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ADVANCES IN PEDIATRIC RESEARCH

Immune thrombocytopenic purpura in a twin girl revealed by a traumatic injury in parakou (North Benin)

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Abstract

Background: ITP seems to be rare but in tropical settings thrombocytopenia is often encountered among children. Objective: Authors through this case report are putting emphasy on the diagnosis and management of ITP in a 4 year old twin girl admitted in the pediatric emergency ward for hematuria and bleeding from various origins seen in the context of a domestic trauma. Results: The various clinical signs have been analyzed to confirm ITP through exclusion of other possible health conditions. The management of ITP depend on the severity of clinical signs and in some cases the situations can be life threatening. In this case report, Blood transfusion and corticosteroids were the main treatment tools. The hospital stay was about 47 days and an ambulatory follow up was conducted for almost 6 months.

Conclusion*:* In the context of various bleeding disorders, hematuria and thrombocytopenia, autoimmune thrombocytopenia in a twin girl was revealed by a domestic trauma.

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Introduction

Immune Thrombopenic Purpura is defined as an « autoimmune disease» in which the immune system reacts against its own platelets considered as foreign bodies [1] responsible of their destruction, especially in the spleen. It is also defined as thrombopenia resulting from lack of bone marrow production of platelet of immunologic origin according to the High French Authority of Health (HAS) [2]. Its symptoms are function of platelets count. Thus, under a certain platelet count, blood clotting disorders occur leading to ecchymotic or purpuric spots without trauma, or spontaneous hemorrhage (rare) meaning an advance stage of disease [1,3]. All ages (child and adults) and all sexes are equally involved. Pathophysiology is still hypothetical and new treatments are being experienced to improve the outcome of the disease like thrombopoietin agonists for instance.

The aim of this work was to report a case of Immune Thrombopenic Purpura (ITP) in a 4 years old twin girl revealed by a trauma with a brief scientific literature review.

Clinical Observation

Case history

A 4-years-old twin girl was admitted in the pediatric ward of Parakou University Hospital (PUH) for multiple bleeding: gingival bleeding and bleeding of the internal face of the cheeks, bilateral epistaxis and generalized purpura (7 days before admission), and two days after a domestic trauma (fall with forehead against metallic front door pillars). It results in a wide frontal wound on the left with an abundant bleeding and palpebral edema, persistent bleeding at different injection sites. The occurrence of hematuria was the main

admission motive. She has been admitted in the emergency room of the pediatric ward of PUH.

The history recall a previous history of febrile onset treated at home with paracetamol and also that the girl was the 2nd twin of a sibling of two. Her twin sister was in an apparent good health condition and has never bled. Their growth and psycho motor development were normal. There was no known family history of bleeding or thrombocytopenia reported. The feeding regimen at home was not specific. There was no history of known allergy notified.

Physical examination

At the general examination she shows good and healthy condition; her body temperature was at 37.5°C; her weight and height were respectively 15 kg and 101.5cm. Weight to Height index (W/H) was between -1 to 0 Z score i.e., normal; her heart rate was 140 ppm and respiratory rate at (RR) 35 cycles/min; Her arterial blood pressure was normal (BP = 9/6). She had a good hydration and there was no edema on the limbs.

Examination of the facial skin showed some large bilateral periorbital ecchymotic spots (Figure 1). Disseminated non extensive and non necrotic petechial spots were observed on the neck (Figure 2), thorax, abdomen and legs (Figure 3) resistant to vitropression. The oral cavity shows petechial spots (on the internal face of the cheeks) and oral hemorrhagic bubbles. The tongue was clean with some petechial elements and gingival bleeding was noted. A hematoma was remarkable at the internal face of the lips. Mild palmar pallor was found. Buchannan score was graded III without internal bleeding (Table 1).

Table 1: The Buchannan score grading table.

Grade	Bleeding severity	Description
0	No	No sign
1	Minor	- Skin: <100 petechial spots or <5 ecchymotic spots - (< 3 cm diameter) - normal epithelial mucosa
2	Little/less severe	- Skin: >100 petechial spots or >5 ecchymotic spots (< 3 cm diameter) - normal epithelia
3	Moderate	- Mucosal bleeding: epistaxis, oral bubles, intestinal bleeding, hematuria
4	Severe	- Mucosal bleeding needing an intervantion or internal bleeding suspected
5	Life-threatening	- Intra cranial hemorrage or life-threatening internal bleeding

Examination of the abdomen wall showed a flat non painful abdomen with no organic swelling especially no spleen enlargement and no superficial ganglionic swelling. The remaining examination was normal (no joint pain). Psychological evaluation of the girl, her twin sister and their mother's clinical state showed no instability.

