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CASE REPORT

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Moschcowitz Disease in pediatric

Samira AGGOUNE[1], Mohamed Faouzi SEDDIKI[2]

[1] Service de pédiatrie EPH Belfort Alger, Algérie
[2] EHS TOUGGOURT, Algérie

ABSTRACT

Hemichorea Moskowitz disease is a rare hematological disorder known to be an autoimmune disease in most patients. Most cases of thrombotic thrombopenic purpura (TTP) are caused by problems with an enzyme or protein in the blood called ADAMTS13. The disorder may be inherited throughout the patient's life or may develop (acquired). Hereditary TTP primarily affects newborns and children, and most individuals with hereditary TTP develop symptoms soon after birth. However, some people do not develop symptoms until they are adults. Once TTP begins in adulthood, it is acquired in 97% of cases, is more commonly diagnosed in women and African Americans. A specific cleaving metalloprotease of von Willebrand factor (VWF) results in circulating supergiant VWF multimers that cause platelet aggregation and systemic microvascular thrombosis. A rare mechanism of severe ADAMTS13 deficiency is constitutional and associated with biallelic mutations in the ADAMTS13 gene. These mutations are responsible for congenital TTP or Upshaw-Schulman syndrome, whose transmission follows an autosomal recessive fashion. Affected individuals are either homozygous or compound heterozygous. We present the case of a 6-month-old girl who suffered despite Upshaw Shulman Syndrome and whose diagnosis was very difficult to find, given the complexity of the case and the differential diagnoses to be invoked.

ARTICLE HISTORY

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CORRESPONDING AUTHOR

Samira Aggoune
aggounesamira@hotmail.com

1. INTRODUCTION

Thrombotic microangiopathy, known as Moschcowitz Disease defined by spontaneous formation of thrombi in the microcirculation. It's rare disease that primarily affects young women. The annual incidence of TTP has been estimated of 1,5-6 per million people. [1] Previously, antibody-mediated her ADAMTS-13 deficiency was thought to cause her TTP in adults and hereditary ADAMTS13 deficiency in children, but recently both types were identified in both age groups. [2]

In most cases, the mechanism of ADAMTS13 hypoactivity is autoimmune in nature and is associated with the presence of IgG-type anti-ADAMTS13 autoantibodies present in 75% of patients with acute TTP. In autoimmune acquired PTT (iPTT), the presence of anti-ADAMTS13 antibodies causes protease inhibition or enhanced clearance. The mutations reported in Upshaw Shulman Syndome (USS) are distributed throughout the gene, but mostly in the N-terminal region. 70% are missense codon-causing mutations and 30% are into truncated proteins. The worldwide frequency of TTP is 1.5–4 per million population per year. [3] This congenital form is estimated to affect 1 in every million people.[4]

Certain features have been correlated with ADAMTS13 deficiency and are considered risk factors for acquired TTP. Female Gender, Ethnicity Sub-Saharan Africa ,HLA-DRB1*11 alleles and obesity. [5].

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2. OBSERVATION

A 6-month-old girl was tested for thrombocytopenia. Of her brothers, three sisters died.The first had fetal fever on the first day of life, the second had shortness of breath and anemia

on the second day of life, and the third had anemia and thrombocytopenia at 3 years of age, all of which were attributed to Evans syndrome. She was born full-term by caesarean section, her birth weight was good, and her height was

normal. She weighs 3.5 kg, is 50 cm tall, and has a head circumference of 35 cm. This child was born presumably due to her Rhesus incompatibility with early jaundice because her mother was her Rh-negative and required an exchange transfusion. At the age of 2 months, she was rehabilitated for bicitopenic anemia with thrombocytopenia. Complete blood count shows 7.7 g/dl for hemoglobin and 54,000/mm3 for platelets. Blood smears showed macrocytosis, schistocytes , and hypochromia. Myellogram showed hyperactive erythroblasts and thrombocytopenia. Negative direct coombs tests. Vitamin especially vitamin B12 and folic acid, were normal. Laboratory tests show lower-than-normal hemoglobin, increased reticulocytes, increased indirect bilirubin, increased LDH, decreased haptoglobin, normalized clotting time, and direct negative Coombs test. Schistocytes cells or klenoocytes are mechanically fragmented as they pass through occluded capillaries and are therefore recognizable on peripheral blood smears. An immunoglobulin weight test, lymphocyte phenotype, Coombs test, and autoimmune tests were performed and no

abnormalities were found. The initial diagnosis was Evans Syndrome. Initial corticosteroid therapy did not significantly improve the child's biological parameters, especially blood

counts.

