CASE REPORT

Poorly differentiated cutaneous squamous cell carcinoma with osteoclast-like giant cell: A rare, aggressive variant

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Key Clinical Message
Squamous Cell Carcinoma (SCC) with Osteoclast-like giant cell (OLGC) is a rare SCC variant; only 10 cases have been reported. Our case suggests OLGC are resultant of a reactive process, driven by the fusion of adjacent macrophages. Knowledge regarding SCC with OLGC is of great importance as this entity has greater prometastatic potential compared to conventional SCC.

KEYWORDS
osteoclast-like giant cells, skin cancer, squamous cell carcinoma

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Cutaneous Squamous Cell Carcinoma (SCC) is the second most common form of skin cancer, and the incidence is rising. While some cutaneous SCC can be relatively indolent, with low-risk malignant potential, they account for the majority of keratinocyte related metastases and death. A wide diversity of SCC variants exists, some of which are associated with more aggressive behavior.

Osteoclast-like giant cell (OLGC) proliferation has recently been described in cutaneous malignancies. The distinctive stromal changes containing OLGC were first described in 1967 and since have been reported in numerous malignant tumors of breast, liver, renal, uterus and more recently, skin. Since 2007, only 10 cases of SCC with OLGC have been reported. To date, the majority have been described in male elderly patients, occurring on sun-exposed skin. High-risk features such as moderate-to-poor differentiation, greater tumor size, recurrence and metastatic spread have been described. We aim to present the 11th case reported to our knowledge of cutaneous SCC with OLGCs, with the objective to promote awareness of this rare SCC variant.

An 88-year-old man presented with an asymptomatic nodule on the temple which had grown rapidly over several weeks. He had a past history of SCC and basal cell carcinoma. There was no past history of melanoma or immunosuppression. On examination, an erythematous, hyperkeratotic nodule had grown over the left temple with a background of chronic sun-damaged skin. No locoregional lymphadenopathy was detected. The lesion was clinically suspicious for SCC and complete excision was performed for histopathologic examination.

Histopathological examination revealed an invasive, poorly differentiated carcinoma measuring 3.0 mm in thickness extending to subcutis (Figure 1A). Atypical cells were spindled and slightly ovoid with prominent nucleoli and plentiful OLGC within the carcinoma (Figure 1B). No perineural or lymphovascular invasion was evident. Immunohistochemical staining of the spindled cells was positive for P63 and P40 indicating squamous cell origin (Figure 1C,D). Multi-nucleated cells stained positive for mesenchymal marker CD68 (Figure 1E), and negative for giant cell tumor marker of bone (anti-histone H3.3G34W rabbit monoclonal antibody) (Figure 1F). P63 and P40 showed no immunoreactivity of OLGCs. The
cytomorphology and immunohistochemistry staining was characteristic and consistent with poorly differentiated SCC with OLGC.

OLGC resembles osteoclasts morphologically and immunohistochemically, but it has been unclear whether they possess the functional capabilities of true osteoclasts. The exact etiology of OLGC has been a source of controversy in both cutaneous and visceral malignancies. Proposed origins of OLGC have included neoplastic epithelial cells, neoplastic mesenchymal cells, and reactive mesenchymal cells. In the current case, CD68 positivity was suggestive of mesenchymal origin, and lack of H3.3G34W tumor marker, a highly sensitive and specific marker, supports the hypothesis that OLGC are benign, reactive histiocytes generated by the fusion of adjacent macrophages, (as opposed to neoplastic) histiocytes.

On review of the literature, the majority of SCC with OLGC have been reported in older (mean 79.6 years), and predominantly male (2:7.1) patients. The current case confirms the following characteristic features as described in the literature: sun damage, head and neck distribution, and rapid progression. Furthermore, the majority of cases have reported high-risk features including moderate-to-poor differentiation and tumor size >2 cm. A review by Chung et al reported 33% recurrence and nodal metastases in 17% of SCC with OLGC cases. This rare subtype of SCC appears to present with high-risk SCC features. Some studies reported nodal metastasis in only 3.7% of cutaneous SCC. OLGC infiltration appears to exert more invasive and prometastatic phenotypes. The exact cause for this is unknown. However, tumor osteoclastic cells in vivo have been found to actively promote tumor growth and lymphangiogenesis by secreting VEGF-C.

In summary, knowledge regarding the differential diagnosis and proper classification of these tumors is of great importance. Diagnosis of SCC with OLGC may pose challenges, due to its often high-grade and poor differentiation. Clinicians and pathologists should be aware of this rare SCC variant to avoid misdiagnosis of a morphologically similar entity, as the malignant potential and prognosis of cutaneous SCC with OLGC may vary.

**CONFLICTS OF INTEREST**

None declared.
AUTHOR CONTRIBUTION

JP: involved in patient management. EM and SC: provided histopathological analysis. VLV, EM, JP, and SC: provided editing and review of the manuscript. VLV, EM, and JP: wrote the manuscript.

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REFERENCES

1. Australian Institute of Health and Welfare 2016. Skin cancer in Australia. Cat. no. CAN 96. Canberra: AIHW.
2. Hanofsky VR, Mercer SE, Phelps RG. Histopathological variants of cutaneous squamous cell carcinoma: a review. J Skin Cancer. 2011;2011:1-13.
3. Chung HJ, Wolpowitz D, Scott G, et al. Squamous cell carcinoma with osteoclast-like giant cells: a morphologically heterologous group including carcinosarcoma and squamous cell carcinoma with stromal changes. J Cutan Pathol. 2016;43:148-157.
4. Wooff J, Werner D, Murphy J, et al. Osteoclast-like giant cell reaction associated with cutaneous squamous cell carcinoma: a report of 2 cases and review of the literature. Am J Dermatopathol. 2009;31:282-287.
5. Amary F, Berisha F, Ye H, et al. H3F3A (Histone 3.3) G34W Immunohistochemistry: a reliable marker defining benign and malignant giant cell tumor of bone. Am J Surg Pathol. 2017;41(8):1059-1068.
6. Geraud C, Marx A, Goerd S. Cutaneous squamous cell carcinoma with osteoclast-like giant cells: a very rare variant of cutaneous squamous cell carcinoma. JEADV. 2015;26:2051-2065.
7. Schmults CD, Karia PS, Carter JB, et al. Factors predictive of recurrence and death from cutaneous squamous cell carcinoma: a 10-year, single-institution cohort study. JAMA Dermatol. 2013;149(5):541-547.
8. Hatano Y, Nakahama K, Isobe M, et al. Tumor associated osteoclast-like giant cells promote tumor growth and lymphangiogenesis by secreting vascular endothelial growth factor-C. Biochem Biophys Res Commun. 2014;446:449.

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