Journal of Clinical Case Reports

Case Report Open Access

An Unusual Case of Paediatric Atypical Haemolytic Uraemic Syndrome with Bilateral Purtschers-Like Retinopathy and Sub-Retinal Detachment

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Abstract

Atypical haemolytic uremic syndrome (aHUS) is a rare disease caused by chronic, uncontrolled activation of the alternative complement pathway that leads to thrombotic microangiopathy, haemolytic anaemia, acute renal impairment and thrombocytopenia. If left untreated, aHUS can progress into end stage renal disease and permanent renal impairment. Extrarenal manifestations have also been reported in the literature. Ocular involvement is usually rare in aHUS. This is a rare case report where a 13-year-old boy with aHUS presented with bilateral purtschers like retinopathy and sub retinal detachment in addition to renal impairment. The patient's hematologic and renal parameters and ocular manifestation improved following appropriate therapy.

Keywords: Haemolytic uraemic syndrome; Retinal detachment; Retinopathy

Introduction

Haemolytic uremic syndrome (HUS) is a condition affecting the blood and blood vessels that results in the destruction of platelets, low red blood cell count (anemia) and renal impairment due to the damage of small blood vessels of the kidney. It is one of the most common causes of acute renal failure in children, and the incidence of this syndrome in children is increasing worldwide [1]. HUS is broadly classified as typical (Diarrhoea related) or atypical HUS (non diarrhoea related) [2]. Atypical HUS is a rare genetic disease which is caused by chronic and uncontrolled alternative complement activation that results in life threatening thrombotic microangiopathy (TMA), hemolytic anemia, thrombocytopenia and acute renal failure [3-5]. About 79% of them progress to permanent renal failure and might need dialysis or die within 3 years from the time of onset [6]. Extra renal manifestations of HUS are reported in about 50% of the patients while ocular involvement is a very rare phenomenon [7].

Central nervous system manifestations occur in a few patients but portend a poor prognosis. Purtscher's retinopathy is a rare retinal disorder that manifests as acute visual loss, cotton-wool spots and intraretinal haemorrhages or retinal whitening following a chest or head trauma. When the etiology is not trauma, the condition is called Purtscher- like retinopathy [8]. Various other systemic conditions that cause Purtscher- like retinopathy are acute pancreatitis, autoimmune diseases, pregnancy related diseases and TAM [9]. aHUS are rare but life threatening, and the pathology of the disease is through complement system dysregulation and it is differentiated from HUS by the absence of diarrhoea and shiga toxin- induced infection. The complement system dysregulation leads to vascular endothelial damage and complement aggregations [10].

Since the approval of eculizumab (a terminal complement inhibitor) in 2011 for the treatment of aHUS, only two cases of ocular involvement in HUS has been reported (one with bilateral serous retinal detachment and the other with bilateral retinal vein occlusion) [11]. Herein a case of aHUS with bilateral purtschers like retinopathy and sub retinal detachment is discussed. This alarm the ophthalmologist in a way as they come as the first line of contact in a variety of systemic diseases and play an important role in the early diagnosis and management of the associated symptoms, thereby reducing fatality. This case describes the favorable outcome of atypical HUS with ocular involvement.

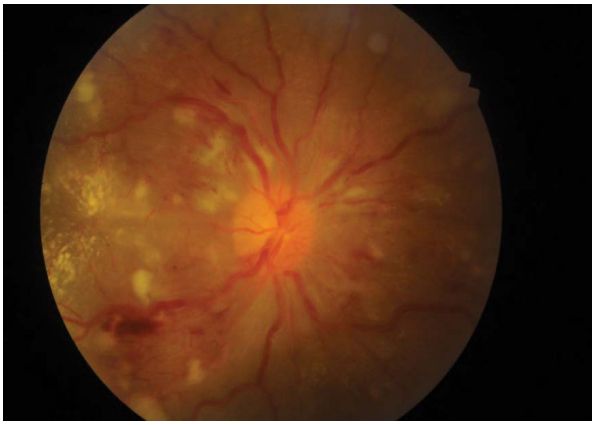

Figure 1: Right eye fundus photograph: Flame shaped haemorrhages, cotton wool spots.

