

# Hemangioma reticular do membro inferior associado a anomalias estruturais congénitas: abordagem terapêutica

*Reticular hemangioma of the lower extremity associated with congenital structural anomalies: therapeutic approach*

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## Resumo

O hemangioma reticular é uma variante do hemangioma infantil descrita recentemente, que apresenta uma predileção pela extremidade inferior e pelo períneo. Associa-se, frequentemente, a ulceração recalcitrante, anomalias ano-génito-urinárias e sacrais e, raramente, a sobrecarga cardíaca. Uma recém-nascida prematura apresentava uma mancha com aspecto reticular ao nível do membro inferior esquerdo, nádegas e períneo, dilatações venosas proeminentes na superfície lateral do membro envolvido, genitália externa dismórfica e ânus imperfurado. A ressonância magnética mostrou imperfuração anal, fistula rectovestibular, hipoplasia coccígea, cavidadeiringomiélica medular e envolvimento hemangiomaso retroperitoneal. As características clínicas e imagiológicas eram consistentes com o diagnóstico de hemangioma reticular com anomalias ventro-caudais. Os autores descrevem a abordagem terapêutica adoptada nesta doente e a eficácia do encerramento assistido por vácuo de uma úlcera extensa e refractária aos cuidados de penso convencionais.

**Palavras-chave:** hemangioma reticular, hemangioma infantil, ulceração, encerramento assistido por vácuo, síndrome SACRAL, síndrome PELVIS, síndrome LUMBAR.

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## Summary

Reticular hemangioma is a recently described variant of infantile hemangioma that has a predilection for the lower extremity and perineum. It is often associated with recalcitrant ulceration, ano-genito-urinary-sacral anomalies, and rarely with cardiac overload. A premature newborn female presented with patchy, network-like cutaneous staining of the left lower limb, buttocks and perineum, prominent lateral venous dilations of the involved limb, dysmorphic external genitalia and imperforate anus. MRI revealed imperforate anus, rectovestibular fistula, coccygeal hypoplasia, medullary syringomyelic cavity and retroperitoneal hemangiomas involvement. The clinical and imaging features were those of reticular hemangioma and ventral-caudal anomalies. The authors describe the therapeutic approach of this patient and the efficacy of vacuum-assisted closure of a large intractable ulceration.

**Key words:** reticular hemangioma, infantile hemangioma, ulceration, vacuum-assisted closure, SACRAL syndrome, PELVIS syndrome, LUMBAR syndrome.

Infantile hemangiomas (IH) are the most common vascular tumors of the pediatric age group. They consist of clonal endothelial cells associated with pericytes, dendritic cells, and mast cells, and are characterized by a period of rapid growth followed by gradual involution[1]. The tumor presents in a broad spectrum of clinical phenotypes, from tiny to large regional lesions. The “segmental” subtype usually

presents as a large plaque-like lesion involving a specific territory and is at much higher risk for complications [2]. When located on the face, a segmental IH is most commonly recognized as a potential indicator of PHACE syndrome (Posterior fossa brain malformations, Hemangiomas, Arterial anomalies, Coarctation of the aorta and cardiac defects, and Eye abnormalities)[3]. One variant, characterized by lum-

bosacral, perineal and/or lower extremity hemangiomas, and ventral-caudal congenital anomalies has been infrequently reported in the literature[4-8]. This condition has been called PELVIS syndrome (Perineal hemangioma, External genitalia malformations, Lipomyelomeningocele, Vesicorenal abnormalities, Imperforate anus, and Skin tag)[9], SACRAL syndrome (Spinal dysraphism, Anogenital anomalies, Cutaneous anomalies, Renal and urologic anomalies, associated with an Angioma of Lumbosacral localization)[10] and, more recently, LUMBAR syndrome (Lower body hemangioma and other cutaneous defects, Urogenital anomalies, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Arterial anomalies, and Renal anomalies)[11]. In 2007, Mulliken and colleagues[12] described a “reticular” variant, consisting of a large flat pink stain with a macular network-like pattern involving the lumbosacral area and lower extremity, associated with structural anomalies of the ventral-caudal region. PELVIS/SACRAL/LUMBAR syndromes share many similarities with PHACE syndrome, and might be considered its extracraniofacial equivalent[11].

The authors present a case of reticular type hemangioma, and describe the therapeutic approach, including the role of systemic corticosteroid and the efficacy of vacuum-assisted closure (VAC) of a large ulcerated wound.

