Infrequent associations of cutis marmorata telangiectatica congenita: a two-case report

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ABSTRACT

Introduction. Cutis marmorata telangiectatica congenita (CMTC) is a rare capillary malformation characterized by persistent reticular and violaceous erythema. We present two cases of CMTC.

Clinical observation. The first case involved a 13-month-old male with a reticular violaceous macule on the left gluteal region and a brownish papule with Darier's sign on the inner malleolus of the left foot, which was biopsied, revealing > 15 mast cells per field, leading to a diagnosis of CMTC and solitary cutaneous mastocytoma. The second case involved a newborn with a characteristic CMTC lesion without other malformations at birth, who subsequently developed two cutaneous tumors consistent with infantile hemangiomas during follow-up.

Discussion. CMTC is a benign condition. However, approximately 50% of cases exhibit associated anomalies. When CMTC is suspected, musculoskeletal, ophthalmological, and cutaneous malformations should be ruled out. To the best of our knowledge, this is the first report of CMTC associated with mastocytoma and one of the few cases associated with infantile hemangioma.

KEY WORDS: Cutis marmorata telangiectatica congenita; Mastocytoma; Hemangioma; Pediatrics.

ASOCIACIONES INFRECUENTES DE LA CUTIS MARMORATA TELANGIECTÁSICA CONGÉNITA: REPORTE DE DOS CASOS

RESUMEN

Introducción. La cutis marmorata telangiectásica congénita (CMTC) es una rara malformación capilar caracterizada por eritema reticular y violáceo persistente. Presentamos dos casos de CMTC.

Observación clínica. Un varón de 13 meses presentaba una mácula violácea reticular en glúteo izquierdo y una pápula parduzca con signo de Darier en el maléolo interno del pie izquierdo, que fue biopsiada identificando > 15 mastocitos/campo, con lo cual se diagnosticó de CMTC y mastocitoma cutáneo solitario. El segundo caso, una recién nacida con una lesión característica de CMTC sin otras malformaciones al nacer, que durante el seguimiento desarrolló dos tumoraciones cutáneas compatibles con hemangiomas infantiles.

Comentarios. La CMTC es una condición benigna, sin embargo, aproximadamente el 50% de los casos presentan anomalías asociadas. Ante la sospecha de CMTC se deben descartar malformaciones musculoesqueléticas, oftalmológicas y cutáneas. Hasta donde tenemos conocimiento, este es el primer reporte de CMTC asociada con mastocitoma y uno de los pocos con hemangioma infantil.

PALABRAS CLAVE: Cutis marmorata telangiectásica congénita; Mastocitoma; Hemangioma; Pediatría.

INTRODUCTION

The congenital form of cutis marmorata was described by Van Lohuizen in 1922 with the name cutis marmorata telangiectatica congenita (CMTC)[1]. According to the International Society for the Study of Vascular Anomalies (ISSVA)[2] classification, it is a capillary malformation and has a slight female predominance (1.2:1). It is characterized by a persistent violaceous, marbled, or reticular erythema that blanches under diascopy and does not improve with increasing temperature. Although it is a benign condition with a good prognosis, it is often associated with a wide spectrum of diseases with different levels of severity. To date, approximately 500 cases have been reported, and almost half of them have some associated abnormality[3]. We present two illustrative cases of cutis marmorata telangiectatica congenita associated with other skin diseases, which are rare in this context.

CLINICAL OBSERVATION

Case 1

A 13-month-old male referred for suspected vascular anomaly. Born at 40 weeks following eutocic delivery to a healthy mother with normal prenatal check-ups; birth