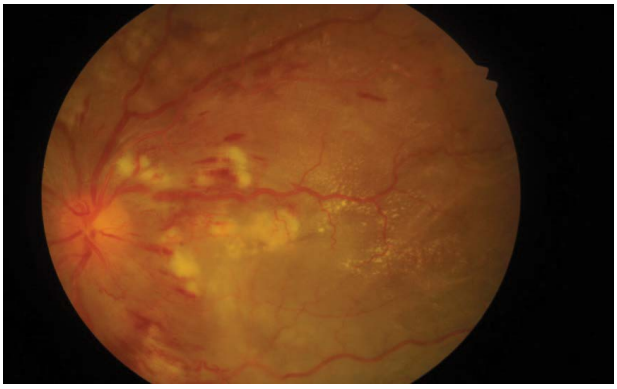

Figure 2: Left eye fundus photograph: Multiple flame shaped haemorrhages, cotton wool spots and mild papilledema.

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Received April 26, 2019; **Accepted** June 03, 2019; **Published** June 10, 2019

Citation: Parekh R (2019) An Unusual Case of Paediatric Atypical Haemolytic Uraemic Syndrome with Bilateral Purtschers-Like Retinopathy and Sub-Retinal Detachment. J Clin Case Rep 9: 1251.

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Case Report

A 13-year-old boy who was healthy until 5 days back was admitted in the intensive care unit with history of fever, jaundice and decreased vision for 5 days and haematuria for 2 days. There was no history of diarrhoea. There was no family history of any renal involvement. On examination he was febrile (temp -38.6℃) and lethargic with tachypnoea (RR-32/min), tachycardia (PR-110/min), pallor and icterus. His blood pressure was 200/130 mmHg. On respiratory system examination he had bilateral equal air entry with no adventitious sounds, and he maintained an oxygen saturation of 100%. Other system examinations were all normal.

On ophthalmic examination presence of scleral icterus was noted. Fundus showed shallow serous retinal detachment in the posterior poles and optic discs showed mild papilloedema. Bilateral retinal vascular tortuosity and retinal edema was observed with cotton-wool patches around the peripapillary region and retinal hemorrhages, mainly in the posterior pole of both the eyes (Figures 1 and 2).

Laboratory tests showed renal derangement with blood urea levels 49.27 mg/dl (normal value 7-20 mg/dl), serum creatinine 1.6 mg/dl (normal value-0.6- 1.2 mg/dl), hemolytic anemia with hemoglobin 6.4 g/dl (normal value 13.5-17.5 mg/dl), lactate dehydrogenase 528.32IU/L (60- 170 U/L), total bilirubin 3.0 mg/dl (0.1- 1.2 mg/dl), indirect and direct bilirubin 2.5 mg/dl (<0.3 mg/dl) and thrombocytopenia with platelet count 71,000/mm^3 (1,50,000 to 4,50,000/mm^3). Serum amylase was slightly elevated to 88.43U/L (normal 23-85 U/L). Peripheral blood smear showed dimorphic anaemia, thrombocytopenia with presence of schistocytes. Malarial antigen and leptospira IgM were negative. Urinalysis showed plenty of proteinuria along with plenty of red blood cells and a urine protein-creatine ratio of 2.25 (normal <0.11mm/hg). Complements were within normal limits. He had a normal international normalized ratio (INR), prothrombin time (PT) and partial thromboplastin time (PTT).

Renal ultrasonography revealed small contracted left kidney (LK-45 × 07 mm) with loss of corticomedullary differentiation and compensated hypertrophy of right kidney (RK- 95 × 15 mm). A renal biopsy was not done due to a contracted left kidney. MRI brain showed T2 hyperintense and T1 hypointense regions in the brainstem predominantly involving pons and medulla as well as bilateral lentiform nuclei and fronto-parietal white matter, suggestive of hypertensive encephalopathy (Figure 3). Echocardiography revealed left ventricular hypertrophy but no pericardial effusion or pulmonary arterial hypertension (PAH).