## Case report

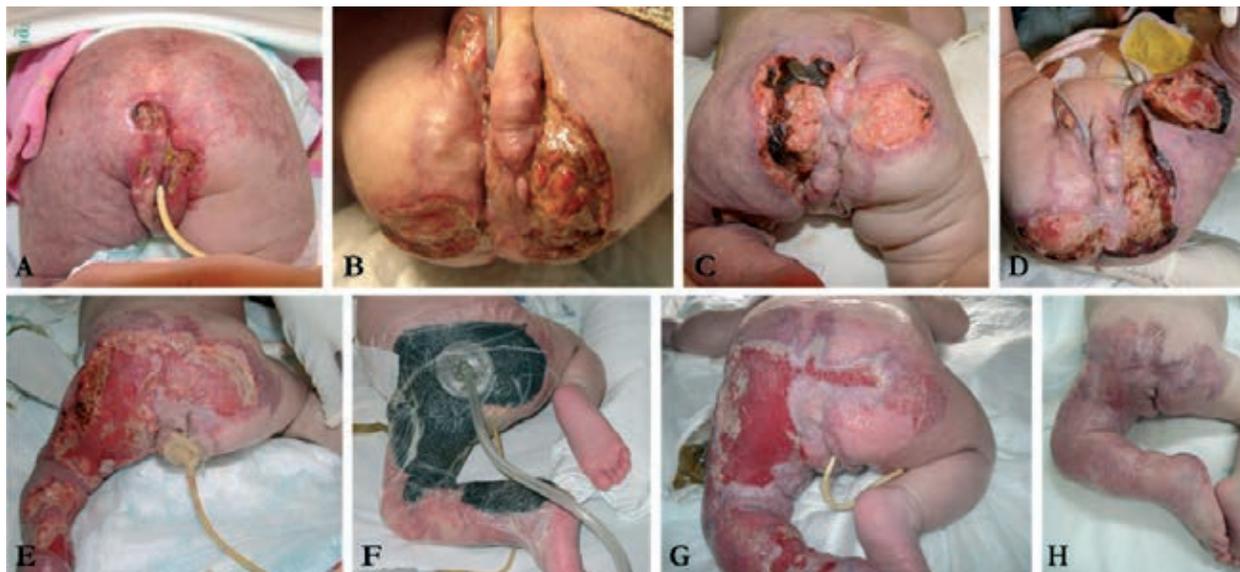
A newborn female delivered at 34 weeks gestation presented with patchy, network-like cutaneous staining of the left lower limb, buttocks and perineum, prominent lateral venous dilations of the involved limb, dysmorphic external genitalia with possible sexual ambiguity, and imperforate anus (Figure 1). She was the first child of a 36-year-old insulin-dependent diabetic mother; the pregnancy was complicated by pre-eclampsia. Prenatal ultrasonograms were interpreted as normal. Chromosome study revealed a normal female karyotype (46, XX). MRI/Angio-MRI, performed at 2 weeks old, revealed imperforate anus, rectovestibular fistula, coccygeal hypoplasia, medullary syringomyelic cavity and retroperitoneal involvement by hemangioma. The clinical and imaging features were those of reticular type hemangioma in association with ventral-caudal anomalies.

At the fifth day of life, perineal ulcers appeared, followed by necrosis of the labia majora (Figure 3A). Intravenous prednisolone (2 mg/kg/day) was started. To facilitate dressings a colostomy was done. Despite increasing corticotherapy to 3 mg/kg/day and topical wound care, new ulcerations appeared in the left thigh and leg, with obvious infection (Figures 2B to E). Cultures grew: *Acinetobacter baumannii*,



**Figure 1.** Global profile of our patient at birth. Note the ischemic whitish discoloration of the labia majora (box inset).

*Enterobacter cloacae*, *Enterococcus fecalis*, *Escherichia coli*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Antibiotic treatment included flu-cloxacillin, ampicillin, ceftriaxone, gentamycin and imipenem. Furthermore, fixed dose morphine was added to the therapeutic schedule, with bolus prior to dressing changes for pain control. Poor sleep and long periods of crying and irritability were noticed. Due to the extent and severity of the ulcers, and unsatisfactory results with conventional dressings, a VAC device was applied to the wound, after removal of the nonviable tissue with a hydrosurgical system (Figure 2F). Negative pressures ranging from 50 to 75 mmHg were delivered in intermittent mode; dressings were changed every 48 hours. Gradually the ulcers began to heal and after 20 weeks of VAC treatment and 34 weeks of corticosteroid, skin grafting was not needed (Figures 2G and H). Some impairment of full extension of the left lower limb was noted. The patient was discharged at 9 months of age but started to experience recurrent episodes of wheezing and bronchiolitis, with frequent need of bronchodilators and hospitalization. Chest x-ray revealed cardiomegaly. Cardiac and abdominal ultrasound disclosed pulmonary and portal hypertension (estimated right ventricular systolic pressure [RVSP]  $\pm$  65 mmHg). Angio-MRI was repeated and showed a massive and diffuse infiltrative angiomatous lesion starting in the left thigh, spreading to the perineum, pelvis and the entire retroperitoneal area; the bladder was totally surrounded by the lesion and compression and lateral displacement of the rectum and left iliac vessels were observed (Figure 3). Cardiac catheterization confirmed the absence of structural heart disease but showed pulmonary hypertension with ele-



