A vasculitis mimic during pregnancy: autoimmune progesterone dermatitis

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**Key message:** Autoimmune progesterone dermatitis during pregnancy can present as a vasculitis mimic.

Dear Editor,

A 41-year-old pregnant woman following assisted conception was reviewed at 10 weeks of gestation in the combined Obstetric and Rheumatology clinic with a history of Eosinophilic Granulomatosis with Polyangiitis (EGPA) and two previous miscarriages in the first trimester. Her vasculitis was well-controlled with a baseline daily dose of Prednisolone 7.5mg. Previous EGPA symptoms included asthma, purpuric rash, and nasal bleeding. Following the ESHRE (European Society of Human Reproduction and Embryology) guideline, the In Vitro Fertilization (IVF) team started her on vaginal progesterone (micronised progesterone 400mg pessaries) twice daily for luteal phase support after IVF. Progesterone is usually continued at least until the day of the pregnancy test, but in this case progesterone was continued even further because of vaginal bleeding. The patient was also commenced on routine pregnancy supplements. She was allergic to aspirin.

During her second review at 16 weeks, she complained about an intermittent, widespread pruritic rash for the last 3 weeks. She had already been seen by her GP who prescribed her emollients without any improvement. On examination, the active lesions looked urticarial and were tender (fig 1). There was also residual hyperpigmentation. The lesions persisted for 48-72 hours before spontaneous resolution. Cutaneous vasculitis rather than urticaria was suspected based on the duration of the rash for more than 24 hours, the hyperpigmentation, tenderness, and the history of EGPA. Otherwise, she was well in herself with no symptoms of active vasculitis and no recent infections. Prednisolone increased to 15mg daily and loratidine was given for the pruritus. Her repeat blood tests were reassuring with normal eosinophil count (<0.1 x 10^9/L) negative ANCA (Antineutrophil Cytoplasmic Antibodies), normal C3 and C4, CRP (C-reactive protein), and eGFR (estimated glomerular filtration rate). Urine dipstick was negative for proteinuria and haematuria.

She was seen again at 19 weeks with persistent rash despite the higher dose of steroids. During this review, the patient reported that the rash is worse in the morning and at night. Autoimmune progesterone dermatitis (APD) was suspected at that point. Urticarial or EGPA vasculitis would have improved with steroids. Further, there were not any symptoms suggestive of systemic vasculitis and the relevant blood
tests were normal (eosinophil count, complement, ANCA, CRP). Of note, the rash was worse in the morning and at night which corresponded to the time of vaginal exposure to progesterone. The patient stopped the progesterone pessaries after discussion with the obstetrician about the pros and cons of withdrawing treatment. The rash improved gradually and resolved in five days, confirming the diagnosis of APD. The rash did not reappear during the pregnancy; therefore, the patient was not referred to dermatology to consider skin biopsy or skin prick testing.

In summary, a 41-year-old pregnant lady with a history of vasculitis presented initially to her GP and then to the combined Obstetric & Rheumatology clinic with urticarial lesions. The disease trajectory suggests that the pruritic rash was caused by APD induced by vaginal exposure to progesterone. The rash could have been mistaken for urticaria or vasculitis. Consequently, the patient may have had antihistamines and increment of glucocorticoids dose during her pregnancy, the latter which could increase risk of gestational diabetes and other toxicities were avoided.

APD is a rare autoimmune hypersensitivity reaction to endogenous or exogenous progesterone. APD varies greatly from patient to patient and can present as urticaria, eczema or vesiculobullous eruptions. It usually develops in the luteal phase of the menstrual cycle with spontaneous resolution after menstruation due to endogenous fluctuation of progesterone. Confirmatory tests, such as skin prick testing with progesterone can be considered. APD following vaginal progesterone exposure in pregnancy is much rarer. In our case, withdrawal of progesterone confirmed the clinical suspicion of APD. In APD caused by vaginal progesterone, treatments, such as corticosteroids and antihistamines, frequently fail to provide any relief, as illustrated also in our case. Cutaneous lesions resolve a few days after suspension of the progesterone pessaries; therefore, the clinical suspicion of APD during pregnancy is paramount. In November 2021, the National Institute for Health and Care Excellence (NICE) recommended vaginal progesterone in women who experience bleeding in early pregnancy and have a history of miscarriage as it slightly reduces the risk of a further miscarriage. The new guidelines suggest that more pregnant women with miscarriages will use topical progesterone during pregnancy and given the association between active rheumatic disease and poor pregnancy outcomes, we may see APD more frequently in our rheumatology practice.
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References
Fig 1. Urticarial lesion on patient's left arm proved to be autoimmune progesterone dermatitis