

A Metastatic Well-differentiated Squamous Cell Carcinoma in a Patient with an Arteriovenous Fistula

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Summary: Patients receiving hemodialysis have an increased risk of developing nonmelanoma skin cancers, such as cutaneous squamous cell carcinoma (SCC). Management of SCC usually relies on complete surgical excision of the primary tumor and may require regional lymph node dissection due to lymphatic spread. An 81-year-old man with an arteriovenous fistula (AVF) presented with an unusually aggressive metastatic well-differentiated SCC, necessitating an axillary dissection for lymph node metastasis. He had been referred for radiotherapy to complete his oncological treatment following excision of the primary SCC on his forearm. An AVF site is subjected to significant changes in circulatory pressure, leading to reduced lymphatic drainage and likely focal immunosuppression. Increased lymphatic burden, combined with repeated trauma to the fistula in an immunosuppressed patient, potentially precipitated the development of an SCC on the affected limb. The individual risk factors for SCC such as sites of chronic inflammation and repeated trauma, host immunosuppression, and renal disease are well established. This patient demonstrates the perfect storm of all these risk factors, leading to a highly malignant metastatic SCC. As the standards of renal care improve and the number of patients with AVF increases, we must remain vigilant in the management of SCCs in these patients. (*Plast Reconstr Surg Glob Open* 2022;10:e4100; doi: 10.1097/GOX.0000000000004100; Published online 28 February 2022.)

Cutaneous squamous cell carcinoma (SCC) is a malignant tumor arising from keratinizing cells in the epidermis, classified as nonmelanoma skin cancer (NMSC). A large study of 79,688 hemodialysis patients found a significantly increased rate of NMSC when compared with the general population.¹ SCCs can be categorized according to the degree of differentiation from undifferentiated to poorly differentiated, conferring varying risk of metastasis. SCCs are risk stratified according to parameters such as subtype, stage, and grade. A high-risk status correlates to a greater risk of local recurrence, nodal

metastases, and disease-specific mortality.³ Risk factors for developing SCCs include immunosuppression, male gender, older age, and lighter skin. SCCs in areas of chronic skin damage such as burn scars, ulcers, and radiation dermatitis demonstrate higher potential for metastasis.²

SCC treatment usually relies on complete surgical excision of the primary tumor. These tumors commonly metastasize via lymphatics to the regional lymphatic basins, which are usually managed with regional node dissection.

An arteriovenous fistula (AVF) is a surgically created anastomosis of a vein to an artery to form a robust high-volume vessel for vascular access in hemodialysis for patients with end-stage renal disease. An effective AVF can have a flow rate in excess of 1000 ml per minute compared with a circulatory flow rate of 15–40 ml per minute in a normal peripheral artery.^{4,5} The increased circulatory pressures have been linked to focal immunosuppression through reduced lymphatic drainage⁶ and limb ischemia from hypoperfusion distal to the AVF.⁵

PRESENTATION OF CASE

An 81-year-old man presented with a firm, painful, and rapidly growing axillary mass. Clinically, the mass was large and tethered to the skin, although it was mobile deeply.

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Fig. 1. Computed tomography scan of neck, thorax, abdomen, and pelvis (sagittal view) demonstrating a large necrotic lymph node within the left axilla with signs of extracapsular spread.

This occurred 4 months following a complete excision of a well-differentiated SCC on his left forearm, which was present for 1 month before the patient was listed for urgent excision due to the fast growth of the lesion. The primary lesion was a 22-mm thick (pT3), high-risk tumor, with invasion of the subcutis and suspicion of lymphatic invasion on initial histology. The patient's prior medical history included previously excised basal and squamous cell carcinomas, atrial fibrillation, gout, myocardial infarction, leading to an out-of-hospital cardiac arrest and chronic kidney disease requiring an AVF in his left forearm for



Fig. 2. Computed tomography scan of the neck, thorax, abdomen, and pelvis (coronal view) demonstrating a large necrotic lymph node within the left axilla with signs of extracapsular spread.

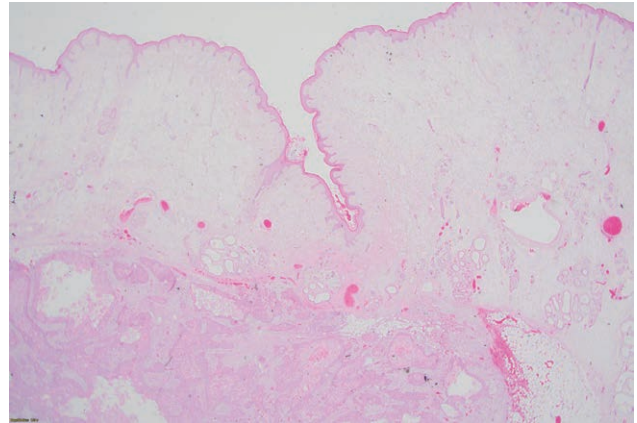


Fig. 3. Hematoxylin and Eosin (H&E) stained slide (×1.25 magnification): well-differentiated squamous cell carcinoma focally invading into reticular dermis.

dialysis. The fistula was created 7 years before the patient developed the aforementioned SCC on his left forearm. At the time of development of the SCCs, the patient was not on any immunosuppressants.