Given the presence of schistocytes in blood smears, positive assessment of hemolysis, and similar symptoms prior to death, a genetic study by sequencing of 29 exons of the ADAMTS13 gene was performed, confirming the presence of homozygosity with presence of 760777 excl. (Ala254-Gly259del) a dose of ADAMTS13 activity that showed less than 1% loss. An autoantibody test was also performed, but no anti-ADAMTS13 autoantibodies were detected. Genetic testing of the parents revealed a heterozygous mutant C.760_777 in p.(Ala254_Gly259 del) .The infant was replaced with fresh frozen plasma every 21 days of her and there after monitored monthly for early thrombocytosis with complete blood count and lactate dehydrogenase levels. Its progression is summarized in Table 1.

3. DISCUSSION

The term Thrombotic Microangiopathies (TMA) defines a syndrome encompassing a variety of conditions characterized by the association of mechanical hemolytic anemia with the presence of anemia, peripheral thrombocytopenia, and organ failure of varying severity. The two main conditions that make up TMA syndrome are thrombotic thrombocytopenic purpura (TTP) (or Moshowitz syndrome) and hemolytic uremic syndrome (HUS), although other conditions also meet the criteria for TMA, such as HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count) in pregnant women. TMA syndrome can occur in a variety of tumor conditions, human immunodeficiency virus (HIV) infection, hematopoietic stem cell transplantation, devastating antiphospholipid syndrome, heparin-induced thrombocytopenia type 2, malignant hypertension (HTA), and even giant angioma. Less than 10% (or IU/dl) reduction in ADAMTS13 activity was specific to TTP [6]

Table 1. Results of biological tests and treatment development.

Date	GB	PNN	LYMPHOCYTE	HB	VGM	CMMH	PLAQUETTE	Taux de LDH
01/10/2022	17	4,20	12,51	13	88	31,82	45	345
15/10/2022	24,68	5,54	17,16	10,8	87	32,20	30	300
24/10/2022	21,99	6,03	13,86	10,3	94	31,40	26	
27/10/2022	19,23	13,17	4,23	10.90	94	31.40	13	616230 16,70%
08/11/2022	20.92	10.14	9.37	12	99.5	30.50	1828	265
21/12/2023	5.92	1.29	3.26	10.59	75	34		200
14.02.2023	12,83	2,82	8,38	11,4	78,30	32,90	1900	265
12.04.2023	12	2.68	8,53	9,80	81.10	34	341	322

Antibodies are present in autoimmune acquired PTT (iPTT). Anti-ADAMTS13 inhibits or promotes clearance of anti-ADAMTS13. protease. The use of anti-CD20 therapies (such as rituximab) has proven to be superior. Effect of reducing the number of times of plasmapheresis required for collection prevention of remission and relapse during or on acute treatment For prophylactic treatment. However, the nature of the immune cells involved Anti-ADAMTS13 autoantibody production has not yet been confirmed. Our patient and his deceased sister had suspected Evans infection. A syndrome characterized by hemolytic anemia with documented thrombocytopenia. Attention may have been the key to early detection, especially in infants with persistent jaundice due to rhesus maladaptation. The failure in our patient's history was most likely due to underdiagnosis of her sister, who is a congenital PTT (c PTT) carrier, and our patient's diagnosis of microangiopathy was suspected and confirmed by the detection of erythrocyte fragmentation (schistocytes cells and helmet cells) in blood smear. In our patient, USS was confirmed by a precipitous drop of <5% in ADAMTS13 activity, genetic analysis

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for infant and parents and presence of biallelic variants, specifically lack of anti-ADMAS13 antibodies. Plasma treatment has been appeared to be viable in patients with persistent repetitive TTP. [7]

If acquired, treatment is usually with immunosuppressants, but in USS cases, an infusion of fresh frozen plasma is used. 1-2 units infusion provides complete symptom relief Platelet count and LDH levels. Platelet checks can be kept up inside the ordinary extend for 2 weeks, whereas ADAMTS13 movement returns to ordinary 2.5–3.5 days after plasma infusion [8] Plasma treatment dosages and dosing interims are right now based on clinical side effects, platelet checks, and lactate dehydrogenase levels. It is well known that the systemic clearance of a drug decides its steady-state presentation.

