CASE REPORT

Granuloma Gravidarum on the Post-Excisional Scar for an Atypical Melanocytic Lesion During Pregnancy
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Abstract

Introduction: Granuloma gravidarum represents a rare lesion, defined as a reactive vascular hyperplasia of pregnancy, that affects mainly the oral mucosa. Very few cases were reported on non-mucous sites. Case presentation: We present the case of a 32-year-old, 18 weeks pregnant patient, that developed a granuloma gravidarum on the excision scar of a volar atypical melanocytic lesion. She presented to the dermatology department with a recently developed melanocytic lesion on her left heel. Dermoscopy showed asymmetry and brown globules in a ring pattern. The lesion was excised with 5 mm margins, under local anesthesia and sedation. The path report and immunohistology revealed a dysplastic melanocytic acral nevus. The excision site closed nicely, but after 5 days a red friable 0,5 cm vascular bleeding tumor developed in one extremity of the scar. Patient refused biopsy. The new tumor raised diagnostic difficulties between a vascular lesion and an amelanotic recurrence of the melanocytic lesion. Due to the path report which showed a benign pigmented lesion and because the lesion was excised completely, granuloma gravidarum was suspected. Patient received local antibiotic treatment and the vascular lesion involuted completely after 3.5 weeks. Conclusion: Pregnant women are at high risk of developing vascular tumors at trauma sites, due to hormonal changes. It’s important to be aware of this surgery complication in pregnant patients, as evolution is usually benign and complete spontaneous resolution is possible.

Keywords: granuloma gravidarum, dysplastic nevus, pregnancy, dermatology, surgery, surgical complications.

Rezumat

Introducere: Granuloma gravidarum este o hiperplazie vasculară reactivă ce apare în sarcină, de obicei la nivelul mucoasei orale, existând doar rare cazuri raportate cu alte localizări. Prezentare de caz: Pacientă în vârstă de 32 de ani, gravidă în 18 săptămâni, s-a prezentat în clinica de dermatologie pentru o leziune melanocitică recent apărută la nivel calcanean stâng. Dermatoscopia leziunii a arătat elemente de apel, precum globule periferice circumferenţiale și asimetrie. Leziunea melanocitică a fost excizată cu margini de siguranţă de 5 mm, sub anestezie locală și analgesie. Examenul histopatologic și imunohistochimia au confirmat un nev displazic acral. La 5 zile după excizie, într-una din extremitățile cicatricii postoperatorii s-a dezvoltat o tumoară vasculară friabilă, sângerândă, de 0,5 cm. Pacienta a refuzat biopsia. Tumora a pus probleme de diagnostic între o formă vasculară și o leziune melanocitică acromică recurrentă. Având în vedere că examenul histopatologic al leziunii excizate a fost benign, iar excizia completă, s-a suspectat diagnosticul de granuloma gravidarum. Pacienta a efectuat tratament local antibiotic, iar leziunea vasculară a involut complet în 3,5 săptămâni. Concluzie: Pacientele grăvite sunt la risc să dezvolte proliferări vasculare care răspund la traume locale. Este important de avut în vedere această complicație postchirurgicală la gravidă, întrucât, deși clinic poate ridica numeroase suspiciuni, evoluția este de obicei benignă, iar remisuirea spontană posibilă.

Cuvinte cheie: granuloma gravidarum, nev displazic, sarcină, dermatologie, excizie, complicații post-chirurgicale.
that presented to the dermatology department, in January 2019, for the evaluation of a melanocytic lesion on her left heel. The patient observed this lesion during pregnancy and noted rapid growth and change in appearance. She had been monitored for atypical mole syndrome (AMS) (Figure 1), but was lost for follow-up for the last year and a half. During this time, she was diagnosed with unexplained infertility and underwent numerous fertility treatments, including 3 in vitro fertilizations, the last of which resulted in her pregnancy. There were no other notable comorbidities in her history.