Immune thrombocytopenic purpura was discussed and retained after paraclinical investigations and after having ruled out others possible diagnoses.

Paraclinical results: Blood Count showed severe microcytic and hypochromic anaemia with severe thrombocytopenia and hyperleucocytosis with neutrophilic predominance: RBC: 2.54 × 10^{12}/L; Hb 5.8 G/dL; Hte: 18%; MGV: 72.8 fL; MCCH: 31.1g/dL; TCMH 22.6 pg; Platelet Count: 36 × 10^{9}/L, WBC: 24.59 × 10^{9}/L; polynuclear neutrophils accounted for 58% and lymphocytes for 42%. No schizocytic cells were found.

The Blood clotting factors were normal (Normal Factor VIII: 58% (Normal value: 60-120%); Normal Factor IX: 92% (Normal value: 60-100%); Normal Prothrombin value (100%) and Normal TCK 32 seconds (Normal value 24-41s)).

ASLO titer was normal. Human Immunodeficiency Virus serology was negative.

The blood urea nitrogen and creatinine were normal.

Urine Dip stick showed leucocytes (+/-); Blood (+++); Urobilinogen (++); Bilirubin (+); Nitrites (-); Glucose (–); Cetone (–); urine density of 1.020 and pH 6.5.

The Addis count was 677 × 10^3 RBC/minutes (i.e., gross hematuria).

The chest X ray and brain CT scan were normal.

Therapy

She received 6 packed pockets of Red Blood Cells (RBC) and 3 pockets of Fresh Frozen Plasma (FFP), Corticotherapy through Methyl prednisolone 20 mg/kg in unique IV administration followed by Prednisone administration of 2 mg/kg/j and adjuvant treatment for 6 weeks after prophylactic deworming. After initial treatment, Prednisone degressive dose with ½ tablets every 2 weeks till complete course was done. The feeding regime after steroid therapy was made of reduced sodium daily intake till the end of hospital stay.

Evolution

Persistent gingival bleeding, ecchymotic and macroscopic hematuria after plasma transfusion, were observed showing possible blood transfusion inefficacy. With the persistency of thrombopenia, abstention from plasma transfusion and continuation of simple blood transfusion (packed red blood cells) was considered. Progressive improvement of mucosal coloration was observed with progressive disappearance of hematuria, ecchymosis and cutaneous bleeding after prednisone therapy at 2 mg/kg/once a day (Figure 4 showing platelet count and hemoglobin level trend over duration of hospital follow up). Body temperature trend remained normal in the range 36 to 37.5°C during hospital stay after admissions (Figure 5). Blood and urine biochemistry progressively became normal.

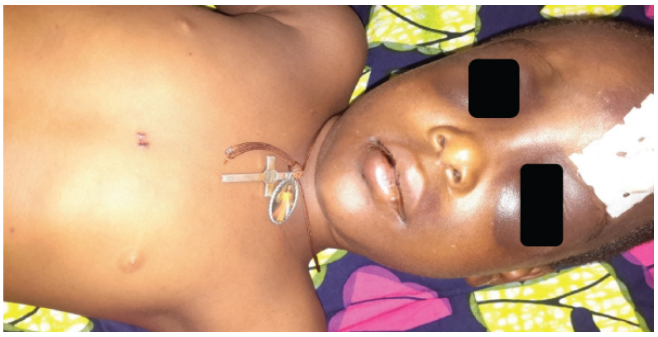

Figure 1: Large periorbital ecchymotic spots and blood clots on the lips.

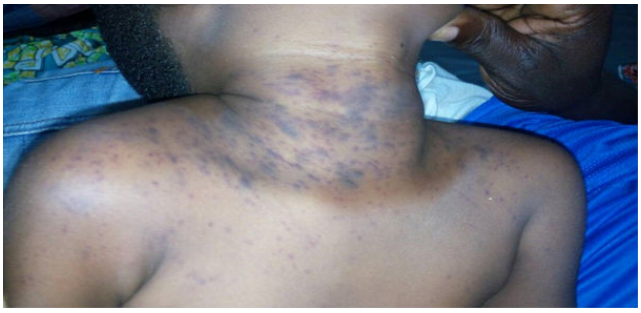

Figure 2: Numerous petechial spots on the girl's neck.