However, it is controversial whether graded plasma therapy is appropriate for the treatment of the most common triggers of his TTP attacks in childhood, such as infections and vaccination. Total reaction to treatment is characterized as a platelet tally >150 x 109/l for 2 continuous days with typical LDH or normalization and clinical enhancement and eternal answer to treatment continues for at least 30 days after discontinuation of TPE (therapeutic plasmapheresis), relapsed within 30 days after treatment response. [8] When the clinical result definition for iTTP was to begin with proposed by the Worldwide Working Bunch (IWG) in 2003, the platelet number was the essential implies of evaluating reaction. At this point, reaction to treatment was characterized as accomplishing a normal platelet count. Supported palliation was characterized by maintaining supported normal platelet control for 30 days after TPE cessation. [9]

Clinical response: The International Working Group IWG 2017 report defined a sustained platelet count of 150 x 109/L and a lactate dehydrogenase (LDH) of 1.5 times the upper constrain of ordinary. No prove of unused or dynamic organ harm or movement - Platelet number less than 150 x 109/L inside 30 days after cessation of anti-VWF or therapeutic plasmapheresis after clinical response. The normal survival rate from the primary TTP occurrence is 80% to 90% on the off chance that TPE is begun early. Age, very high LDH levels (10-fold above normal), mainly reflecting basically reflecting organ harm, and raised cardiac troponin levels at determination (0.25 ng/mL troponin level) are all related with mortality and therapeutic resistance. TTP survivors are reported to suffer from neurocognitive impairment, arterial hypertension,and major depression more frequently than expected compared with the general population. This can lead to high mortality. ADAMTS13 activity testing (and antibody screening by his ELISA if ADAMTS13 activity <10%) and standard biologic surveillance are scheduled for the following dates:- Weekly after normalization of platelets (and discontinuation of PE) until partial normalization of ADAMTS13 activity to levels of 20-30%. Then repeat the check after 28 days to confirm normalization (preferably 50% percentage). It is then given every 3 months for several years for lifelong monitoring. Deferring monitoring to every 6 months or even annually should only be considered after several years of successful ADAMTS13 activity (50%). [10]

4. CONCLUSION

The rarity of this disease makes it difficult to diagnose TTP in an emergency, as treatment may be delayed and prognosis may be affected. A growing number of countries are developing various measures to address this, including training programs for general practitioners, emergency physicians and other professionals who may be involved in managing TTP.

DECLARATION D'INTERETS

none relevant to this article.

5. REFERENCES

1. Mariotte E, Azoulay E, Galicier L, et al. Epidemiology and pathophysiology of adulthood-onset thrombotic microangiopathy with severe ADAMTS13 deficiency (thrombotic thrombocytopenic purpura): a cross-sectional analysis of the French national registry for thrombotic microangiopathy. Lancet Haematol. 2016;3(5):e237– 245.

2. Kinoshita S, Yoshioka A, Park YD, et al. Upshaw-Schulman syndrome revisited: a concept of congenital thrombotic thrombocytopenic purpura. Int J Hematol 2001; 74:101–108. 9.

3. Reese JA, Muthurajah DS, Kremer Hovinga JA et al. Children and adults with thrombotic thrombocytopenic purpura associated with severe, acquired Adamts13 deficiency: comparison of incidence, demographic and clinical features. Pediatr Blood Cancer 2013; 60: 1676 – 82

4. Kokame K, Kokubo Y, Miyata T. Polymorphisms and mutations of ADAMTS13 in the Japanese population and estimation of the number of patients with UpshawSchulman syndrome. J Thromb Haemost 2011; 9: 1654 – 6.

5. Martino S, Jamme M, Deligny C, et al; French Reference Center for Thrombotic Microangiopathies. Thrombotic thrombocytopenic purpura in black people: impact of ethnicity on survival and genetic risk factors. PLoS One. 2016;11(7): e0156679.

To cite the article: Aggoune S et al. Moschcowitz Disease in pediatric. Batna J Med Sci 2024; 11(1): 80-83

6. Levy GG, Nichols WC, Lian EC, et al. Mutations in a member of the ADAMTS gene family cause thrombotic thrombocytopenic purpura. Nature. 2001;413:488---94

7. Lotta, L.A.; Wu, H.M.; Mackie, I.J.; Noris, M.; Veyradier, A.; Scully, M.A.; Remuzzi, G.; Coppo, P.; Liesner, R.; Donadelli, R.; et al. Residual plasmatic activity of ADAMTS13 is correlated with phenotype severity in congenital thrombotic thrombocytopenic purpura. Blood 2012, 120, 440–448

8. Taylor A, Vendramin C, Oosterholt S, et al. Pharmacokinetics of plasma infusion in congenital thrombotic thrombocytopenic purpura. J Thromb Haemost 2019;17:88-98.

9. Adam Cuker,Spero R. Cataland,Paul Coppo,Javier de la Rubia,Kenneth D. Friedman et al. Redefi ning outcomes in immune TTP: an international working group consensus report. Blood: 8 April 2021 | Volume 137, Number 14

10. Kathrin Eller , Paul Knoebl , Sevcan A. Bakkaloglu , Jan J. Menne , Paul T. Brinkkoetter et al. European Renal Best Practice endorsement of guidelines for diagnosis and therapy of thrombotic thrombocytopaenic purpura published by the International Society on Thrombosis and Haemostasis. Nephrol Dial Transplant (2022) 37: 1229–1234

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