatosplenomegaly, and edema. A serum CMV IgM antibody test was performed and was positive, supporting this possibility.

The anemia, microcytosis, and hypochromia observed in the complete blood picture were consistent with iron deficiency anemia. The low serum iron and elevated ferritin levels further supported this diagnosis. Iron deficiency anemia could result from inadequate iron intake, malabsorption, or increased iron requirements. Given the patient's history of exclusive breastfeeding up to one month and subsequent inadequate calorie intake, nutritional iron deficiency is a likely cause. However, other causes, such as chronic blood loss or impaired iron absorption, should also be considered and investigated further.

The proteinuria, hypoalbuminemia, and ascites suggested a renal component to the patient's presentation. Nephrotic syndrome, characterized by heavy proteinuria, hypoalbuminemia, and edema, should be considered. It was crucial to determine the underlying cause of nephrotic syndrome, which could be either primary (idiopathic) or secondary to various systemic diseases, including infections, autoimmune disorders, and malignancies. A renal biopsy might have been necessary to establish the specific diagnosis and guide further management.

Similar cases have also been reported worldwide, and a summary is provided in Table 3 [3-7].

In summary, when evaluating INS, it was important to consider infectious causes, such as Cytomegalovirus (CMV). If CMV was found to be the primary cause, early and appropriate treatment could lead to a good outcome. However, it was important to consider other viral and bacterial infections that might present with similar symptoms, such as Epstein-Barr Virus (EBV), adenovirus, or tuberculosis. Additional investigations, including viral and bacterial cultures, should be considered to rule out these possibilities.

Limitation

This case report has a few limitations. First, the follow-up time was limited due to the public sector hospital setting. Consequently, the duration of monitoring and assessment of the patient's condition was restricted, which might have limited our understanding of long-term outcomes and potential complications. Second, only necessary tests were conducted, which ensured essential information was obtained. However, this approach may have resulted in limited data availability for a comprehensive analysis. Additional tests or investigations could have provided a more in-depth understanding of the patient's condition and response to treatment. These limitations should be considered when interpreting the findings of this case report.

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