A diagnosis of atypical hemolytic uremic syndrome was made based on laboratory evidence of microangiopathic hemolysis, thrombocytopenia and acute renal impairment in the presence of normal complements with no preceding history of diarrhoea. The patient was managed with supportive measures including hydration, packed cell transfusion and intravenous nitroglycerine to control his blood pressure. His condition stabilized yielding normal diuresis and blood pressure. After day 5, azotemia improved (BUN mg/dl, Cr mg/dl) without any proteinuria or microscopic hematuria, and uric acid and LDH levels normalized. Repeat fundus examination after one month showed total resolution of the serous retinal detachment.

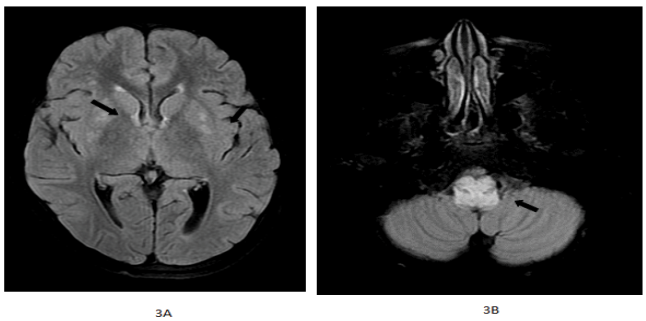

Figure 3: MRI of brain (a) T2 FLAIR demonstrating hyperintensities (black solid arrows) in bilateral lentiform nuclei and (b) brainstem.

Discussion

To the best of our knowledge this is the first case of a paediatric aHUS patient presenting with haemorrhaghic or Purtscher-like retinopathy. HUS is a syndrome due to the combination of findings it presents with, that has different causes. It occurs after a severe bowel infection in children with toxic strains of *E. coli* and may occur after intake of certain medicines. Apart from renal impairment, it can also damage the brain and heart due to damage to the smaller blood vessels [12]. Typical HUS is also known as the D+ form where D+ means 'with diarrhoea' which occurs with gastroenteritis caused by bacteria (usually *E. coli* 0.157) that produce verotoxin. It usually affects the very young (below 5 yrs.) or the very old and develops a few days after a bout of bloody diarrhoea. It may occur in outbreaks or one at a time with 1 in 20 people getting HUS following *E. coli* infection. HUS is the most frequent cause of acute kidney failure in children in Western Europe and North America [13].

Atypical HUS (also called D-) may be inherited or occur due to pre-eclampsia, drug reaction or rarely as a complication of cancer or bone marrow transplantation. It is characterized by a triad of nonimmune hemolytic anemia, thrombocytopenia and renal failure. It usually follows bloody diarrhea secondary to infection with shiga like toxin (Stx) producing bacteria or Streptococci. The commonest clinical presentation of HUS is acute pallor and oliguria following diarrhoea or dysentery and commonly occurs in children less than 5 years of age. Around 10% cases are atypical (aHUS), may be preceded by viral or bacterial illness (other than Stx producing bacteria or Streptococci), connective tissue disease or history of drug intake. Family history may also be present. Uncontrolled activation of alternate pathway of complement system due to mutations in complement regulatory proteins underlies the pathogenesis of aHUS [14].

The tiny filter units or the glomeruli become clogged with platelets and damaged RBCs that alter the kidney's ability to filter and eliminate waste products. These patients have more insidious and sometimes fluctuating symptoms at onset and the degree of hypertension and duration of oligo-anuria is greater compared to that in typical HUS [15]. Extrarenal complications like cerebrovascular events and pulmonary hemorrhages and retinopathy occurring due to multiorgan thrombotic microangiopathy are also more common in aHUS. Ocular involvement in HUS has been documented in both adults and pediatric age group [16]. Findings consistent with Purtschers like retinopathy has also been reported in HUS [17].

