Journal of african clinical cases and reviews / Journal africain des cas cliniques et revues

www.jaccrafrica.com ISSN 1859-5138 Open access

Clinical case

Autoimmune thrombocytopenia refractory to prednisone during pregnancy: A case report

Thrombocytopénie auto-immune réfractaire à la prednisone pendant la grossesse : un rapport de cas

M Oumara[1], S Oumarou Garba[2], A Abdou Issa[3], A Adamou[4], H Soumana Diaouga*[5], M Nayama[5]

Abstract

Immune thrombocytopenic purpura is a rare autoimmune hemorrhagic pathology. It's association with pregnancy is also rare. The management of immune thrombocytopenic purpura in pregnancy can be a challenge in limited resource setting. We report the prenatal monitoring and delivery management of a patient with a severe form of immune thrombocytopenic purpura that became resistant to prednisone. The diagnosis was made at the 28th week of amenorrhea during a previous pregnancy. During this new pregnancy, severe biological signs appeared at 7th week of amenorrhea despite prednisone therapy. Betamethasone administered for fetal lung maturation in the 3rd trimester of the pregnancy showed in the same time a platelet count rebound which improved maternal and perinatal prognosis. This case report aims to show the interest of Betamethasone in the management of refractory immune thrombocytopenic purpura in pregnancy as an alternative therapy to prednisone with low cost and helped to minimize heavy platelet transfusions and gamma globulin in the peripartum period.

Keywords: Immune thrombocytopenic purpura, pregnancy, Betamethasone, Niger.

Résumé

Le purpura thrombocytopénique immunitaire est une pathologie hémorragique auto-immune rare. Son association avec la grossesse est également rare. La prise en charge du purpura thrombocytopénique immunitaire pendant la grossesse peut constituer un défi dans un contexte de ressources limitées. Nous rapportons le suivi prénatal et la prise en charge de l'accouchement d'une patiente présentant une forme sévère de purpura thrombopénique immunologique devenu résistant à la prednisone. Le diagnostic a été posé à la 28ème semaine d'aménorrhée lors d'une précédente grossesse. Lors de cette nouvelle grossesse, des signes biologiques sévères sont apparus à la 7ème semaine d'aménorrhée malgré un traitement par prednisone. La bétaméthasone administrée pour la maturation pulmonaire fœtale au 3ème trimestre de la grossesse a montré dans le même temps un rebond de la numération plaquettaire qui a amélioré le pronostic maternel et périnatal. Ce rapport de cas vise à montrer l'intérêt de la bétaméthasone dans la prise en charge du purpura thrombocytopénique immunitaire réfractaire pendant la grossesse comme thérapie alternative à la prednisone à faible coût et a permis de minimiser les transfusions lourdes de plaquettes et de gamma

globuline en période péripartum.

Mots-clés : Purpura thrombocytopénique immunitaire, grossesse, Bétaméthasone, Niger.

Introduction

Immune thrombocytopenic purpura (ITP) is a rare autoimmune hemorrhagic pathology defined by an isolated platelet count below 150,000 elements/mm3. The incidence varies from 2 to 6.1 per 100,000 adults per year [1,2,3]. The association of ITP and pregnancy is also very rare. The pathophysiology involves an immunological mechanism which combines peripheral destruction of platelets and inappropriate bone marrow production [2]. For decades, knowledge of the pathophysiology of ITP was limited to the concept of increased destruction of platelets in the reticuloendothelial system, resulting from the presence of autoantibodies directed against platelets [2,3]. The main cause of immunologic thrombocytopenia is immunologic thrombocytopenic purpura [2]. ITP is most often asymptomatic but could be revealed or aggravated by pregnancy. When ITP is discovered during pregnancy, it then poses the differential diagnosis with gestational thrombocytopenia. It is a relatively benign pathology, however, with a risk of neonatal thrombocytopenia and rare serious hemorrhagic complications in mother and child [4,5]. The aim of treatment, based mainly on prednisone, is to reduce platelet destruction while avoiding any unnecessary and potentially harmful escalation of therapy [3,6,7]. Thrombopoietin receptor agonists (Romiplostim, Eltrombopag and Avatrombopag), Rituximab (anti-CD20 monoclonal antibody reducing the production of anti-platelet antibodies by lymphocytes), Cyclosporine or Azathioprine have considerably modified the treatment of ITP. Response rates of 80 to 90% are consistently achieved and generally maintained with continued treatment [3]. We report a case of ITP during pregnancy in a 37-year-old patient treated in our hospital. The aim of this report was to show the possibility of treatment that would minimize heavy platelet transfusions and gamma globulin infusions. We also describe the particularities of our patient's care.

