SHORT COMMUNICATION



# Unanticipated Squamous Cell Carcinoma in a Giant Verrucous Venous Malformation

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Submitted Jun 23, 2025. Accepted after revision Jul 19, 2025
Published Aug 13, 2025. DOI: 10.2340/actadv.v105.44208. Acta Derm Venereol 2025; 105: adv44208.

Verrucous venous malformations (VVM) are typically benign congenital vascular anomalies managed conservatively or surgically if symptomatic (e.g., recurrent infection, oozing, or bleeding) (1). We report an extraordinarily rare case of a 55-year-old woman with a giant right-lumbar VVM who developed cutaneous squamous cell carcinoma (SCC) with distant lymph node metastasis.

## CASE PRESENTATION

A 55-year-old woman presented with a congenital red patch on her right lumbar region that had gradually expanded since birth. Over time, the lesion evolved into an area of marked hyperkeratosis, thick crusting, and recurrent ulcerations with persistent itching. Prior interventions including electrochemical therapy and urea sclerotherapy proved ineffective. Approximately 1 year before presentation, several red nodules emerged within the lesion, progressively enlarging and ulcerating following scratching.

On examination, the lesion extended from the right lumbar region to the lower abdomen with an irregular distribution. The affected skin exhibited extensive hyperkeratosis, persistent crusting, and repeated ulceration. Five to 6 nodules of variable size were observed, with some being exophytic, firm, and erythematous, while others showed swelling, bleeding, and focal necrosis, raising suspicion of malignant transformation (**Fig. 1**).

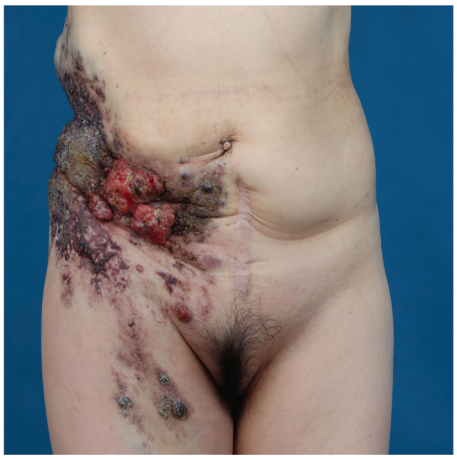
Contrast-enhanced magnetic resonance imaging (MRI) revealed diffuse thickening and nodularity of the skin and subcutaneous tissues without adjacent muscular or osseous involvement. Further imaging with positron emission tomography-computed tomography (PET-CT) demonstrated multiple soft tissue lesions in the right lumbar region, abdominal wall, and thigh with focal increased fluorodeoxyglucose (FDG) uptake, particularly in the right lower abdomen, indicative of malignant transformation. Additionally, several lymph nodes in the bilateral iliac and inguinal regions, along with the right axillary region, showed mildly increased metabolic activity, suggesting possible metastasis.

One year ago, an initial biopsy of an erythematous area had demonstrated proliferative vascular channels of varying calibres (from capillaries to small veins) in the subcutaneous tissue, consistent with VVM (**Fig. 2**). In contrast, histopathological evaluation of the recently resected nodules revealed solid, sheet-like proliferations of atypical squamous cells with focal keratinization, infiltrative growth, and vascular invasion by tumour emboli (**Fig. 3**). Immunohistochemistry demonstrated partial positivity for B-cell lymphoma 2 (BCL-2); positivity for epidermal growth factor receptor (EGFR), cytokeratin 5/6 (CK5/6), p63, p40, and epithelial membrane antigen (EMA); and a Ki-67 proliferation index of 40–50%. Stains for BER-EP4 (EpCAM), cytokeratin 7 (CK7), S100 protein (S100), p16INK4a (p16), and carcinoembryonic antigen (CEA) were negative, supporting a diagnosis of moderately differentiated SCC arising secondary to chronic ulceration over a longstanding VVM. Furthermore, an axillary lymph node biopsy was performed, and histopathological evaluation confirmed metastatic epithelial malignancy.