An ultrasound-guided biopsy of the left axilla confirmed metastatic well-differentiated SCC in a left axillary node. A staging CT scan confirmed metastatic lymphadenopathy in the axilla but no other distant disease (Figs. 1, 2).

Prompt surgical treatment of the axillary metastasis was necessary for pain control and prevention of ulceration and inevitable wound complications. Despite an extensive medical history, he underwent an axillary clearance. Intraoperatively, the tumor was adherent to the overlying skin and encased a hypertrophied axillary vein and the thoracodorsal neurovascular bundle. A small volume of residual tumor was necessary to preserve the axillary vein. The surgery was therefore followed by radiotherapy.

Microscopic evaluation of the axillary mass showed well-differentiated SCC with large areas of necrosis. The tumor was largely confined to the subcutis, but focally invaded into the reticular dermis of the overlying skin (Fig. 3). A small part of the tumor was surrounded by a rim of lymphoid

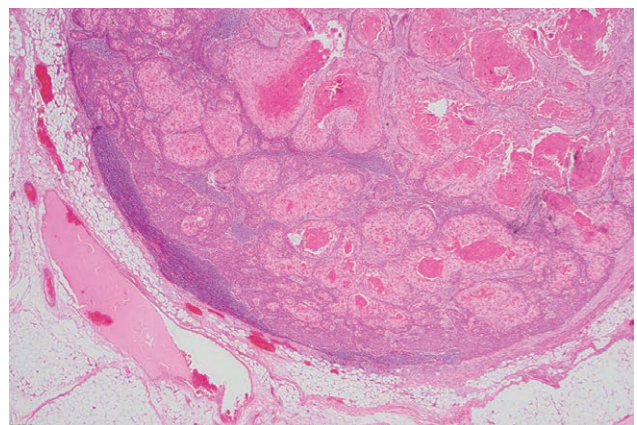


Fig. 4. Hematoxylin and Eosin (H&E) stained slide (×2 magnification): well-differentiated squamous cell carcinoma, partially surrounded by a small rim of lymphoid tissue.

tissue, highly suggestive of a lymph node being replaced by metastatic tumor with extracapsular spread (Fig. 4).

DISCUSSION

There are multiple reports of SCCs developing close to arteriovenous fistulae.^{6,7} Suggested mechanisms include repeated iatrogenic trauma^{7,8} due to hemodialysis and physiological changes that occur as a result of the AVF. Increased lymphatic workload at the site and reduced lymphatic drainage are both thought to contribute to an impaired local immune response.⁶ This, in conjunction with the iatrogenic trauma, may work synergistically to increase cancer risk in patients with an arteriovenous fistula. An estimated 3.7%–5% of dialysis patients can develop upper arm ischemia.⁵ The oxidative stress from the ischemic environment may potentiate the carcinogenic factors for the development of cutaneous SCC on upper limbs, which tend to receive significant UV radiation and remain the anatomical site of choice for AVF formation.⁴

Although the manifestation of multiple well-differentiated SCCs from an ischemic and atrophic hand associated with a patent AVF has been described previously,^{7,8} our case report highlights the presentation of a well-differentiated SCC metastasizing to the regional lymph node basin. The patient's original tumor was high risk, which may also have contributed to the unusually aggressive metastatic spread.

The reported metastatic rate for all grades of cutaneous SCC is low, at approximately 1.9%–2.6%.⁹ However, this is closer to 7% in poorly differentiated SCCs and significantly lower in well-differentiated SCCs.² The average interval to metastasis in a large study involving more than 6000 patients found an average interval to metastasis of 26 months,⁹ suggesting that this patient's mass was highly unusual for its speed of development, particularly given that the original lesion was histologically well-differentiated.¹⁰

Despite the risk of SCC formation in patients with end-stage renal disease and AVF, AVF remains a cornerstone in the long-term care of these patients. Constant vigilance, involving regular skin checks of such patients, is vital to ensure any skin cancers that do develop are treated urgently.

CONCLUSIONS

Risk factors for SCC such as chronic inflammation, repeated trauma, host immunosuppression, and renal

disease are well established. This patient demonstrates the perfect storm of all these risk factors, leading to the unusual presentation of a metastatic well-differentiated SCC in a relatively short time frame. As the standards of renal care improve and the number of patients with AVF increases, we must remain vigilant in detecting SCCs in these patients and be aware of the potentially increased risk of lymph node involvement, even with well-differentiated tumors.

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