**Figure 2.** A) Deep perianal ulcerations at day 5 of life (D5). B) More extensive, deeper, painful and infected ulcers at D80. C) Appearance of the ulcers at D93. D) Extensive necrosis of ulcers borders at D100. E) Confluence of buttocks, perineum and limb ulcers (D115). F) Overview of VAC device on place. G) Note approaching of wound edges and granulation tissue after 11 weeks of VAC treatment (D200). H) Complete healing of the wound at D262.

vated pulmonary capillary pressure and saturation of 92% in the inferior vena cava, hyperkinetic heart and absence of evident pulmonary arteriovenous malformations. Both the respiratory complaints and the increased pressures in pulmonary and hepatic veins were considered secondary to these alterations. The patient was treated with high doses of diuretics (furosemide and spironolactone) and inhalatory therapy, slowly tapered, with progressive improvement. She is now a 2-year-old asymptomatic baby without significant functional disability (Figure 4), having taken the first steps recently. Despite the maintenance of the angiomatous involvement on MRI, the lesion is stable, slightly smaller and both pulmonary and portal pressures significantly reduced to normal values. After physical therapy and surgical release of posterior thigh contracture, her range of motion has substantially improved. Further surgical procedures are planned for cosmetic reasons, as well as for colostomy closure.

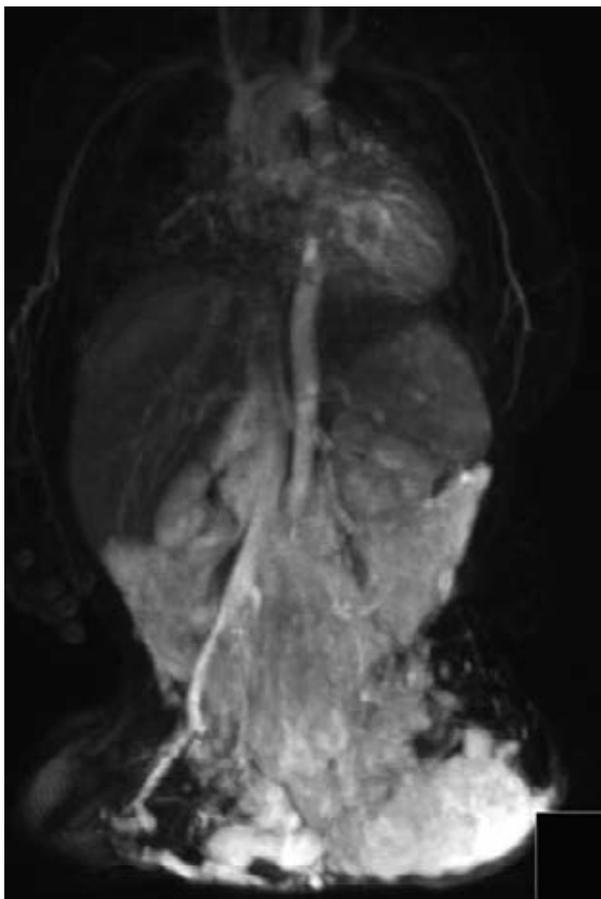
## Discussion

Hemangiomas are the most common benign tumors of infancy, occurring in up to 2% of full-term newborns and as many as 10% to 12% of Caucasian infants by 1 year of age[1]. Risk factors for the development of IH include female sex, white (non-Hispanic) ethnicity, prematurity, low birth weight, multiple gestation, and chorionic villus sampling[1]. Prenatal associations include older maternal age, placenta previa, and pre-eclampsia[13]. Although most IH occur spo-

radically, familial transmission in an autosomal dominant fashion has been reported[1]. Most tumors are solitary but up to 20% of infants may have two or more[14]. Multiple IH more commonly occur in multiple gestations. About one-third of tumors have premonitory cutaneous marks at birth, such as a small red macule, pallor, telangiectasia, or less commonly a bruise or scratch, at the hemangioma site.

