Case Report

Rash. What Lies Beneath.
A Case Report on Polyarteritis Nodosa in Pregnancy

Joan Chavez, * Nerissa Gracia Nano-De Guzman
Department of Obstetrics and Gynecology, The Medical City, Ortigas Avenue, Pasig City
*Contact Details: joan.chavez@gmail.com

ABSTRACT: Polyarteritis nodosa is a rare form of vasculitis affecting single and medium arteries in about 2 to 3 persons in a million. The initial presentation is usually nonspecific, and due to the rarity of the condition is not always recognized. Rashes in pregnancy are often dismissed and the diagnosis of vasculitisis rarely considered. There is a need to systemically identify or rule out this rare condition as timely and appropriate interventions can significantly affect the pregnancy. We present a case of a 40-year-old multigravid diagnosed with polyarteritis nodosa who presented with progressive rashes on bilateral lower extremities during her 2nd trimester of pregnancy. We describe the history and physical examination findings of a pregnant patient with vasculitis and discuss the diagnostic approach to vasculitis in pregnancy.
Keywords: *PAN, panniculitis, polyarteritis nodosa, rash, vasculitis*

INTRODUCTION

Rash is a broad term for any change in appearance, color, or texture of the skin. Pregnancy, as a hormone-dependent state brings about a multitude of physiologic changes and exacerbates underlying pathologic disorders that bring out rashes. Vasculitis is the inflammation of systemic vasculature causing reactive damage to mural structures leading to loss of vessel integrity and compromise of the lumen resulting to downstream tissue ischemia and necrosis.[1] Its effects may be self-limiting or catastrophic, depending on the vasculature affected, the initial manifestation may be nonspecific and as innocuous as a rash.

CASE

Patient is a 40-year-old Gravida 4 Para 3 (3-0-0-2), 34 1/7 weeks age of gestation, who came in for rashes on extremities. She had an unremarkable antenatal history, with regular prenatal check-ups. At 18 weeks age of gestation, approximately 4 months prior, patient noted gradual-onset of multiple painful macular erythematous lesions on bilateral lower extremities, concentrated around the ankle,. There was easy bruisability with no other associated signs and symptoms. Persistence of symptoms prompted consult, and patient was advised observation.

At 28 weeks age of gestation, the patient noted progression of lesions, now affecting bilateral lower extremities, up to her thighs (Figure 1). She described severe joint pains on her ankles and knees affecting ambulation, which prompted consult. Upon physical examination, patient was noted to have multiple hyperpigmented nontender, movable nodules about 0.5 to 1 cm in diameter on bilateral lower extremities (Figure 2). There were no sensory or motor deficits and systemic exam was essentially unremarkable. Abdominal exam showed a nontender gravid abdomen with a fundic height of 30 cm, with good fetal heart tones and movement. At the time, patient denied any obstetric symptoms, no perceived uterine contractions, or watery or bloody vaginal discharge.

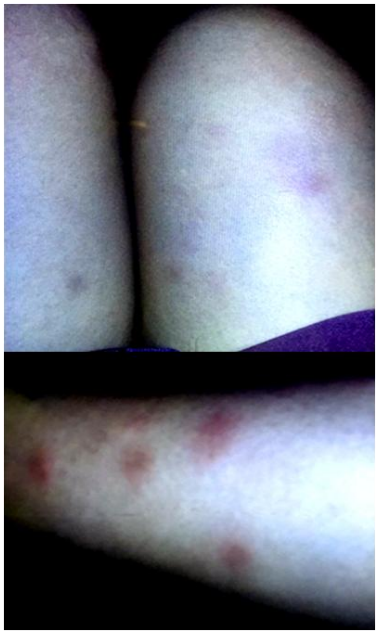

Figure 1. At 28 weeks age of gestation, erythematous, maculopapular lesions affecting bilateral lower extremities (up to the thighs)

The progressive development of the patient's symptoms warranted further assessment and the patient was admitted for work-up and fetomaternal surveillance. Fetal monitoring with daily non-stress tests revealed reactive tracings with no uterine contractions. The biophysical profile score was 8/8 with no signs of intrauterine fetal growth restriction. Maternal doppler studies revealed findings suggestive of the development of maternal hypertension in the future, but no current fetal compromise. Betamethasone was given for fetal lung maturity in the event that expeditious delivery was necessary.