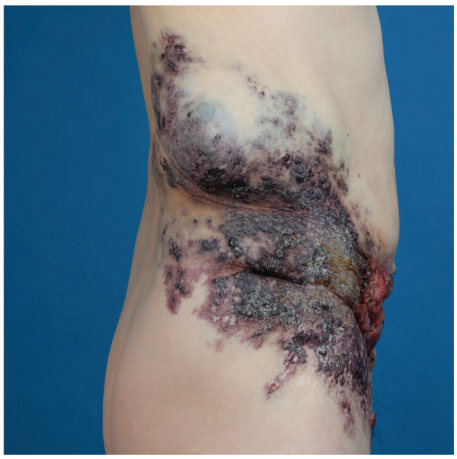
Given the locally advanced disease and nodal metastasis, after multidisciplinary consultation we plan to initiate immunotherapy with a programmed cell death protein 1 (PD-1) inhibitor. The treatment response will be evaluated after 2 cycles to guide further management.

## DISCUSSION

VVM is a rare congenital vascular anomaly according to the International Society of Vascular Anomalies (ISSVA) classifications (1). VVM typically presents at birth as a



**A.** Anterior view of patient



**B.** Lateral view of patient

**Fig. 1. Clinical photographs showing the anterior and lateral views of a patient with verrucous venous malformation complicated by secondary squamous cell carcinoma.**

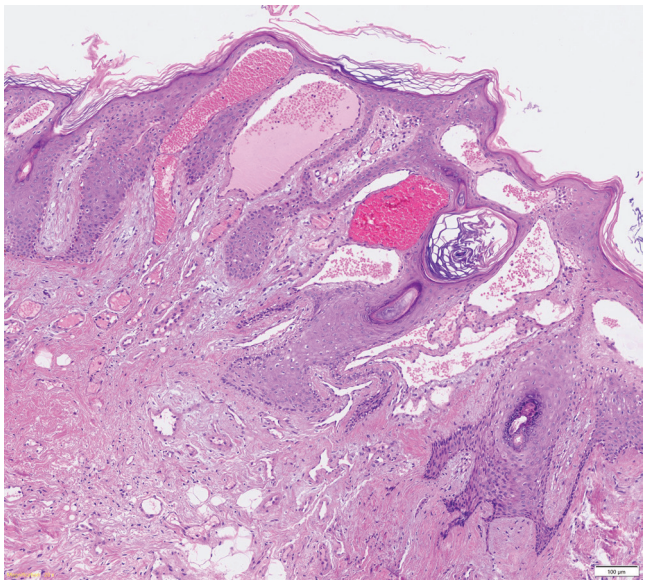


**Fig. 2. Haematoxylin-eosin staining of an erythematous lesion biopsy demonstrates proliferative vascular channels of varying calibres (from capillaries to small veins) in the subcutaneous tissue (original magnification ×40).**

localized erythematous patch that gradually enlarges with growth, developing pronounced hyperkeratosis and, as the skin barrier becomes compromised, progressing to ulceration and crusting (2). Histologically, VVM shows proliferative vascular channels of varying calibres (from capillaries to small veins) extending from the dermis into the subcutaneous tissue. Through the gradual convergence of channels, nodular lesions can be formed (3). VVM lesions predominantly occur on the extremities and may be accompanied by mild pain or pressure. The lesions are characteristically fragile, and prone to bleeding and secondary infection.