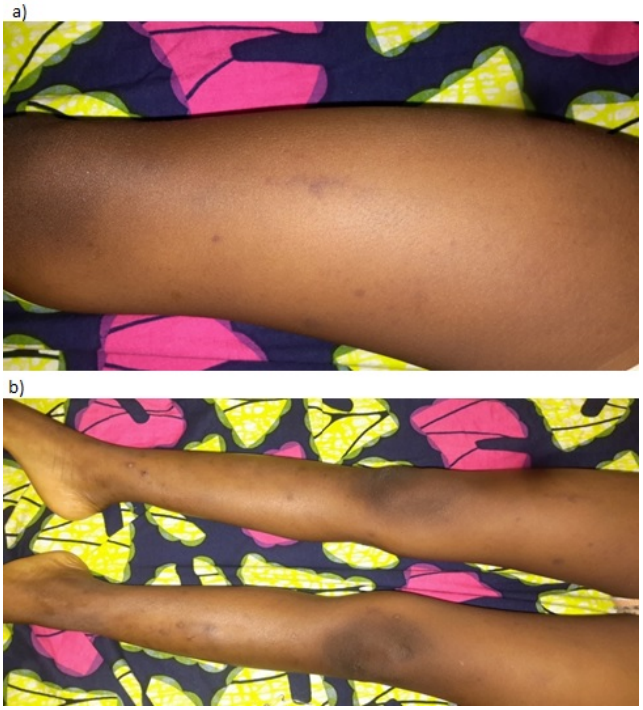

Figure 3: a) and b) Numerous petechial spots on the limbs.

Erythrocyte and platelet count were progressively normalized with healing of post-traumatic wound. Long-term corticosteroid therapy with degressive course has been introduced. Platelet count normalization occurred from the 47th day of

hospital stay, followed by 1.5 mg/kg/day Prednisone and adjuvant treatment. The patient has been seen and currently still under Prednisone (Cortancyl®) 0.5 mg/kg/day. In that situation, and in the fear of chronicity, we considered anti-D serum administration for non-accessibility of new treatments which was finally abandoned. The total follow-up was 47 days of hospital stay and nearly six months of ambulatory follow up with complete response of platelet count showing recovery.

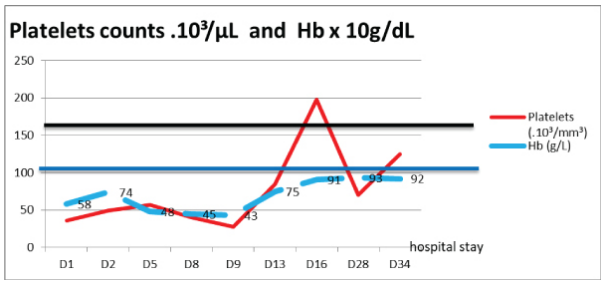

Figure 4: Evolution of Platelets counts and Hemoglobin level in function of Hospital stay.

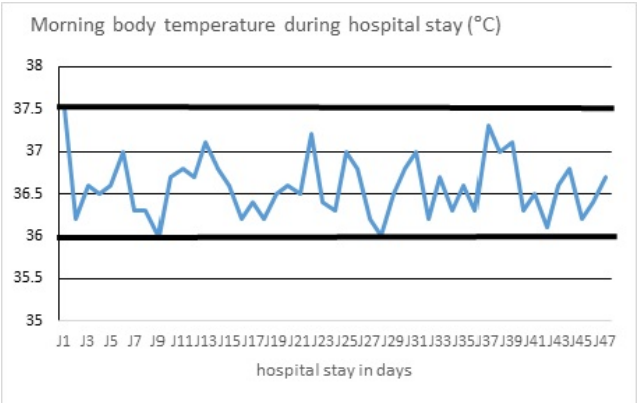

Figure 5: Daily body temperature trend (in °C) during hospital stay of the girl with suspected Persistent ITP.

Discussion

Epidemiological data

According to some authors, ITP is seen in 1 case over 10 000 in the world [1]. For some other authors ITP is seen in 2 cases over 100 000/per year [4], or 5 cases/year/100 000 population [5] classifying ITP among orphan diseases in the western world [1].