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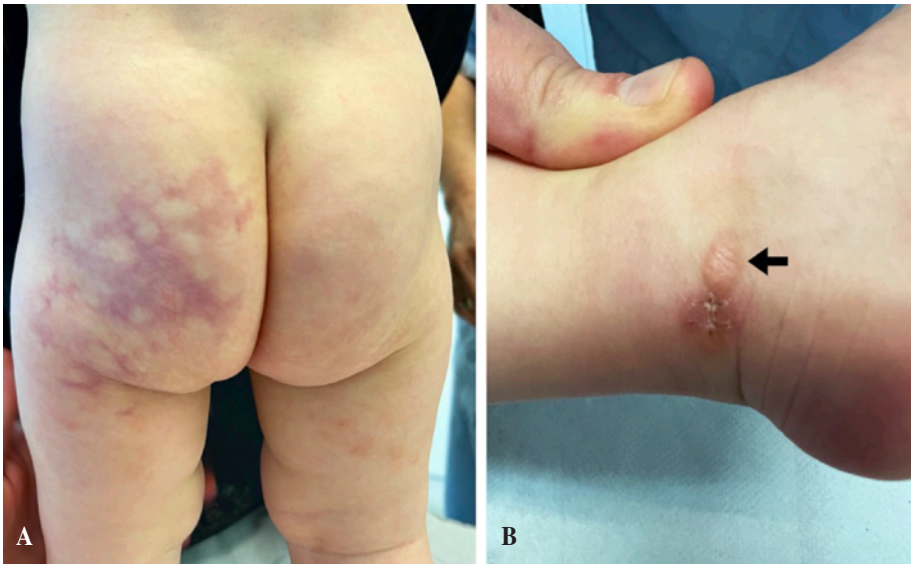

Figure 1. A) Erythematous-violaceous and reticular macule on the left gluteal region with extension to the ipsilateral lower limb. Small scattered telangiectasias and central cutaneous atrophy were observed, but without ulceration or a deep component. B) Brownish maculopapular lesion on the left internal malleolus, firm to the touch, and with an anfractuous surface (arrow). Biopsy reported orthokeratosis and spongiosis of the epidermis and dermis, with >15 perivascular mast cells per high-magnification field (Giemsa stain), confirming the suspicion of solitary cutaneous mastocytoma.

weight of 3,690 g and an Apgar score of 9 at one minute and 10 at five minutes. From birth, an asymptomatic "vascular mark" was observed in the gluteal region that was accentuated by cold, did not improve with heat, and seemed to be growing in proportion to the child. He presented with a violaceous and reticular erythema in the left gluteal region with central cutaneous atrophy and the lesion extending to the proximal third of the ipsilateral thigh (Fig. 1A). The erythematous macule blanched under diascopy, was superficial, and was not associated with venous dilatation or limb asymmetry. The rest of the physical examination was normal. Ophthalmologic assessment revealed no alterations, and a soft tissue ultrasonography ruled out subcutaneous malformations. In addition, on the internal malleolus of the left foot there was a hemispherical, erythematous-brownish, firm to the touch, maculopapular lesion measuring 1.5 x 1 cm, with Darier's sign (Fig. 1B). Given the suspicion of mastocytoma, a biopsy was performed and confirmed the diagnosis. The patient had also had 2 episodes of urticarial exanthems on the torso and limbs with erythematous and edematous papules that resolved spontaneously two days later. Therefore, a blood test with serum tryptase was performed, and was found to be normal. The diagnosis of cutis marmorata telangiectatica congenita and solitary cutaneous mastocytoma was established. Currently, at 2 years of age, the malformation remains stable without trophic alterations in the limbs or skin ulcerations. The mastocytoma is still present and there have been no new exanthems.

Case 2

A 24-hour-old female newborn assessed for an extensive vascular malformation of unknown origin present since birth. Born at 39.2 weeks following eutocic delivery, with a maternal history of gestational diabetes and a birth weight of 2,920 g, with an Apgar of 9 at one minute and 10 at 5 minutes after birth. During examination, a violaceous and reticular macule was identified on the postero-external side of the right lower limb, especially on the feet, which blanched under diascopy and was accentuated by cold or crying without improving with heat, without venectasia, a deep component, or limb asymmetry; all of which were suggestive of a cutis marmorata telangiectatica congenita capillary malformation (Fig. 2A). At the one-month check-up, the capillary malformation was stable, but two new tumors with a vascular appearance were observed, one on the left side and the other on the ipsilateral foot, which had increased in size over the previous few weeks and were suggestive of infantile hemangiomas (Fig. 2B). In subsequent check-ups, the cutis marmorata and hemangiomas were found to be stable, with no new lesions appearing. Currently, at 12 months of age, the cutis marmorata is stable, with progressive involution of both hemangiomas. However, atrophy of the subcutaneous cellular tissue has been observed in the right gluteal region, apparently without functional repercussions (Fig. 2C).