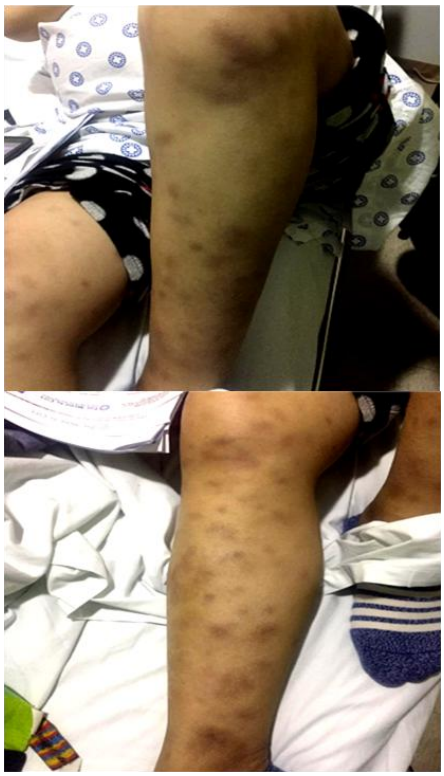

Figure 2. At 32 weeks age of gestation, multiple erythematous to hyper pigmented nontender, movable nodules about 0.5-1 cm in diameter on bilateral lower extremities

Given the patient's presentation, she was referred to Hematology and Rheumatology services for co-management. Initial work-up was done revealing unremarkable liver and kidney function tests with normal bleeding parameters and no underlying coagulopathies.

Further assessment of the patient's rash revealed non-specific areas of erythema with multiple tender hyperpigmented nodules. Palpation revealed deep-seated nodules characteristic of an inflammatory process located beneath the dermis; hence a form of panniculitis was entertained[2]. Despite a normal initial work-up, the patient's symptoms progressed during the course of the admission. The nodules on bilateral lower extremities became tender to touch, with difficulty in ambulation due to the pain.

Further work-up was then warranted to rule out an underlying systemic illness. Tumor markers were negative. Due to the cutaneous manifestations, the apparent lack of internal organ involvement, and the elevated ESR, the working impression was erythema nodosum. To confirm this, she was referred to Dermatology for a biopsy of a nodule on the left thigh. Patient was started on low-dose Prednisone which immediately resulted in improvement of pain and tenderness. Patient was sent home stable awaiting biopsy results, which later revealed medium sized polyarteritis nodosa. She was advised to continue Prednisone therapy with careful monitoring of symptoms. Perinatology planned to monitor the pregnancy via sonography and NST twice a week until delivery at term.

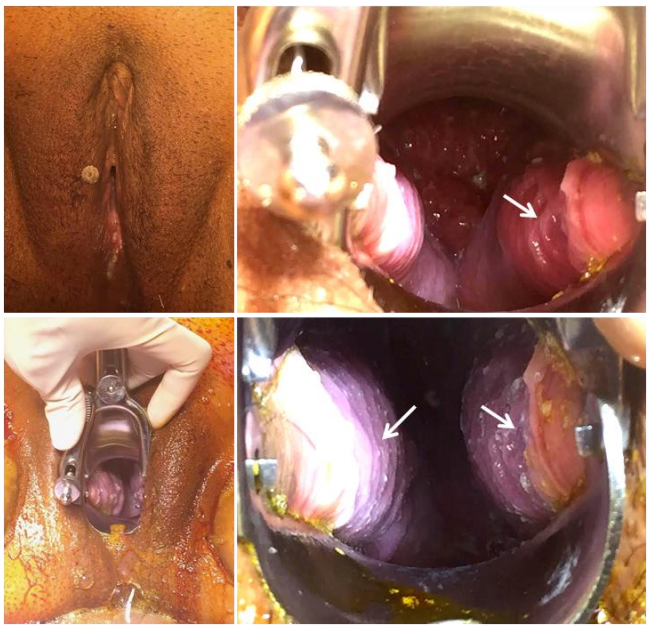

Figure 3. At 34 weeks age of gestation, active Condyloma Acuminata (arrows) along the cervical and vaginal canal

At 36 weeks age of gestation, patient was re-admitted for labor pains with gross blood in her urine. Internal exam revealed 1 cm dilatation of the cervical os, with note of erythematous papillary outgrowths on her cervix and vulvar areas aggregately measuring >2 cm (Figure 3),. Further work-up was done to differentiate systemic vs cutaneous polyarteritis nodosa. Patient's repeat urinalysis revealed microscopic hematuria despite little cervical change pointing to the possibility of renal involvement. In the background of preterm labor with at least 48 hours of steroid therapy for fetal lung maturity, the decision to expedite the delivery was made. Patient underwent primary cesarean

section with bilateral partial fimbriectomy and electrocautery of warts under spinal anesthesia. Post-operatively, patient tolerated the procedure well. She delivered a live preterm, baby girl at 2853 grams, 36 weeks appropriate for gestational age with no signs and symptoms of vasculitis or cutaneous lesions. Post-operatively, the immunosuppressive therapy was continued with a decrease in number of cutaneous lesions and improvement of joint pains.