Physiopathology

ITP is an auto-immune disease meaning that the immune system is turned against its own body using its own platelets as targets. In ITP, «auto-antibodies» are produced against the immune system [6]. But some others authors define it as a muco-cutaneous hemorrhagic syndrome linked to the diminution of circulating platelet in absence of systemic auto-immune disease [3]. On the contrary, Blanchette and Bolton-Maggs explain that it is due to the loss of self-tolerance leading to the production of autoantibodies directed against platelet's antigens [7]. Glycoproteins are considered to be the platelet antigens that are inducing the synthesis of class G immunoglobulin in their plasma according to the same authors [7]. Unfortunately, it is also known that accurate detection of autoantibodies against platelet linked antigens in ITP patients is not possible in current laboratories [8] and is not clinically available in low resource settings. Thus, a negative platelet antibody result does not exclude the diagnosis.

Clinical data

The main problem in this condition is the difficulty in the diagnosis and in its management. Concerning the diagnosis, in daily pediatric practice, thrombocytopenia is often seen. Specifically, ITP is a diagnosis of exclusion [2]. Thus, in tropical Africa, there is a necessity to differentiate it with any other health conditions among which, spurious thrombocytopenia, malaria, bacterial infectious diseases, febrile purpura, hemophilia, hemolytic and uremic syndrome, acute glomerulonephritis, and even leukemia for different symptoms and signs occurring in these situations are also common to ITP.

- Spurious thrombocytopenia (false thrombocytopenia) in laboratory errors is recognized using the difference between taking blood sample in EDTA tube comparing that one in sodium citrate anticoagulant tube. In the first one there will be platelet aggregation and clumping whereas in the second situation there won't be any in most of cases [7].

- Severe Malaria was to be ruled out for low platelet count and bleeding disorders, can be seen in these conditions. However, in our context, thick blood smear or rapid diagnostic test (RDT) helped us to rule severe malaria out in that girl.

- In front of low platelet count and bleeding disorders, clinician's first reflex is to think about primary or secondary hemostasis disorders. In this

case, the primary and secondary hemostasis test (Prothrombin, TCK and Prothrombin percentage) were all normal. In addition, these bleeding disorders can mislead clinicians to think about febrile purpura in case of association of febrile onset. But the absence of typical forms of purpuric spots characterizing febrile purpura, helped us to rule out this intensive care condition in our case.

- In the situation of bleeding plus traces of bruises or ecchymosis, hematoma in the context of trauma, diagnostic misguidance is also possible. But in this situation, hemophilia has been ruled out for the patient was a girl, and her normal twin sister presents no similar events. The Factors VIII and IX explorations were also normal in the two twin sisters and platelet counts was low in the girl.

- Hemolytic and Uremic Syndrom (HUS) has been eliminated through the absence of hypertension (BP=9/6) and of renal failure (normal urea and creatinine values), absence of hemoglobinuria in the urine dip stick result and a lack of schizocytic cells in the blood smear.

- Acute glomerulonephritis has been eliminated though repeated gross hematuria (confirmed by Addis count) was present. But the normal BP, the absence of spontaneous morning facial edema, the absence of proteinuria and negative ASLO titer were important reasons helping us eliminating that condition although complement dosage (C3 and CH50) were not available in our setting. Occurrence of hematuria in ITP is considered to be a warning sign for intracranial hemorrhage (ICH) according to some authors [4]. In our case, the brain CT scan was normal.

- Constitutional thrombocytopenia was eliminated for the following reasons: The beginning of the onset was not in the earlier years of life (less than 18 months), the platelet count were less than 30×10^9 /L sometimes, there was no family history of PTI (her parents and her twin sister were not affected) [9], and at long, thrombocytopenia has slowly been corrected after corticosteroid treatment (Figure 4). In such a case the blood smear and platelet counts can help the Physician as the key to the diagnosis (diameter and aspects of platelets) [2]. In our case, we did not study the aspects and diameter of platelets.

- Finally, we have ruled out Leukemia in the absence of tumoral syndrome (no lymph node swelling, no spleen enlargement). Ecchymoses are not current in leukemia [10]. According to the 2011 American Society of Hematology ' s (ASH) evidence-based practice guideline, bone marrow examination is not necessary in children and adolescent with the typical features of ITP (grade 1B) [11]. In this specific case, bone marrow aspiration was not performed.

