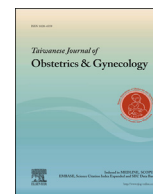




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## Research Letter

## Bier spots on legs associated with deep vein thrombosis during pregnancy

Hung-Che Lin <sup>a, b</sup>, Chi-Huang Chen <sup>c, d</sup>, Her-Young Su <sup>e, \*</sup><sup>a</sup> Department of General Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan<sup>b</sup> Department of Otolaryngology-Head and Neck Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan<sup>c</sup> Department of Obstetrics and Gynecology, Taipei Medical University Hospital, Taipei, Taiwan<sup>d</sup> Department of Obstetrics and Gynecology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan<sup>e</sup> Department of Obstetrics and Gynecology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

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Bier spots often present as asymptomatic, irregular white macules on an erythematocyanotic background [1]. They are mainly visible when a patient is in a standing position. These spots were first described by Bier in 1898. When the blood supply is restored, the spots disappear; however, they tend to recur in the same place when the occlusion is repeated. Gniadecki and Gniadecka [2] described this physiological condition in young adults, which occurs mainly on the lower limbs. Previous studies have described that patients with Bier spots might have underlying diseases [3–5]. During gestation, both physiological and pathological changes can occur in the skin, nails, and hair shafts. A previous study classified these changes into the following five categories: (1) physiological changes caused by the hormonal milieu; (2) cutaneous tumors affected by pregnancy; (3) diseases specifically associated with pregnancy; (4) genital infections of prenatal importance; and (5) other dermatological diseases influenced by pregnancy [6]. However, only a few studies have described such vascular modifications of the skin during pregnancy [7].

Our patient was a 35-year-old woman who was diagnosed with deep vein thrombosis from October 12, 2011 to November 11, 2011, during her first pregnancy. She received several test to make the diagnosis. She came to our outpatient department with complaints of swelling and a painful sensation in her left lower limb. Her Wells score was 1, indicating moderate probability [8,9]. She also showed symptoms of skin-color change on her legs. Heparin was prescribed

prior to admission (5000 IU q.d.), as she was in her second trimester. Because of the persistent symptoms and a tentative diagnosis of deep vein thrombosis, she was admitted to our hospital. Physical examinations revealed irregular borders against a background of blanching erythema on her lower limbs in the dependent position. However, the lesions disappeared when her limbs were raised (Fig. 1). No palpable cord, calf tenderness, or thigh pain was noted. In addition, no acrocyanosis was observed and her symptoms were not affected by cold temperatures. A Doppler sonography image of the left lower limb deep vein revealed partial thrombus in the common femoral vein. Following medical treatment, her deep vein thrombosis resolved, and this was verified using repeated sonography, which revealed no evidence of thrombus in the deep venous systems of both limbs. The laboratory test results were all normal; however, the symptoms of skin-color change on her legs persisted. We made the diagnosis as Bier spots based on the characteristic manifestation. The patient was discharged and all lesions disappeared after delivery. During her second pregnancy, the symptoms of deep vein thrombosis and Bier spots reappeared and resolved gradually after delivery. She did not receive any treatment during her second pregnancy.

Bier spots were first described by Bier in 1898 and were thoroughly studied by Lewis in 1927 [1,7,10]. These spots are also called “physiological anemic macules, angiospastic macules, and exaggerated physiological speckled mottling of the skin” [5]. Clinically, the affected patients are often aged between 20 years and 40 years. The current information on Bier spot suggests a male-to-female ratio of 2:1, indicating that men are predominantly affected by the condition. However, we reviewed all the cases reported in English and found that the male-to-female ratio is close to 1:1 (Table 1). Bier spots are characterized by multiple asymptomatic, pale, irregularly shaped macules measuring approximately 10 mm, which are commonly distributed on the extensor sites of four extremities.

Moreover, the white spots disappear when raising the limbs or by blanching the surrounding skin. Previous studies have revealed that these spots are associated with miscellaneous conditions such

\* Corresponding author. Department of Obstetrics and Gynecology, Tri-Service General Hospital, Number 325, Section 2, Chenggong Road, Neihu District, Taipei, Taiwan.

E-mail address: [su108868@gmail.com](mailto:su108868@gmail.com) (H.-Y. Su).



**Fig. 1.** (A) Scattered white macules on both lower limbs. (B) The lesions disappear when the patient raises her lower limbs.

as palmar hyperhidrosis, insomnia, tachycardia, pregnancy, cryoglobulinemia, scleroderma, renal crisis, aortic hypoplasia, varicosity, lichen planus, alopecia areata, and Peutz–Jeghers syndrome; skin biopsy shows normal histopathologic findings [1,3,5,7,11]. The differential diagnosis includes disorders with white macules caused by hypopigmentation (pityriasis versicolor, vitiligo, achromic nevus, postinflammatory hypopigmentation, etc.) or those caused by vascular abnormalities (nevus anemicus) [5,11].

Clinicians must recognize that Bier spots might be the first sign of an underlying systemic disease. In our case, we observed the rare combination of Bier spots on the legs and deep vein thrombosis. The anemic macules were not caused by circulatory obstruction, but by venous hypertension in accordance with the stage of pregnancy. The peripheral venous pressure rises gradually during normal pregnancy, whereas the central venous pressure remains stable; subsequently, when the venous return slows down, venous hypertension is produced in physiological conditions, suggesting a possible etiology of deep vein thrombosis [7,12].

**Table 1**

Summary of all cases reported in English.

Study references	Case no.	Country	Ratio of men to women
Liaw and Chiang [10]	1	Taiwan	1:0
Fan et al [5]	6	China	5:1
Peyrot et al [1]	1	France	0:1
Schoenlaub et al [7]	1	France	0:1
Gniadecki and Gniadecka [2]	8	Denmark	3:5
Bessis et al [3]	1	France	0:1
Cabanillas et al [11]	1	Spain	1:0
Khera and English [13]	1	USA	0:1
Graham and James [14]	1	England	0:1
Tey [15]	1	Singapore	1:0
Miura et al [16]	4	Japan	3:1
Sarifakioglu and Erdal [17]	1	Turkey	1:0
Heller [18]	1	USA	1:0
Tunca et al [19]	2	Turkey	1:1
Tan and Zhu [20]	1	China	0:1
Present case	1	Taiwan	0:1
Summary	32		17:15

Pregnancy is commonly accompanied by a disturbance of the skin caused by either physiological or pathological changes. Bier spots can manifest as an overstated physiological response of small vessels to the venous hypertension observed in certain predisposed conditions in gestating patients. Although Bier spots are typically a physiological condition that can occur during pregnancy, other systemic diseases such as deep vein thrombosis must be considered while making the diagnosis.

#### Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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