DISCUSSION

The patient presented with cutaneous lesions on the lower extremities. In a hormone driven state such as pregnancy, rashes are often manifestations of physiologic changes that come with pregnancy. The most common benign rash in pregnancy is pruritic urticarial papules and plaques of pregnancy (PUPP), which is managed conservatively. PUPP rash often manifests in the extremities but is always associated with abdominal involvement, which our patient did not have. Further assessment of the patient's 6-week rash also revealed non-pruritic hyperpigmented tender nodules unlike the characteristic plaques and papules seen in PUPP. The characteristics of the lesions, the progressive course of the disease entity and the development of associated signs and symptoms such as arthralgia, joint pains, and gross hematuria were more consistent with a systemic disease, such as vasculitis.

Vasculitis, especially in pregnancy, presents several diagnostic challenges. The clinical presentation often involves bilateral lesions on the lower extremities, which could be from an isolated cutaneous vasculitis or a clue to multisystem involvement. A rational approach is required in patients with suspected vasculitis[3]. An article published in the British Medical Journal suggests a systematic approach to the diagnosis of vasculitis by answering these 4 questions: Is this a condition that could mimic the presentation of vasculitis? Is there a secondary underlying cause? What is the extent of vasculitis? What specific type of vasculitis is this?

Several conditions such as infection, coagulopathies, and other inflammatory conditions such as Antiphospholipid Antibody Syndrome (APAS) mimic the presentation of vasculitis. The need to identify and rule out these disease entities is important as they warrant a different approach[4]. Infections such as hepatitis B and C, are closely related to PAN and prognosis is significantly worse than non-HBV related PAN[5]. Our patient's hepatitis screening was unremarkable. Vasculitis is seldom the initial presenting manifestation in the setting of rheumatoid arthritis or systemic lupus erythematosus making these less likely[6]. Drug exposure, a common secondary cause of vasculitis[7]was not elicited in this patient.

After thoroughly ruling out other disease entities, there is a need to confirm the diagnosis polyarteritis nodosa (PAN), and assess its extent, as systemic involvement may call for more aggressive management. Confirmation of PAN is often done via biopsy of active lesions. In general, biopsy of a relatively new vasculitic lesion is most likely to show representative histologic changes[8]. These include fibrinoid necrosis of a medium-sized muscular artery in the deep dermis with disruption of the internal elastic lamina, neutrophilic inflammation, and leukocytoclasis as seen in our patient (Figure. 4). Our patient's work-up did not show systemic involvement and her PAN appeared limited to the cutaneous form. She responded well to Prednisone therapy and delivered a preterm baby girl via cesarean section with no complications. Post-operatively, the plan was to continue immunosuppressive therapy for 6 months to control symptoms.

Polyarteritis nodosa is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries, with occasional involvement of small muscular arteries[9-10]. In the Philippines, data regarding PAN in pregnancy is very limited. As such, the specific effect of PAN in pregnancy and vice versa has only been studied in a small number of cases. It appears pregnancy does not have an effect on PAN nor does it cause progression. However, patients diagnosed with PAN late in pregnancy appear to have high maternal morbidity or mortality from complications of systemic involvement such as renal failure, gastrointestinal hemorrhage, and respiratory failure. Specific prognostic factors identified in surviving patients with PAN, followed up to 6 years, include heavy proteinuria, high serum creatinine, cardiomyopathy and gastrointestinal or neurological involvement[11]. Our patient's initial presentation was limited to cutaneous PAN but there was concern for possible progression to systemic PAN given her hematuria, which consequently led to the decision to expedite the delivery. There are case reports which have identified the development of cutaneous PAN in the fetus either at birth or neonatally. Our patient delivered a live preterm baby girl with no signs of cutaneous or systemic vasculitis, who was immediately roomed-in after delivery and sent home stable with her mother.

CONCLUSION

Polyarteritis nodosa in pregnancy is an underdiagnosed and under-reported phenomenon. Early recognition of a disease flare and differentiation from other disease entities in a pregnant patient can positively affect the pregnancy course and outcomes. A systemic diagnostic approach is necessary to allow for prompt identification and management of PAN. These patients are best cared for in a multidisciplinary setting, with access to specialized care. The cornerstone in the management of PAN during pregnancy is the use of corticosteroids. Its use has to be monitored thoroughly to avoid drug toxicity on both the mother and the growing fetus.

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