Purtscher-like retinopathy is a rare retinal disorder with signs of cotton wool spots, retinal haemorrhages, macular edema, pseudo cherry red spots and purtscher flecks [18]. The incidence of this retinopathy is 0.24 patients per million per year [19] and it is seen associated with acute pancreatitis, renal failure, autoimmune diseases and thrombotic microangiopathies like TTP, HUS and DIC. The pathophysiology behind purtscher-like retinopathy is vascular endothelial damage and arteriolar precapillary occlusion by emboli of leucocytes, fibrin, fat and complement aggregates. Purtscher-like retinopathy is commonly

caused by HUS and aHUS and can be life threatening in childhood and early adulthood. Therefore, a detailed fundus examination is crucial, especially in pediatric patients for recognizing these retinopathies underlying a life-threatening disease.

MRI findings in our patient were like lesions already described in literature [20] and believed to be the result of microvascular damage. The pathogenesis of CNS involvement in aHUS is multifactorial secondary to metabolic abnormalities, uraemia, hyponatraemia, or hypocalcaemia. Also, toxin-mediated mechanisms resulting in focal vascular endothelial injury or multifocal thrombotic pathology may occur. Hypertension has been cited as an additional factor. Mutations of factor H, factor I, factor B, membrane cofactor protein, C3 convertase component, and thrombomodulin gene can cause aHUS [21]. These abnormalities cause thickening of arterioles and capillaries, endothelial detachment, subendothelial accumulation of proteins, cell debris and fibrin-platelet thrombi obstruction due to the dysregulation of complement alternative pathway.

All these mechanisms cause multi-organ involvement but there are only very few reported cases of ocular involvement in aHUS [22,23]. aHUS with ocular involvement patients responded well to hemodialysis, plasmapheresis and eculizumab therapy [24]. General medical care by close monitoring of fluid volume (IV fluids and nutritional supplementation by IV or tube feeding) is mandatory. Blood transfusion and short-term dialysis is also done in a few cases. Early and correct treatment, as described above, is pivotal to the child's outcome, so it is important to identify the differences in presentation and manage typical HUS and atypical HUS appropriately as treatment and prognosis is always dependent on the type of HUS.

Our case had extra renal manifestations. Treatment was initiated early and so probably he had a favorable outcome. During the course in hospital, his urine volume and generalized edema subsided with prompt treatment. His platelet count rose to 2,03,000 /mm^3, hemoglobin rose to 10.6 g/dl, reticulocyte count reduced to 1.5%, lactate dehydrogenase decreased to 200 IU/L, and blood urea nitrogen and serum creatinine improved to 20 mg/dl and 0.8 mg/dl, respectively. Peripheral blood smear did not show evidence of hemolytic anemia.

Conclusion

Recent progress in diagnosis of Anti-factor H antibodies-HUS and therapeutic options, including early aggressive plasma exchange along with various immunosuppressive modalities helps in the betterment of prognosis in the future. The extent and severity of non-renal involvement become an important determinant of ultimate prognosis. Prompt recognition of the syndrome and effective therapy for acute renal failure helped the patient to improve in due course and resulted in a successful treatment outcome. This case report states that Ophthalmologists play a pivotal role in the diagnosis and management of many new health diseases in this setting.