DISCUSSION

Cutis marmorata telangiectatica congenita is a rare capillary malformation that manifests locally and extracranially in 66% of cases, although it can also occur on the face or be generalized. It appears most frequently on the torso and limbs (60%) but can affect any body segment[4]. Its etiology is unknown, and a multifactorial causation is suspected. Pathogenic variants in GNA11 have been detected in skin biopsies from affected areas, suggesting that it is a postzygotic somatic condition, which might explain the low incidence of familial cases[5,6]. In some

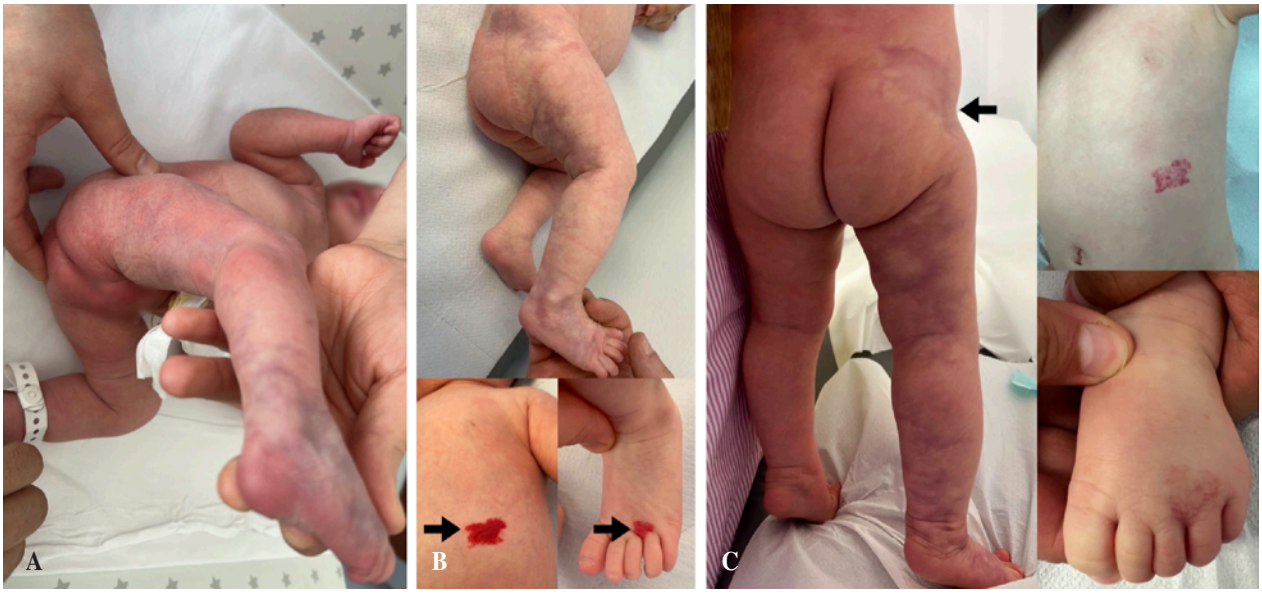

Figure 2. A) Violaceous macule with reticular pattern on the postero-external side of the right lower limb, most apparent on the foot, with scattered telangiectasias, without deep component or limb asymmetry, compatible with cutis marmorata telangiectatica congenita. B) Stability of the malformation in the right lower limb and appearance of reddish tumors with well-circumscribed margins, raised and with a velvety surface on the left side and ipsilateral foot, suggestive of infantile hemangioma. C) Cutis marmorata progression at 12 months of life, with atrophy of the subcutaneous cellular tissue in the lateral part of the right gluteal region (arrow) and progressive hemangioma involution with pale areas and less skin turgor.

syndromic forms, a homozygous truncating mutation in ARL6IP6 has been described, as well as cases related to drugs such as propylthiouracil, but this association has not been demonstrated[7,8].

