

Case Report

Cutaneous Squamous Cell Carcinoma associated with Proliferation of Osteoclast-Like Giant Cells

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Abstract

Proliferation of osteoclast-like giant cells in a cutaneous squamous cell carcinoma is a rare phenomenon and so far only four cases have been reported. In previous reports, osteoclast-like giant cells were admixed with sarcomatoid component of squamous cell carcinoma and it is therefore debatable if the osteoclast-like giant cells represent a reactive phenomenon or a part of the malignant tumour.

A case of cutaneous squamous cell carcinoma associated with osteoclast-like giant cells is reported. However, sarcomatous component of squamous cell carcinoma was not identified in this case. Morphologically, the osteoclast-like giant cells appeared to be benign. The localization of the squamous cell carcinoma and the osteoclast-like giant cells were separate from one another. Immunohistochemically, squamous cell carcinoma was positive for high molecular weight cytokeratin, cytokeratin-5 and p63, whereas the osteoclast-like giant cells were positive for histiocyte marker CD68 and vimentin and negative for epithelial markers supporting a reactive nature of osteoclast-like giant cells to the cutaneous malignancy.

Keywords: Osteoclast-like giant cells, Squamous cell carcinoma, Skin.

Introduction

Although cutaneous squamous cell carcinoma (SCC) shows a diverse range of clinical and pathological subtypes,¹ SCC with osteoclast-like giant cells (OGCs) proliferation is a rare phenomenon that has been described only recently.²⁻⁴ There have been four reported cases, all of which show presence of sarcomatoid component of SCC with associated proliferation of OGCs. OGCs associated with cutaneous sarcomatoid carcinoma have also been reported recently.⁵ Most of the previous reports favour reactive process of the OGC proliferation based on the morphological features and immunohistochemistry, but whether the OGCs proliferation is truly a reactive phenomenon or if these are a part of the SCC due to the coexistence of the sarcomatoid component of SCC is debatable. The SCC in this report differs from the previously reported cases as sarcomatoid component of SCC on routine histology sections and on

immunohistochemistry was un-identified. Although SCC and OGCs were abutting remain un-identified each other, their localization were distinctly separate from one another. SCC were positive with high molecular weight cytokeratin (HMWCK), p63 and CK5, and negative with BER-EP4, CD68, CD31, CD34, vimentin, CD10, factor XIIIa, desmin, SMA, HMB45, S100 and Melan-A. The OGCs morphologically did not exhibit features of malignancy and were immunoreactive to histiocyte marker CD68 and vimentin and negative with HMWCK, p63, CK5, CD31, CD34, Factor XIIIa, Desmin, SMA, HMB45, S100 and Melan A. Morphological features together with immunohistochemistry supported a reactive process of OGCs proliferation associated with SCC.

Case Report

A 79-year-old man attended a dermatology clinic in November 2009 because of an angiomatous pedunculated nodule on his central mid back measuring 4 cm in diameter and 1cm in height (Figure-1A and 1B). The patient had a malignant melanoma with a Breslow thickness of 0.30mm removed from his right chest wall in February 2009. Clinically, there was no evidence of recurrence or metastatic disease. Other medical history included type-2 diabetes mellitus, dyslipidaemia and hypertension. There was no history of organ transplantation or immunosuppressive medication intake. The patient underwent curetting of the skin lesion for diagnostic and therapeutic purposes. Grossly, the specimen consisted of a disc shaped fragment of skin measuring 35 mm in diameter x 12 mm in depth with almost entire ulcerated skin surface. Light microscopic examination showed skin and underlying tissue which is ulcerated and covered with exudate (Figure-2). The surface squamous epithelium showed hyperkeratosis, marked epithelial atypia of the basal layer, which showed invasion up to the upper dermis. The majority of the underlying lesion was composed of abundant OGCs admixed with scattered mononuclear cells, fibroblastic spindle cells and extensive haemorrhage, forming OGC nodule. No malignant features such as high nuclear to cytoplasmic ratio, nuclear hyperchromasia, nuclear membrane irregularities, nucleoli or mitotic activity were seen among OGCs. Fibroblasts, however, showed scattered mitotic figures (two per ten high power fields). Dispersed within the