Upon clinical examination, a small 0.3 mm melanocytic lesion was observed on her left foot, on the lateral aspect of the heel, homogeneously black, asymmetrical and with irregular borders. Dermoscopy showed asymmetry, brown globules both on the surface of the lesion and in a peripheral ring pattern and a dark black-blue homogenous central area (Figure 2). The clinical evaluation, dermoscopy and evolution of the lesion were highly suspicious of an atypical melanocytic lesion, a Reed/Spitz nevus or even an early melanoma. All other melanocytic lesions that had been followed up in the past were without changes.

Taking in account the rapid evolution and the risk of melanoma in pregnancy7, the lesion was excised with 5 mm margin, under local anesthesia and monitored anesthetic care (sedation). The surgical defect was closed per primam with intradermal and skin resorbable sutures. The path report revealed a dysplastic acral melanocytic nevus, excised completely, with free margins (Figure 3) Immunohistochemical stains were performed

### INTRODUCTION

*Granuloma gravidarum* (GG) represents a benign reactive proliferation of capillary blood vessels that affects about 5% of pregnancies and it is also known as *epulis gravidarum* or pregnancy tumor1,2. It is indistinguishable on clinical or histopathological grounds from pyogenic granuloma (PG) developed outside of pregnancy. Pyogenic granuloma is a misnomer, as it is neither infectious, nor granulomatous. Both represent an endothelial proliferation, usually developed on minor trauma sites. The lesions are composed of highly proliferative vascular tissue, with vascular channels bordered by endothelial cells, engorged with erythrocytes. There is a mixed inflammatory infiltrate of neutrophils, plasmocytic cells and lymphocytes. The epithelium is spared, but can be ulcerated or thickened at the periphery of the lesion3.

Clinically, *granuloma gravidarum* is a smooth or lobulated exophytic lesion, that bleeds easily. It can grow slowly or evolve rapidly. It’s non-neoplastic in nature, but can recur after treatment. Also, depending on its localization, it can cause important functional or cosmetic impairment and cancer-related anxiety4. Maybe one of the most important clinical implications of GG is that it can mimic more severe diagnosis, like amelanotic melanoma, basal or squamous cell carcinoma, or skin metastasis5,6.

### CASE PRESENTATION

We present the case of a 32-year-old female patient, 18 weeks pregnant (first pregnancy) with twin pregnancy, that presented to the dermatology department, in January 2019, for the evaluation of a melanocytic lesion on her left heel. The patient observed this lesion during pregnancy and noted rapid growth and change in appearance. She had been monitored for atypical mole syndrome (AMS) (Figure 1), but was lost for follow-up for the last year and a half. During this time, she was diagnosed with unexplained infertility and underwent numerous fertility treatments, including 3 in vitro fertilizations, the last of which resulted in her pregnancy. There were no other notable comorbidities in her history.

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Taking in account the rapid evolution and the risk of melanoma in pregnancy7, the lesion was excised with 5 mm margin, under local anesthesia and monitored anesthetic care (sedation). The surgical defect was closed per primam with intradermal and skin resorbable sutures. The path report revealed a dysplastic acral melanocytic nevus, excised completely, with free margins (Figure 3) Immunohistochemical stains were performed

![Figure 1. One of the many atypical melanocytic lesions of the patient, localized on the left calf, that had been followed-up, due to her atypical mole syndrome. Clinical (A) and dermoscopy (B) images. Dermoscopy shows dark central blotch.](image-url)
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and were positive for Melan A, S100 and HMB45. Ki67 stain was positive in less than 4% of the tumoral melanocytes and distributed mostly close to the dermal epidermal junction (Figure 4). This confirmed that the excised melanocytic lesion was not an early melanoma.

