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Bier's anemic spots, cyanosis with urticaria-like eruption (BASCULE) syndrome: a new entity?

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DEAR EDITOR, Bier's anemic spots (BAS) are characterized by multiple asymptomatic anemic white macules usually standing out against a cyanotic background and mainly distributed on the extensor surface of the upper and lower extremities.¹ Herein, we report four cases of a new dermatosis characterized by BAS associated with cyanosis and urticaria-like eruption.

A 14-year-old girl without relevant medical history was admitted for the evaluation of disseminated pruritic cutaneous lesions that had appeared 2 years ago and were progressively worsening. The lesions developed after 1-2 minutes in a standing and immobile position, were associated with disabling pruritus and were always relieved by sitting, walking around or raising the limbs. Cutaneous examination after 1-2 minutes in a standing position revealed multiple irregular white spots standing out from a marked cyanotic background. In the next few minutes, pruritic red-orange papules progressively appeared, always located on the white macules and extending from their center to cover most of their surface (**Figure 1A, 1B**). The lesions faded completely within minutes of lying down (**Figure 1C**). Histopathologic examination of a biopsy specimen from a papule showed multiple dilated capillaries of the upper dermis with rare interstitial and scattered eosinophils and mast cells (**Figure 1D**). Desloratadine, 10 mg per day for 7 days, resulted in partial improvement of the pruritus, whereas the cutaneous lesions remained unchanged.

A 15-year-old girl without relevant medical history was seen for the evaluation of pruritic cutaneous lesions of the lower limbs that had appeared 10 months earlier. The lesions developed in a standing and immobile position and were relieved by sitting or walking around. The patient also reported ankle edema after more than 20 minutes of immobile standing. Clinical cutaneous findings after one minute in a standing position were quite similar to those of the previous case. H1-antihistamines and tranexamic acid provided no relief.

A 19-year-old man without medical history was seen for asymptomatic white spots of the lower limbs that had appeared 18 months earlier. Cutaneous examination after 1-2 minutes in a standing position revealed multiple anemic white spots centered by urticaria red-orange papules on the lower limbs. Spontaneous and complete clinical regression of all the cutaneous lesions was observed 2 years later.

A 3-month-old boy was hospitalized for tenderness and limb cyanosis of the upper or lower limbs noted by the parents in the previous days, and depending on how they held the child. Regression of the lesions and symptoms was noted within 1 minute of stopping manual compression and laying the boy down. The cutaneous lesions were reproduced during the examination by holding the boy under the thighs and hanging the legs for 2 minutes. They appeared to be cyanotic, with edema of the left lower limb associated with multiple anemic white macules ranging in size from about 1 mm to 5 cm and mostly centered by edematous and tender red-orange macules and papules (**Figure 2**).

In all cases, routine laboratory tests were normal: full blood count, activated cephalin time, C-reactive protein, urea and electrolytes, liver function tests and protein electrophoresis. Further explorations (cases 1, 3 and 4) failed to detect cryoglobulinemia; antinuclear,

anticardiolipin and antibeta2glycoprotein1 autoantibodies; or circulating lupus anticoagulant.

Lower limb arterial and venous ultrasonography was normal in all cases, except for a superficial and bilateral venous insufficiency of the internal saphenous vein in case 3.

We describe four cases of a vasomotor dermatosis marked by the association of BAS, cyanosis and urticaria-like eruption. They differ from the approximately 50 cases of idiopathic and secondary BAS reported in the English-language literature¹⁻⁹ by (i) the invariable presence of cyanosis, (ii) the occurrence of urticaria-like eruption characterized by red-orange macules and papules always located on the central part of the anemic macules, and spreading like an oil stain (iii) the variable presence of pruritus (2/4) and tenderness (1/4) of the affected areas, and (iv) partial or diffuse edema of the involved limbs (2/4).

Venous stasis appears to be the main cause, although venous occlusion by mechanical compression may be an exacerbating factor as illustrating by the case 4. The absence of a secondary etiology, in particular thrombophilia, and the spontaneous resolution in one case strongly suggest a benign vasomotor dermatosis. The causative mechanism leading to Bier's spots is the exaggerated vasoconstrictive response of arterioles to tissue hypoxia induced by physiological venous stasis and the lack of venoarteriolar reflex in dermal ascending arterioles in response to venous filling,¹ venous² and lymphatic⁷ hypertension, or hyperviscosity.³ In our observations, the development of pruritic papules strictly located on the anemic white macules may indicate a paradoxical urticaria reaction induced by local skin vasoconstriction and/or hypoxia but the exact mechanism remains unknown.

In conclusion, we describe a new benign vasomotor dermatosis and we propose the acronym BASCULE (Bier's anemic spots cyanosis urticaria-like eruption) to designate it.

References

1. Fan YM, Yang YP, Li W, Li SF. Bier spots: six case reports. *J Am Acad Dermatol* 2009;**61**:e11-2.
2. Schoenlaub P, Dupré D, Redon JY, Plantin P. Numerous and large Bier's spot associated with pregnancy. *Eur J Dermatol* 1999; **9**:230-1.
3. Bessis D, Dereure O, Rivière S, Ravi N, Le Quellec A, Guilhou JJ. Diffuse Bier white spots revealing cryoglobulinaemia. *Br J Dermatol* 2002; **146**:921-2.
4. Binois R, Galliot C, Audia S, et al. Multiple anaemic macules and diffuse erythrocytosis revealing mixed cryoglobulinaemia. *Eur J Dermatol* 2011; **21**:269-70.
5. Peyrot I, Boulinguez S, Sparsa A, Le Meur Y, Bonnetblanc JM, Bedane C. Bier's white spots associated with scleroderma renal crisis. *Clin Exp Dermatol* 2007; **32**:165-7.
6. Cabanillas M, Suarez-Amor O, Loureiro M, Ginarte M, Toribio J. Bier's spots in association with hypoplasia of the aorta. *Dermatology* 2007; **215**:166-7.
7. Dean SM, Zirwas M. Bier spots are an under-recognized cutaneous manifestation of lower extremity lymphedema: a case series and brief review of the literature. *Ann Vasc Surg* 2014; **28**:1935.e13-6.
8. Sachs C, Lipsker D. Nevus Anemicus and Bier Spots in Tuberous Sclerosis Complex. *JAMA Dermatol*. 2015 Nov 18:1-2.
9. Lin HC, Chen CH, Su HY. Bier spots on legs associated with deep vein thrombosis during pregnancy. *Taiwan J Obstet Gynecol* 2015; **54**:102-4.

Figure Legends

Figure 1. Clinical and histologic findings of patient 1

A. Multiple irregular red papules on the lower limbs, with a more marked color in their center, over a cyanotic background; some are surrounded by a partial white halo. **B.** Close-up view of an orange-red papule. **C.** All the lesions faded almost completely within minutes of lying down. **D.** Histopathology shows multiple dilated capillaries with normal vessel walls of the upper dermis (hematoxylin and eosin; original magnification x 200).

Figure 2. Clinical findings of patients 2, 3 and 4

A. Patient 2: Lesions similar to those of the first patient observed on the legs and dorsal side of the feet. **B.** Patient 3: Multiple anemic white macules on the lower limbs over a cyanotic background. Some are centered by irregular red-orange macules or papules (see black arrows), surrounded by a persistent slight white halo. **C.** Patient 4: Cyanosis with edema of the left lower limb associated with anemic white macules, 1 mm to 5 cm, and red-orange papules (see black arrows).