Clinical case

It was a 37 years old woman, who was in her second pregnancy, and she's mother of one living child. She was referred by her hematologist to our National Reference Hospital for pregnancy care. In her history, petechias appearance is noted in her previous pregnancy at 28 weeks amenorrhea associated to severe thrombocytopenia at 6,000 elements/mm3. The etiological assessment carried out (hemogram, myelogram, DIC assessment and infectious assessment) concluded to an ITP. She was treated by Prednisone 30 mg/d until 38 weeks where cesarean section was performed for stagnation in active stage of labor on May 25, 2018 with a well alive child. She was transfused with two concentrated platelet bags during the procedure. In Postpartum, she was followed for long-term on prednisolone 30 mg/day with regular monitoring of the platelet count. Controls checks of platelets showed a stable level between 35,000 and 50,000 elements /mm3, which prompted the cessation of corticosteroid therapy. In June 2022 the patient was readmitted in the first trimester of pregnancy to our department to prenatal care of a new pregnancy. On admission, the patient was in good general condition. The conjunctiva and mucous were normally colored. The skin and appendages were clinically normal. The gynecological examination was normal. The ultrasound noted 7 weeks intrauterine evolutive pregnancy. Hemogram showed severe thrombopenia with platelet count of 18,000 cells/mm3. Other assessment was normal. On the advice of the hematologist, she was carried over on prednisone 30 mg/day but the platelet count remained below 20,000 elements/mm3 until the 28th week. It was at this term of pregnancy that petechiae appeared, leading to 4 bags of concentrated platelet transfusion. The platelet counts control then rose to 76,000 elements/mm3. At 33 weeks of gestation, tocolysis and corticosteroid therapy (Betamethasone 12 mg, renewed 24 hours

later intramuscularly) aimed for acceleration of fetal lung maturation was done in a context of premature threat delivery. The hemogram check 24 hours later showed a platelet count of 165,000 elements/mm3. This level dropped to 89,000 elements/mm3 at 36 weeks and 41,000 elements/mm3 at 37 weeks. In view of this refractory thrombocytopenia, a cesarean section was scheduled at the 38th week because of scarred uterus and hemorrhage risk. The multidisciplinary staff (Gynecologist, Anesthetist, Internist and Hematologist) decided to reconduct a new course of betamethasone (12 mg, renewed 24 hours later) before delivery, hoping for an increase in the maternal platelet level. The check-up on the day of the cesarean section showed a platelet level of 179,000 elements/mm3. Four concentrated platelet bags were available in precaution. The cesarean section was performed without platelet transfusion. She received 1g of tranexamic acid during procedure. The postoperative course was simple. The platelet count on postoperative day2 was 117,000 elements/mm3 and then 68,000 elements/mm3 two weeks later. The newborn had a good clinical condition and a platelet level of 192,000 elements/mm3. The patient and her newborn left the maternity on day7 postoperative with a favorable outcome. Subsequent long-term follow-up was provided by a hematologist. During the first 30 days after birth, the newborn did not present any hemorrhagic diseases. At 8 weeks postpartum, the maternal platelet level had dropped to 25,000 elements/mm3 without associated clinical signs (without petechia). A dose of betamethasone (12 mg IM, renewed 24h later) was carried out again, which raised the platelet count to 182,000 elements/mm3. The patient was satisfied with this treatment.