IH can appear anywhere on the skin, internal organs or mucous membranes but have a predilection for the head and neck region (60%)[15]. Fewer than 10% of IH are located in the perineal area, where complications (including ulceration, infection, pain, hemorrhage, and impairment of function by mass effect) seem to be more frequent[16].

Despite their benign and self-limited course, some hemangiomas can impair vital or sensory functions, cause disfigurement and ulceration, or herald underlying developmental anomalies of the spine, central nervous system, circulatory system, and/or eyes. Frieden et al.[3] used the acronym PHACE to define the combination of large, facial hemangiomas with one or more congenital malformations, most commonly structural or cerebrovascular anomalies of the brain. This association is a spectrum, with few infants manifesting the entire constellation of anomalies. The term *reticular* was proposed by Mulliken and co-workers[12] to describe the characteristic pattern previously called "port-wine stain-like", to describe hemangioma seen in PHACE and in the lumbo-sacral area. Often reticular hemangioma involves the lower extremity and occurs with recalcitrant



**Figure 3.** Angio-MRI revealing massive angiomatous involvement in the pelvic and retroperitoneal areas (14 months old).

ulceration, ano-genito-urinary-sacral anomalies, visceral hemangiomas, and rarely with cardiac overload[12]. Our patient fits this subtype of hemangioma with typical coexistent ventral-caudal structural anomalies.

We believe that an insult during embryonic development at a specific critical time may give rise to these congenital malformations. According to Wheeler et al.[17,18] insufficient breakdown of the cloacal membrane and a lack of mesodermal cells in the caudal region of the embryo during the 4-6<sup>th</sup> weeks of development might result in a combination of anorectal, spine, and genitourinary congenital defects (urorectal septum malformation sequence).

Because perineal and lumbosacral hemangiomas are often associated with underlying structural anomalies, adequate clinical and imaging investigation is recommended in all infants or older children with hemangioma in these locations. Iacobas et al.[11] proposed comprehensive imaging guidelines for evaluation of these patients. In our case, investigation started with MR imaging, which is being repeated annually.



**Figure 4.** Clinical aspect of the gluteal and lower limb scar at present.

Systemic corticosteroids have been the first line treatment for problematic IH, other options including interferon alpha and vincristine for refractory tumors. However, the efficacy of corticosteroid was not satisfactory in the present case. Recently, propranolol was reported in the treatment of proliferative and complicated hemangiomas with beneficial effects and favorable safety profile[19], placing at the forefront in the treatment of these tumors. However, this case occurred in the “pre-propranolol era”, and when this drug was announced in the treatment of IH, the patient was experiencing frequent episodes of wheezing, a contraindication for propranolol usage. Management of the ulceration was the central problem in this child. There were adverse local conditions (constant maceration and frictional stress, infection, and bleeding), severe pain and insufficient results with the conventional dressings. Vacuum-assisted closure (also called topical negative pressure, negative pressure wound therapy and sub-

atmospheric pressure wound therapy) proved safe and effective in controlling the recalcitrant ulceration leading to complete healing of the wound without need for skin grafting. This technique has been shown to accelerate debridement and promote healing in many different types of wounds, including acute and traumatic wounds, subacute wounds (i.e. dehisced incisions), pressure ulcers, chronic open wounds (venous stasis ulcers and diabetic ulcers), meshed grafts, and flaps[20]. The application of controlled levels of negative pressure draws wound edges together, removes bacteria and factors that impede healing, reduces edema, and increases perfusion[21]. In addition, tissue microdeformation occurs at the cellular level under negative pressure, leading to cell stretch and resulting cellular proliferation, protein synthesis and fibroblast migration[21].

There is known association between pulmonary capillary hemangiomatosis and pulmonary hypertension, hepatic hemangiomas and portal hypertension, and visceral or large hemangiomas and congestive heart failure. The clinical outcome observed in our patient after resolution of the cutaneous lesion seems to be particularly worrisome and, to our

knowledge, previously unreported in the literature. In fact, the patient developed high-output heart failure caused by the massive pelvic and retroperitoneal hemangiomatosis, with consequent pulmonary and portal hypertension. This aspect has direct implications in the prognosis. The spontaneous involution of the vascular lesion has led to clinical and imaging improvement as well as decreasing pulmonary and portal pressure values and suggests that a conservative approach with control of vascular overload may be recommended. However a regular long-term follow-up will be needed. Furthermore these complicated IH require a multidisciplinary team, including pediatric dermatologists, plastic and/or pediatric surgeons, neonatologists/pediatricians, and nurses.

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