Her twin sister was completely normal during hospital stay and all the biological investigations done on her blood or urine samples were completely normal.

The presence of other disorders in red blood cell lines in our case can be explained by the numerous bleeding episodes encountered by the girl before and after admission leading then to anemia on admission. According to some authors, in PTI, there is no other blood lines disorder involved except that of megakaryocytic cell line on the contrary of what have been observed in this case [3,5]. Moreover, the importances of bleeding correlates inversely with platelet count (Table 1) [12]. In the same order, other hemostatic parameters were normal in our case confirming the diagnostic orientation too. Hyperleucocytosis encountered in this case can be explained by an intercurrent viral infectious onset preceding the present situation.

Concerning the difficulty in its management, multiple blood transfusions were considered with long term corticotherapy according to the American Society of Hematology [3,5], and the French Cerevance group [10,13]. Fresh frozen plasma or platelet concentrate was inefficient in our case as stated already by French authors [10]. Symptomatic treatment was one of the key points to look after. First line treatment with corticoid was the key treatment [14] to obtain complete platelet count response as stated by the 2011 ASH's evidence-based practice guideline [11].

Conclusion

PTI should systematically be evoked in front of hemorrhagic manifestations (purpura and ecchymosis) with thrombocytopenia in the absence of infectious call signs. This case was concluded as persistent ITP grade III with favorable outcome. Simple confirmation is possible in ordinary cases through blood and platelet count. Treatment through blood transfusion is sometimes necessary. Long term corticoid can also help. Recovery is

possible but treatment seems long especially in this case where we thought of persistent PTI. Clinicians especially in low resource settings should think about it in front of every suspicious case.

References

Reynaud CA, Weill JC. Rare diseases: Thrombopenic Purpura : Toward a new therapeutic approach of thrombopenic purpura? Research Foundation for Medical Research. Unity 783 Inserm – immune system developpement,Paris 2017.

HAS. National Protocol of Diagnostic and Care (PNDS): immune thrombopenic purpura in children and adult 2017.

Frikha I, Mellouli F, Dhoub N, Rehayem S, Ouederni M, Ben Khaled M, et al. Idiopathic Thrombopenic Purpura: review of 53 pediatric cases. Rev Maghr Pediatr. 2011,21(4):175-182.

Ahmed FE, Younies EH. Demographic and Clinical Charachteristics of Immune Thrombocytopenia in Sudanese Children. Int J Pediatr Neonat Care. 2016;2:117.

Godeau B. Immune thrombocytopenias: pathophysiology and treatment. Bull Acad Natle Méd. 2013;197(2):407-17.

Khellaf M, Michel M, Schaeffer A, Bierling P, Godeau B. Assessment of a therapeutic strategy for adults with severe autoimmune thrombocytopenic purpura based on a bleeding score rather than platelet count. Haematologica. 2005;90(6):829-832.

Blanchette V, Bolton-Maggs P. Childhood Immune Thrombocytopenic Purpura: Diagnosis and Management. Pediatr Clin N Am. 2008;55:393–420.

Hoffbrand AV, Moss PAH. Essential haematology. 6th edn, London. Wiley-Blackwell. 2011;p.334-337.

Boutroux H, Favier R, Héritier S, Lapillonne H, Ballerini P, Leverger G. Constitutional thrombocytopenias: From clinical features to the new inputs of genetics. J Ped Pue. 2018;31:160-7.

Aladjidi N, Santiago R, Pondarré C, Lambilliotte A, Leverger G, Godard Sebillotte C, et al. Revisiting splenectomy in chilhood Immune Thrombopenic Purpura in the era of new therapies: the french experience. J Blood Disorders Transf. 2012;S3:003.

Neunert C, Lim W, Crowther M, Cohen A, Solberg LJ, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190-4207.

Buchanan GR, Adix L. Grading of hemorrhage in children with Idiopathic Thrombopenic purpura. J Ped. 2002;141(5):683-688.

Boutroux H, Leblanc T, Courcoux M.-F, Pasquet M, Aladjidi N, Leverger G. Childhood immune thrombocytopenia. J Ped Pue. 2018;31:79-85.

Leverger G, Courcoux MF. Chronic Immune Thrombocytopenic Purpuras chroniques in Children: News et new therapeutic approaches. Réalités pédiatriques. 2013;176(1):1-5.