Discussion

This observation reports the clinical and biological illustrations of a severe form of ITP during pregnancy. Because of absence of a satisfactory therapeutic response to prednisone, the administration of betamethasone in a short 48-hour course showed a spectacular improvement in the platelet count and clinical signs of the disease over the long term. The association of pregnancy and ITP is an uncommon situation. Pregnancy can reveal asymptomatic ITP or aggravate acute attacks of previously well compensated ITP. In our observation, pregnancy was the circumstance of discovery and diagnosis at the 28th week. Also, the acute outbreak of the disease revealing the lack of response to prednisolone also occurred during the second pregnancy at the same term. Therefore, the term of 28 weeks would be a critical period in the monitoring of ITP during pregnancy. Clinically, the revealing symptoms before or during pregnancy consist of bruising, gingival bleeding, fever and sometimes splenomegaly. However, ITP is very often asymptomatic [8]. The diagnosis is made in half of the patients during pregnancy [8] as is the case in our observation. Therapeutically, most authors recommend treatment regardless of clinical signs or other factors as soon as the platelet count is below 20 to 30,000 elements/mm3 [3]. During pregnancy, prednisone or prednisolone are usually used at a dose of 1 mg/Kg/day and followed by a rapid reduction in doses in stages in order to maintain a platelet count of 20 to 30,000 elements/mm3. Thus, intra venous Immunoglobulins are an alternative to high doses of steroids, particularly at the end of pregnancy. However, the availability and high cost of these drugs limits their use in our context. Rituximab, an anti-CD20 monoclonal antibody, which reduces the production of anti-platelet antibodies by lymphocytes, is an integral part of the second- or third-line recommendations in all current guidelines outside of pregnancy. However, rituximab is only recommended very cautiously in pregnant women. Cyclosporine and Azathioprine can be used if the benefit for the mother justifies it [3]. For some authors, splenectomy may be indicated in cases of severe thrombocytopenia and bleeding in refractory cases [7,8].

Betamethasone, in addition to being widely used during pregnancy to accelerate fetal lung maturation, represents an interesting alternative in the management of ITP in pregnant women or even outside pregnancy

[6]. It's use in this context allowed us to discover a good response to thrombocytopenia even though prednisone at a dose of 30 mg/24 hours had not been able to slow down the decline in the platelet count in our patient. It is to highlight that dose equivalence between these drugs is about 1 mg prednisone (with intermediate duration of action) for 0,15 mg betamethasone (with long duration of action). Also, taking these drugs in the prenatal period may cross the placental barrier and lead to birth defects in the fetus [9]. One such medication is corticosteroids, which may increase the risk of orofacial clefts and genitourinary anomalies [10]. However, it was found that the newborn of the current case was free of these birth defects probably due to its administration in the third trimester. Otherwise, the short-term use of corticosteroids antepartum for the prevention of respiratory distress syndrome does not seem to pose a risk to the fetus or newborn infant [11]. In our case, the short course of betamethasone allows the patient to avoid the harmful effects of prolonged corticosteroid therapy during pregnancy. However, more in-depth studies on large samples are necessary to determine an effective threshold dose and the optimal duration between two courses for long-term management of IPT during or outside pregnancy. From an obstetrical point of view, the mode of delivery depends on the platelet level at the end of pregnancy. Values above 50,000 are required for vaginal delivery and 70 to 80,000 elements/mm3 for cesarean section [3]. In our observation the platelets were at 179,000 elements/mm3, cesarean section was indicated to minimize the risk in scarred uterus during labor. The prognosis for ITP is generally good during pregnancy. However, there is a risk of severe postpartum hemorrhage between 8 and 21% [8]. Outcome was simple in our case. Hemorrhagic disease and thrombocytopenia are expected complications in the newborn. In fact, ⅓ of newborns have thrombocytopenia with values lower than 100,000 elements/mm3 and approximately half of them have values lower than 50,000 elements/mm3 [2,8]. These complications were not observed in the newborn in our case.