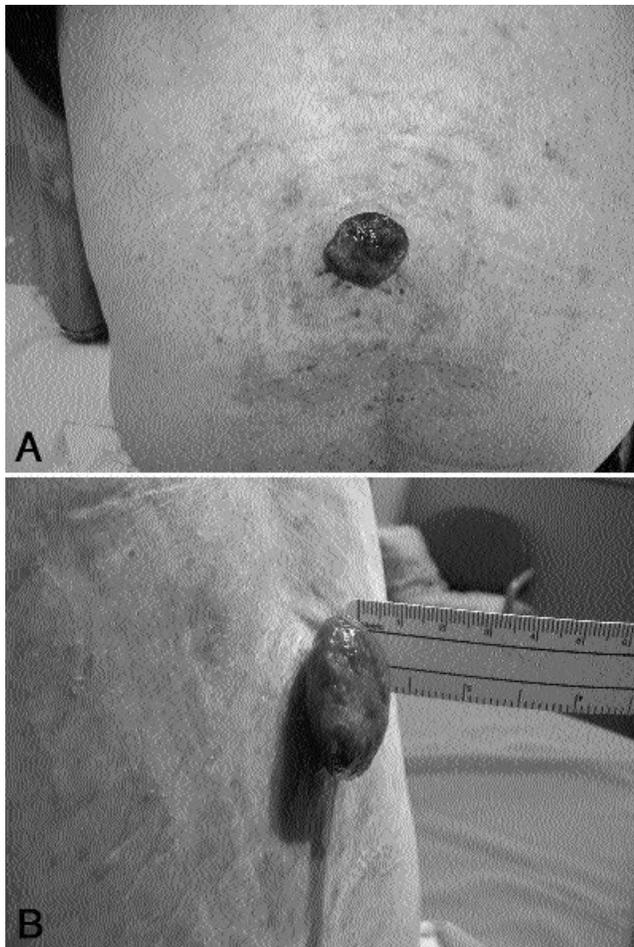


Figure-1: Gross image of the central mid back lesion. A. Frontal view and B. lateral view. There is angiomatous pedunculated lesion which measures 4cm in diameter and 1cm in height.

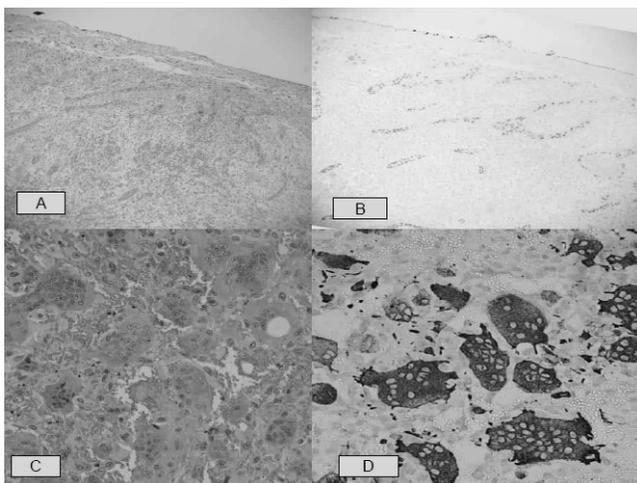


Figure-2: A: Low magnification (x12.5) image with (A) hematoxylin and eosin. B: CK5 immunostain. The lesion is largely ulcerated. Small foci of squamous cell carcinoma within the dermis are highlighted by CK5. C: High magnification (x400) image of OGCs with hematoxylin and eosin. D: OGCs are positive with CD68 immunostain.

