

Escleroterapia no Tratamento de Malformações Glomuvenosas Cutâneas Disseminadas Familiares: Relato de Caso

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RESUMO – As malformações glomuvenosas manifestam-se geralmente sob a forma de pápulas, placas ou nódulos azul-violáceos, dérmicos ou subcutâneos, e podem ser esporádicas ou hereditárias. Apresentamos o caso de uma mulher de 41 anos, referenciada para avaliação de um quadro de lesões cutâneas disseminadas, azuladas, com evolução desde a puberdade. O exame histopatológico foi compatível com o diagnóstico de malformações glomuvenosas. A história familiar de uma irmã com lesões semelhantes motivou o estudo genético do gene da glomulina na nossa doente, que revelou uma variante patogénica e possibilitou o diagnóstico de malformações glomuvenosas cutâneas disseminadas familiares. Malformações glomuvenosas únicas ou escassas, sintomáticas, são frequentemente submetidas a excisão cirúrgica, enquanto que outras modalidades terapêuticas têm sido reportadas no tratamento de lesões múltiplas, com resultados variáveis. A doente foi submetida a escleroterapia com polidocanol, resultando em melhorias sintomática e cosmética muito significativas após seis sessões, sem efeitos adversos e sem recorrência aos 6 meses.

PALAVRAS-CHAVE – Escleroterapia; Neoplasias da Pele; Tumor Glómico/genética; Tumor Glómico/tratamento.

Sclerotherapy in the Treatment of Familial Disseminated Cutaneous Glomuvenous Malformations: Case Report

ABSTRACT – Glomuvenous malformations usually present as soft bluish-purple dermal or subcutaneous papules, nodules or plaques, and can occur as sporadic or inherited lesions. We present the case of a 41-year-old female, referred for evaluation of disseminated bluish lesions developing since puberty. Histopathology was consistent with the diagnosis of glomuvenous malformations. The history of a sister with similar lesions justified a genetic study of the glomulin gene that revealed a pathogenic mutational variant allowing the diagnosis of familial disseminated cutaneous glomuvenous malformations. Whereas surgical management is often used for symptomatic solitary lesions of glomuvenous malformations, other treatment modalities have been reported for treatment of multiple lesions, with variable results. The patient underwent sclerotherapy with polidocanol and there were significant symptomatic and cosmetic improvements after six sessions, with no adverse effects and no recurrence after 6 months.

KEYWORDS – Glomus Tumor/genetics; Glomus Tumor/therapy; Sclerotherapy; Skin Neoplasms.

INTRODUCTION

Glomuvenous malformations (GVM), also known as glomangiomas, are benign abnormal vascular proliferations arising from glomus cells,¹ which are considered modified smooth muscle cells of the glomus body, a specialized form of arteriovenous anastomosis involved in thermal and

baroregulation.^{2,3} GVM are most often sporadic but familial forms exist, caused by mutations in the glomulin (*GLMN*) gene.^{1,4} Disseminated lesions are uncommon, representing less than 10% of all reported cases.⁵ We present a patient with multiple hereditary GVM who was successfully treated using sclerotherapy techniques.

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DOI: <https://dx.doi.org/10.29021/spdv.77.3.1087>

Recebido/Received 2019/06/16 | **Aceite/Accepted** 2019/08/11 | **Publicado/Published** 2019/10/10

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CASE REPORT

A 41-year-old female, with irrelevant medical history, presented to our department with multiple bluish-purple cutaneous lesions evolving since puberty, with a slow but sustained development of new lesions. There were no other related local or systemic manifestations. Her sister had similar lesions, although with a more circumscribed pattern.

On examination there were bluish-purple firm papulonodules, ranging in size from 2 to 10 mm, distributed over the upper and lower limbs, trunk and face, but most numerous on the right lumbar area (Fig. 1). Lesions were tender on palpation.



Figure 1 - Grouped bluish-purple papulonodules on the right lumbar region.

Keeping the possibilities of GVM, blue rubber bleb nevus syndrome (BRBNS) and venous malformation, an excisional biopsy of one of the lesions was performed, demonstrating clusters of dilated vascular channels lined by glomus cells (Fig. 2). These findings supported a diagnosis of GVM.

Attending to the family background, the patient underwent mutational analysis for the *GLMN* gene (1p21-22), which revealed heterozygosity for a pathogenic variant not previously reported in the literature – c.971dupT p.(Leu324Phefs*19). At this point the diagnosis of multiple familial GVM/familial disseminated cutaneous GVM was made.

The benignity of the diagnosis and prognosis were explained to the patient. Due to the associated pain and for cosmetic reasons, treatment of the most symptomatic lesions was decided. Surgical excision was not achievable because the lesions were multiple and disseminated. A literature review showed many therapeutic options have been attempted in disseminated GVM, with variable and frequently unsatisfactory results, but revealed sclerotherapy as a promising option.