The excision site closed nicely initially, but after 5 days a red friable 0.5 cm vascular bleeding tumor suddenly developed in one extremity of the scar, without signs of scar dehiscence or infection (Figure 5). Patient reported some pain, but refused another intervention during pregnancy (biopsy). The new tumor raised diagnostic difficulties between a vascular pyogenic granuloma-like lesion and an amelanotic recurrence of the melanocytic lesion. Dermoscopy of the newly develop-
Patient was monitored for the next month, twice a week. The vascular lesion involuted completely after 3.5 weeks. The patient went on to have a normal pregnancy and delivery (c-section) and the vascular lesion did not recur. The last clinical evaluation was done 5 months post-partum and the surgical scar was barely visible, with no clinical or dermoscopical signs of granuloma gravidarum (Figure 6).

Ped tumor showed only red background and bleeding, without any atypical vascular pattern. Considering that the path report of the excised nevus was benign and that the excision was complete with free margins, granuloma gravidarum was suspected and close monitoring of the lesion was decided with the patient. Also, local antibiotic treatment was prescribed, twice daily, and avoidance of local trauma was recommended.

Figure 4. Immunohistology slide, x100, Ki 67 stain positive in less than 4% of the tumoral nuclei, mostly at the dermal epidermal junction.

Figure 5. Red, friable nodule developed in one extremity of the scar, 5 days after the excision of the atypical melanocytic lesion (lateral aspect of the left heel).
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A 25-year-old pregnant patient and another case of subungual GG on the foot of a pregnant woman\textsuperscript{15,16}. All cases found in literature were treated surgically, either during pregnancy or post-partum, due to local complications, lack of involution or the need to accurately differentiate from an amelanotic melanoma.

Pregnant women are at high risk of developing vascular tumors due to hormonal changes and an increase in pro-angiogenetic factors, although the exact mechanism that leads to the development of granuloma gravidarum is not fully understood\textsuperscript{17,18}. Estrogen and progesterone may not be directly involved in the formation of these lesions, as the expression of receptors for these hormones were not found to be increased in GG\textsuperscript{19}. The strong angiogenetic effects of female sex hormones are probably modulated by vascular endothelial growth factor (VEGF) and angiopoietin-2. Their concentrations increase in pregnancy under the influence of estrogen. In non-pregnant women this effect is balanced by androgens. There are studies that show the amount of VEGF is high in granuloma gravidarum in pregnancy and almost undetectable post-partum and that this difference might account for spontaneous regression after parturition, at least in some cases\textsuperscript{20}.

Granuloma gravidarum typically develops in the oral cavity (gingiva, tongue, palate, lip) and is taught to be associated with poor oral hygiene and chronic low-grade irritants, like minor trauma, dental calluses or bacterial biofilm\textsuperscript{21}. Most affected is the third trimester, followed by the second one, but lesions can develop anytime during pregnancy. Management of granuloma gravidarum depends on the severity of symptoms and, if possible, treatment is delayed post-partum\textsuperscript{22}. Most tumors in pregnant patients develop in areas where surgery may pose technical difficulties and recurrences are frequent. On the other hand, evolution can be benign and treatment is not always necessary while the patient is pregnant\textsuperscript{23}. The therapy decision should be case-based, as some GG involute post-partum and some persist after parturition. Nevertheless, some studies show that as much as 50\% of cases may require surgical treatment during pregnancy, due to severe local complications\textsuperscript{21,24}. Less frequently, granuloma gravidarum can involute completely, without any intervention, during the course of pregnancy.

We presented the case of a GG developed on the post-excisional scar of an atypical acral nevus, excised during pregnancy, in the second trimester. The exact cause for the development of a GG is not yet clarified, but local trauma and hormonal factors are taught

**DISCUSSION**

In non-pregnant patients, granuloma pyogenic is more frequently found on the skin (88\%) and less on the mucous surfaces (12\%)\textsuperscript{3}. Most frequently, it involves the skin of the head and neck area. In contrast, most cases of granuloma gravidarum are reported on the mucous membranes of the oral cavity, but there are a few less typical cases described, like nasal, aural or laryngeal granuloma gravidarum\textsuperscript{9,10,11}.