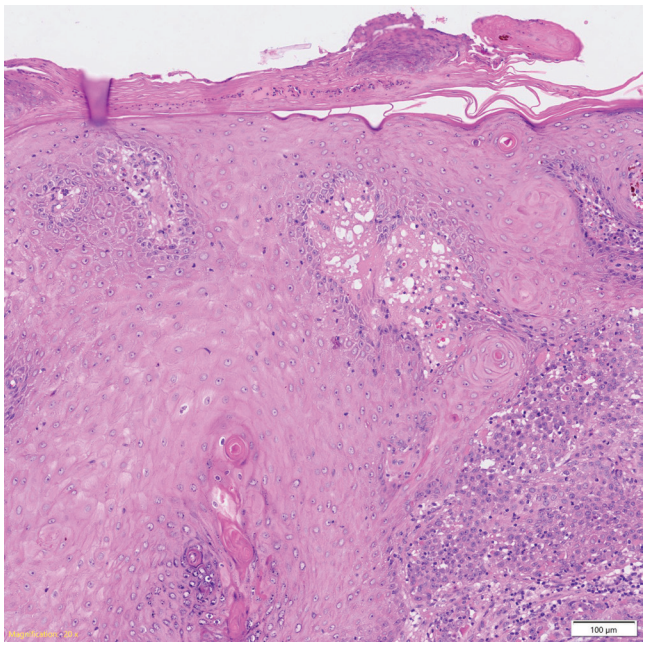


**Fig. 3. Haematoxylin-eosin staining of a representative nodule biopsy reveals invasive sheets of atypical squamous cells with focal keratin pearl formation (original magnification ×40).**

In terms of the treatment of VVM, laser therapy in the early stage has shown satisfying therapeutic effects (4). A large retrospective study that treated patients with early VVM using pulsed dye laser (PDL) and combined dual PDL-neodymium-doped yttrium aluminium garnet (PDL-Nd:YAG) laser has demonstrated significant reductions in surface area and colour intensity, with simple erythematous patches responding particularly better than lesions with incipient hyperkeratosis. Thus, laser intervention is recommended for the treatment of erythematous-stage VVM, potentially delaying progression to hyperkeratosis and ulceration, thus reducing the risk of malignancy. Once lesions progress to marked hyperkeratosis and ulceration, surgical excision remains the mainstay. However, larger resections often necessitate skin grafting, yielding suboptimal cosmesis and a high recurrence rate (5).

Emerging non-surgical options include intralesional bleomycin, which may reduce lesion volume and delay progression, though its durability requires further study (6). Molecular insights have identified a somatic MAP3K3 missense mutation (NM_002401.3, c.1323C>G; NP_002392, p.Iso441Met) in VVM (7), implicating the mammalian target of rapamycin (mTOR) pathway dysregulation. A small retrospective series of 10 patients, refractory to steroids, propranolol, pingyangmycin, laser, or cryotherapy, achieved ≥ 90% lesion reduction with oral sirolimus (8). Despite these promising results, sirolimus is limited by mucosal ulceration, the need for frequent serum-level monitoring, and the absence of large-scale efficacy data.

In our patient, histopathology confirmed that the new nodules were moderately differentiated SCC rather than angiosarcoma originating from VVM. Given her clinical history of longstanding VVM with repeated trauma, the complication of SCC likely arose from chronic ulceration and persistent non-healing wounds. The patient did not seek timely intervention, allowing the nodules of SCC to progress rapidly. The axillary lymph node biopsy confirmed the presence of distant metastasis, which belongs to stage IV according to the American Joint Committee on Cancer (AJCC) staging system (9).

Therefore, early intervention in VVM is critical. Because VVM most often presents in early childhood, initially as erythema and partially with mild hyperkeratosis, early laser intervention is crucial to delay progression. Once significant hyperkeratosis, ulceration, and crusting develop, treatment options include surgical excision, intralesional bleomycin, or oral sirolimus, but their long-term efficacy remains uncertain without larger clinical trials. We therefore advocate vigilant monitoring and early intervention, particularly during the erythematous stage, to prevent chronic ulceration and its potential complication of SCC.

In conclusion, we present the first reported case of lumbar VVM complicated by life-threatening SCC secondary to chronic ulceration and repeated wound breakdown. Clinicians should be aware that VVM lesions with persistent crusting, ulceration, and non-healing wounds carry a risk of malignant transformation and must be managed early and aggressively to mitigate this risk.

## ACKNOWLEDGEMENTS

*Funding sources:* This work was supported by the fund of the Clinical Cohort of complex vascular malformations and related syndromes for Genetics-Based Targeted Therapies from the Top Priority Research Center of Shanghai—Plastic Surgery Research Center, Shanghai (No. 2023ZZ02023).

*IRB approval status:* The participant has consented to the submission of this case report to the journal.

*The authors have no conflict of interest to declare.*

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