The patient underwent sclerotherapy with growing concentrations of polidocanol, starting from 0.5%, to minimize the risk of cutaneous ulcerations and pain. These possible

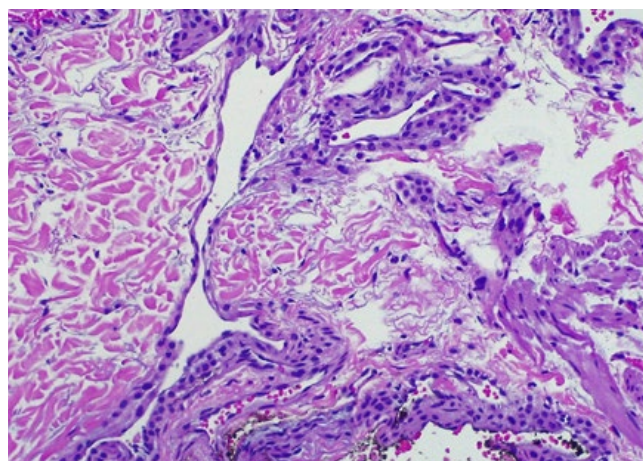


Figure 2 - Dilated vascular spaces lined by glomus cells (H&E, 200x).

adverse events were explained to the patient and a total number of sessions was not established – it would depend on the results after each session. The first step was to delimitate the lesions to be treated in each session. The right lumbar cluster of lesions was the first to be treated, as these were the most exuberant and symptomatic, and the other foci were treated subsequently. Lesions were injected directly using a 30 gauge needle. Initially blood was drawn back to ensure intraluminal position of the needle and the sclerosant was injected slowly, inducing the swelling and mild blanching of the lesion. After the injection of each lesion, cotton balls were applied and the area was compressed using a short stretch compression bandage. The patient was then instructed to maintain the compression for at least 36 hours.

A total of six sessions were performed, at 2-3 weeks intervals. Polidocanol concentrations of 0.5% and 1% were used, as the satisfactory clinical response dismissed any further escalation. The average volume of sclerosant was 0.5-0.8 mL per lesion per session. Smaller lesions were injected once, but larger ones required 2 injections of sclerosant. This approach resulted in a significant improvement, with flattening of the lesions and a very satisfactory cosmetic result, but mostly, lesional pain neutralization, the main complaint of the patient (Fig. 3). The procedure was well tolerated, with a minor discomfort during and immediately after each session. Besides a residual hyperpigmentation that faded over the weeks after the treatment, there were no immediate or long-term complications and in particular there was no ulceration or scarring. The patient is under follow-up and there was no recurrence of lesions over treated sites after 6 months. First degree relatives were referred for genetic counseling.

DISCUSSION

GVM may either be acquired or inherited.⁴ The inheritance pattern is believed to be autosomal dominant with incomplete penetrance and variable expression. Heterozygous germline mutations in the *GLMN* gene on chromosome



Figure 3 - Resolution of the lesions with residual hyperpigmentation, 9 weeks after treatment.

1p21-22 have been found to contribute to the formation of GVM.^{1,6,7} In this case a new pathogenic variant, not previously reported in the literature, was detected, highlighting the familial predisposition for the disease. Like most of the pathogenic variants identified in this gene so far, this one caused the insertion of a premature termination codon.

GVM typically present as blue-to-purple papules or nodules, grouped and limited to a specific area, usually an extremity.⁵ Multiple GVM present as bluish nodules, anywhere from two to more than one hundred, and may be localized, segmental or disseminated over the entire body.^{8,9}

Multiple GVM must be distinguished from BRBNS, due to the important risk of gastrointestinal hemorrhage associated with the latter: lack of mucosal and gastrointestinal involvement and glomus cells on histopathology are distinguishing features of GVM.¹

The prognosis for patients with GVM is excellent. Malignant transformation is extremely rare and typically represents a locally infiltrative malignancy.⁵ Lesional size larger than 2 cm, rapid growth and deeper soft tissue involvement are clues to suspect malignant transformation.¹⁰

Abstaining from therapy and regular observation may be an option in asymptomatic lesions, while the treatment of choice for symptomatic solitary GVM is surgical excision.^{8,11} However this may not be feasible for multiple or large segmental lesions^{8,12} and there is a possibility of recurrence even with complete surgical excision.¹¹ Several therapeutic modalities have been used for the treatment of multiple GVM, including sclerotherapy, argon and carbon dioxide laser therapy and electron-beam irradiation, with variable efficacy, recurrence rates and residual scarring.^{5,13}

Sclerotherapy involves introduction of a sterile solution into the lumen of a blood vessel or a vascular lesion to induce permanent endofibrosis and ablation. Sclerotherapy has been attempted with polidocanol, sodium tetradecyl

sulfate, hypertonic saline and absolute alcohol, among other agents.⁵ Potential complications of sclerotherapy include necrosis and ulceration, hyperpigmentation and telangiectatic matting, localized hypertrichosis, tromboflebitis and localized paresthesia, and these adverse effects are recognized to be concentration dependent.¹³

Sclerotherapy resulted in significant symptomatic and cosmetic improvements in our patient, with no complications, and at 6 months post-procedure no recurrence of the treated lesions was noticed. A cautious approach, starting with low concentrations of the sclerosant and increasing according to the response is advisable to avoid the risk of cutaneous ulceration. Given the scarcity of good options to treat multiple GVM, our experience corroborates previous reports that sclerotherapy appears to be an effective and safe method for treatment of disseminated lesions.

Conflitos de interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Suporte financeiro: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

Conflicts of interest: The authors have no conflicts of interest to declare.

Financing support: This work has not received any contribution, grant or scholarship.

Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Patient consent: Consent for publication was obtained.

Proveniência e revisão por pares: Não comissionado; revisão externa por pares

Provenance and peer review: Not commissioned; externally peer reviewed

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