At 8 weeks postoperative, the maternal platelet level had dropped to 25,000 elements/mm3 but without associated clinical signs (without petechia). A course of betamethasone (12 mg IM, renewed 24h later) was again carried out, which raised platelet count to 182,000 elements/mm3.

Conclusion

Pregnancy associated to IPT is rare. Management requires close collaboration between obstetrician, hematologist, and neonatologist. Betamethasone commonly used for fetal indications could help with a rebound in platelet counts in certain cases of resistance to usual corticosteroids in the management of ITP when the availability and high cost of new drugs remain to be a barrier to ITP care as in our country.

Consent

Consent was obtained from the patient for publication of this case report.

***Correspondence**

Soumana Diaouga Hamidou

hamidousoumana21@gmail.com

Available online : August 27, 2024

1 : Abdou Moumouni University, Department of Obstetrics and Gynecology, General Reference Hospital in Niamey, Niger
2 : André Salifou University, Department of Obstetrics and Gynecology, Zinder, Niger
3 : Dan Dicko Dankoulodo University, Department of Obstetrics and Gynecology, Maradi, Niger
4 : Abdou Moumouni University, Department of Anesthesia, Isska Gazoby Maternity in Niamey, Niger
5 : Abdou Moumouni University, Department

of Obstetrics and Gynecology, Isska Gazoby Maternity, Niger

Conflict interest : None

References

[1] Benachi A, Luton D, Mandelbrot L, et al. Pathologies maternelles et grossesse. In: Elsevier Masson; 2022. p. 358-366.

[2] Khellaf M, Godeau B. Thrombopénies immunologiques. In: Maladies rares en médecine d'urgence. Références en médecine d'urgence. Collection de la SFMU. Paris: Springer; 2013.

[3] Matzdorff A, Alesci SR, Gebhart J, et al. Experten report Immunthrombozytopenie – Aktuelle Diagnostik und Therapie. Oncol Res Treat. 2023;46(1):7-56.

[4] Kuter DJ. The treatment of immune thrombocytopenia (ITP) - focus on thrombopoietin receptor agonists. Ann Blood. 2021;6.

[5] Lambert C. Actualités dans la prise en charge du purpura thrombocytopénique immun primaire de l'adulte. Louvain Med. 2021;140:437-443.

[6] Song F, Al-Samkari H. Management of adult patients with immune thrombocytopenia (ITP): a review on current guidance and experience from clinical practice. J Blood Med. 2021;12:653-664.

[7] Sailer T, Lechner K, Panzer S, et al. The course of severe autoimmune thrombocytopenia in patients not undergoing splenectomy. Haematologica. 2006;91(8):1041-1045.

[8] Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology. Guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866.

[9] Hegazy A. Clinical embryology for medical students and postgraduate doctors. Saarbrücken: LAP Lambert Academic Publishing; 2014.

[10] Thalluri V, Woodman RJ, Vollenhoven B, Tremellen K, Zander-Fox D. Exposure to corticosteroids in the first trimester is associated with an increased risk of urogenital congenital anomalies. Hum Reprod. 2022;37(9):2167-2174. doi: 10.1093/humrep/deac142.

[11] Horizon Therapeutics USA Inc. Product Information: Rayos (prednisone). 2016.

To cite this article :

M Oumara, S Oumarou Garba, A Abdou Issa, A Adamou, H Soumana Diaouga, M Nayama. Autoimmune thrombocytopenia refractory to prednisone during pregnancy: A case report. Jaccr Africa 2024; 8(3): 206-210
https://doi.org/10.70065/24JA83.010L012708