Its diagnosis is clinical and based on the criteria described by Kienast and Hoeger, where the presence of 3 major and 2 minor criteria[9] are considered indicative of CMTC. The major criteria include: 1) congenital reticulated (marbled) erythema; 2) absence of venectasia; and 3) lack of response to local skin heating. The minor criteria are 1) disappearance of erythema within 2 years; 2) telangiectasias within the affected area; 3) port-wine stain outside the areas affected by CMTC; 4) ulceration; and 5) cutaneous atrophy, but these have not been validated. In the cases presented, the 3 major criteria and 2 minor criteria (telangiectasias and atrophy) were met. Histologic findings in skin biopsies are nonspecific and do not play a role in the diagnostic process, so no biopsy of the malformation was performed in either of the cases. However, exceptionally, atypical vascular proliferation similar to that of infantile hemangiomas has been documented[10]. These findings raise the clinical concern as to whether there may be some degree of relationship between CMTC and infantile hemangioma or whether it is simply a coincidence. In our two-case report, in the patient with infantile hemangiomas, malformations progressed according to the natural history of the disease and therefore we opted not to perform invasive studies or procedures in favor of a watchful-waiting approach. Imaging tests are only indicated if associated anomalies are suspected or there are phenotypic findings suggestive of a syndromic manifestation. In the first case, an ultrasound was performed to rule out the presence of deep components or underlying vascular anomalies, since the disease was localized.

Differential diagnosis should include physiologic cutis marmorata, congenital livedo reticularis, and other conditions with worse prognosis, such as Klippel-Trenaunay and Sturge-Weber syndrome or other phenotypes derived from alterations in the PI3K/Akt/mTOR pathway[3,11-13]. The distinguishing feature between CMTC and physiologic cutis marmorata is that the latter disappears with local skin heating and has a symmetrical distribution. In the other cases, the distinction is simpler, mainly due to the characteristic abnormalities and mutations associated with each syndrome[14]. In our patients, presentation was typical and there were no significant difficulties in diagnosis, although both cases were accompanied by infrequent malformations such as solitary cutaneous mastocytoma and infantile hemangioma.

Although CMTC is a benign condition, up to 50% of cases have associated anomalies, primarily body asymmetry (37%), neurological, ophthalmological, cardiovascular, or genitourinary defects[3]. Body asymmetry mainly affects the limbs and presents as hypertrophy or hypotrophy: Therefore, these patients require strict follow-up to control limb growth. In our case series, there

was no limb asymmetry, but there was focal subcutaneous cellular tissue atrophy in the second case. However, the malformations in these patients were mainly gluteal and a lower rate of trophic alterations has been reported in this location[15]. Neurological defects are present in 1 in 10 patients and consist mainly of seizures and neurodevelopmental delay. Visual problems occur in 10% of cases and half of these correspond to glaucoma, with the facial manifestations having the highest risk of glaucomatous pathology (24%)[3]. In cases of localized CMTC, such as those described, only 2% are associated with glaucoma. Although this is a low percentage, these patients require ophthalmologic evaluation due to its potential severity and the risk of amblyopia or blindness.

Our patients did not present limb asymmetry or visual alterations, and the associated anomalies were the lesion in the malleolus and the hemangiomas. Consequently, the studies performed were focused on that direction, histologically confirming the clinical suspicion of mastocytoma. Diagnosis could have been achieved clinically and without the need for biopsy. However, in the presence of CMTC and considering that this is associated with a large number of anomalies, it was decided to rule out other types of tumors or underlying malformation. To our knowledge, this is the first case described in which solitary cutaneous mastocytoma is associated with CMTC. In the case of infantile hemangioma, although also an infrequent association, given that the lesions were clinically very suggestive, no other diagnostic studies have been performed. Generally, CMTC does not require treatment beyond moisturizing the affected skin. Although there are reports of laser therapy with effective results for erythema and ulceration[16], these are isolated cases and, in general, the results of this type of therapy are poor, so treatment is focused on the associated anomalies[17]. Prognosis is good and more than 50% of patients experience improvement of skin lesions in the first two years of life due to skin thickening and maturation. However, they rarely disappear completely, and limb asymmetry often persists[18].

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