Outside of the mucosal area of the head and neck region, granuloma gravidarum reports are extremely rare. A case of an unusual giant granuloma gravidarum on the scalp was reported in 2006 in Mexico\textsuperscript{12}. The lesion developed in the third trimester, was preceded by local trauma and increased rapidly in size. There are 6 cases reported of histologically proved pyogenic granuloma occurring on the hands of pregnant patients, 5 of which not preceded by trauma\textsuperscript{13,14}. In addition, two cases have been reported: one of a giant GG on the cheek of a
to play an important role. The surgical excision of the nevus may have represented the trauma trigger in our patient, combined with the localization on the foot (heel), an area prone to continuous micro-trauma and pressure. There are a few reports of pyogenic granuloma complicating eyelid surgery or hair transplants, but all regard non-pregnant patients and the reported risk is low. Also, it is known that pyogenic granulomas may arise after grafting burn lesions, but it’s difficult to assess whether the burn itself represents the trigger for PG or the grafting surgery. Although the exact molecular mechanism is unclear, pregnancy hormones play a crucial role in numerous vascular changes, including the development of GG. As our patient underwent numerous hormonal fertility treatments prior to her pregnancy, she was under a pro-angiogenetic influence long before she became pregnant and this may have also influenced the development of GG.

Dermatologic surgery during pregnancy requires deliberate consideration and should be performed only in selected cases. The second trimester is the optimal period, although, if necessary, surgery can be performed safely during any time in pregnancy. In no circumstance should surgery be delayed in melanoma or in high-risk patients for melanoma. The decision to excise the melanocytic lesion in our pregnant patient was taken after carefully analyzing all the individual risks and benefits in her case. Due to her atypical mole syndrome (AMS) she was at high risk for developing melanoma and a new melanocytic lesion at the age of 32, with rapid growth and evolution was highly suspicious. Also, dermoscopy showed worrisome aspects, like brown globules in the periphery. Although pregnancy appears not to increase the risk for melanoma, melanocytic lesions do change significantly during pregnancy and melanomas developing in pregnant AMS patients were reported, especially after in vitro fertilization.

The most challenging aspect of this case was the development of an amelanotic vascular tumor on the excision site, just a few days after the operation was carried out without events and before the path report for the melanocytic lesion was finalized. This raised important differential diagnosis considerations, mainly with an amelanotic recurrence of a melanoma, as patient denied trauma and no infection was evident. Dermoscopy did not show any specific clues, but amelanotic melanoma is one of the biggest mimickers in dermatology. When the path report of the excised melanocytic lesion (both standard hematoxylin-eosin and immunohistology stains) excluded melanoma, the diagnosis of granuloma gravidarum was the evident choice.

There are two case series, totaling 252 patients, that investigated oral GG. These studies show that more than half of cases required excision during pregnancy, with an additional 30-40% being excised after childbirth. Between 7-15% of cases had spontaneous remission and only 4 of these cases involuted during pregnancy, in both studies combined. Most lesions grew slowly and local irritants were involved.

In the case presented above, GG developed in the second trimester on the skin of the foot, lateral aspect of the heel, related to a surgical trauma, but grew rapidly in a matter of days. Since the patient refused biopsy and the lesion was not excessively large, did not bleed heavily, nor did impair function, close clinical follow-up was decided. Also, local antibiotic treatment and avoidance of further trauma were recommended. Although spontaneous remission is not the rule in GG, in our case the lesion disappeared completely in less than a month, needing no further intervention and showing no recurrence after 8 months of follow-up.

CONCLUSION

Granuloma gravidarum is a pyogenic granuloma developed during pregnancy, usually in the oral cavity. The clinical case presented shows an unusual localization of a GG, on the foot and on the post-excisional scar of an atypical melanocytic lesion. Although complete spontaneous remission during pregnancy is rare, this case shows that this outcome is possible. Also, it emphasizes that conservative management and close monitoring may lead to great results.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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