References

1. Karpman D (2002) Haemolyticuraemic syndrome and thrombotic thrombocytopenic purpura. Cur Paediat 7: 569-574.
2. Noris M, Remuzzi G (2009) Atypical hemolytic-uremic syndrome. N Engl J Med 361: 1676-1687.
3. Andreoli SP (1999) The pathophysiology of the hemolytic uremic syndrome. Curr Opin Nephrol Hypertens 8: 459-464.
4. Zipfel PF, Heinen S, Skerka C (2010) Thrombotic microangiopathies: New insights and new challenges. Curr Opin Nephrol Hypertens 19: 372-378.
5. Benz K, Amann K (2010) Thrombotic microangiopathy: New insights. Curr Opin Nephrol Hypertens 19: 242-247.
6. Noris M, Caprioli J, Bresin E (2010) Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. Clin J Am Soc Nephrol 5: 1844-1859.
7. Campistol JM, Arias M, Ariceta G (2013) An update for atypical haemolytic uraemic syndrome: Diagnosis and treatment. Nefrologia 33: 27-45.
8. Agrawal A, McKibbin M (2007) Purtscher's retinopathy: Epidemiology, clinical features and outcome. Br J Ophthalmol 91: 1456-1459.
9. Miguel AI, Henriques F, Azevedo LF, Loureiro AJ, Maberley DA (2013) A systematic review of Purtscher's and Purtscher-like retinopathies. Eye 27: 1.
10. Dragon-Durey MA, Sethi SK, Bagga A, Blanc C, Blouin J, et al. (2010) Clinical features of anti-factor H autoantibody-associated hemolytic uremic syndrome. J Am Soc Nephrol 21: 2180-2187.
11. Zheng X, Gorovoy IR, Mao J, Jin J, Chen X, et al. (2014) Recurrent ocular involvement in pediatric atypical hemolytic uremic syndrome. J Pediatr Ophthalmol Strabismus 51: 62-65.
12. Donne RL, Abbs I, Barany P, Elinder CG, Little M, et al. (2002) Recurrence of hemolytic uremic syndrome after living related renal transplantation associated with subsequent *de novo* disease in the donor. Am J Kidney Dis 40: 22-23.
13. Gallo GE, Gianantonio CA (1995) Extrarenal involvement in diarrhoea-associated hemolytic-uremic syndrome. Pediatr Nephrol 9: 117-119.
14. Caton B, Diaz de Otazu R, Aldamiz-Echebarria M, Viguri A (1993) Haemolytic-uraemic syndrome with thrombotic microangiopathy of the retina following cytomegalovirus infection: Postmortem findings. Postgrad Med J 69: 653-655.
15. Sturm V, Menke MN, Landau K, Laube GF, Neuhaus TJ (2010) Ocular involvement in paediatric haemolytic uraemic syndrome. Acta Ophthalmologica 88: 804-807.
16. Patel MR, Bains AK, O'Hara JP, Kallab AM, Marcus DM, et al. (2001) Purtscher retinopathy as the initial sign of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome. Arch Ophthalmol 119: 1388-1389.
17. Miguel AI, Henriques F, Azevedo LF, Loureiro AJ, Maberley DA (2013) A systematic review of and Purtscher-like retinopathies. Eye 27: 1-13.
18. Agrawal A, McKibbin M (2007) Purtscher's retinopathy: Epidemiyology, clinical features and outcome. Br J Ophthalmol 91: 1456-1459.
19. Yenerel MN (2014) Atypical hemolytic uremic syndrome: Differential diagnosis from TTP/HUS and management. Turk J Hematol 31: 216-225.
20. Dragon-Durey MA, Sethi SK, Bagga A, Blanc C, Blouin J, et al. (2010) Clinical features of anti-factor H autoantibody-associated hemolytic uremic syndrome. J Am Soc Nephrol 21: 2180-2187.
21. Larakeb A, Leroy S, Frémeaux-Bacchi V, Montchilova M, Pelosse B, et al. (2007) Ocular involvement in hemolytic uremic syndrome due to factor H deficiency are there therapeutic consequences. Pediatr Nephrol 22: 1967-1970.
22. David R, Hochberg-Klein S, Amer R (2013) Resolution of ocular involvement with systemic eculizumab therapy in atypical hemolytic-uremic syndrome. Eye 27: 997-998.
23. Greenwood GT (2015) A case report of atypical hemolytic uremic syndrome with retinal arterial and venous occlusion treated with eculizumab. Int Med Case Rep J 8: 235-239.
24. Green H, Harari E, Davidovits M (2014) Atypical HUS due to factor H antibodies in an adult patient successfully treated with eculizumab. Ren Fail 36: 1119-1121.