OGC nodule were small islands of moderately differentiated SCC. Immunohistochemically, both superficial and deeper islands of SCC were positive for squamous cell epithelial markers such as HMWCK, p63 and CK5, and negative with melanoma markers HMB45, S100 and Melan A, and other epithelial and soft tissue tumor markers as BER-EP4, CD68, CD31, CD34, vimentin, CD10, factor XIIIa, SMA, desmin. The OGCs were immunoreactive with histiocyte marker (CD68) and vimentin and negative for all epithelial, mesenchymal and melanoma markers. The spindle fibroblast cells surrounding the OGCs and island of SCC showed positivity with vimentin only and were negative for all other epithelial, mesenchymal and melanoma markers. The morphological features and immunohistochemical profile is consistent with superficial SCC with exuberant reactive proliferation of OGCs with formation of an exophytic nodular lesion that predominately comprising OGCs, mononuclear cells and fibroblasts with only scattered island of squamous cell carcinoma.

Discussion

Present report demonstrates a fifth case of cutaneous SCC associated with OGCs. Interestingly, two of the four previous cases had history of organ transplantation. One reported case was post kidney and pancreas transplantation² while the other case was post kidney transplantation.⁴ The present case neither had a history of organ transplant nor immunosuppressive medication intake. SCC was located superficially with occasional small islands of well differentiated SCC dispersed within the upper to mid dermis. No sarcomatoid component of the SCC as reported in all of the previous case reports was noted in this case. The OGCs were located subjacent to the SCC forming OGCs nodule admixed with mononuclear cells, fibroblastic spindle cells and extensive haemorrhage. OGCs showed cytologically benign features. Although SCC and OGCs were abutting each other, their localization were discretely separate from one another. Immunohistochemically, SCC was positive for SCC epithelial markers and the OGCs were positive for histiocytic marker only. Both were negative for other epithelial markers, mesenchymal and melanoma markers. All morphologic features, distribution and immunohistochemical profile suggested that the OGCs are reactive phenomenon to the superficial SCC.

Differential diagnosis considered for the case report were SCC with OGC tumor-type sarcomatous differentiation and collision tumor — SCC and primary or metastatic neoplasm containing OGCs. For example, malignant melanoma, atypical fibroxanthoma, giant cell tumour of soft tissue, leiomyosarcoma, dermatofibroma and dermatofibrosarcoma protuberans.

SCC in the current case did not show sarcomatous

differentiation. The tumor nodule was predominantly composed of exuberant proliferation of multinucleated OGCs surrounded by mononuclear cells and fibroblastic spindle cells. Histologically, there were no features suggestive of malignancy in the OGCs and the surrounding spindle fibroblast, was supported by non immunoreactivity of the OGCs and the spindle fibroblasts to epithelial and mesenchymal markers.

As the patient had a history of malignant melanoma, the possibility of a recurrence was considered. Malignant melanoma can have diffuse spindle cell growth and can present with OGCs as reported recently.⁶ Benign morphology of the spindle cells comprising the OGC nodule and lack of immunoreactivity to melanoma markers such as S-100, HMB45 and Melan A excluded this diagnosis.

Atypical fibroxanthoma (AFX) is known to be associated with OGCs.⁷ AFX is characterized by proliferation of polygonal or spindled cells in which the nuclei show wide variations in size and shape with high mitotic index. OGCs nodule in our case showed minimal nuclear pleomorphism and low mitotic activity, which made this diagnosis unlikely. CD10 immunostain was non-contributory in this case.

Due to the abundance of the OGCs, the possibility of giant cell tumour of soft tissue (GCTST) was sought.^{8,9} GCTST typically present as multinodular mass in the subcutis. Microscopically, GCTST shows proliferation of two distinct cell populations, mononuclear cells and OGCs. The mononuclear cells are round to oval and the nuclei resemble those of the giant cells. In contrast to the uniform distribution of mononuclear cells and OGCs throughout the lesion in GCTST, in our case the OGCs were mainly located in the dermis and mononuclear cells were scarce and these were surrounded by reactive spindle fibroblasts. These features opposed the diagnosis of GCTST.

OGCs can also be associated with leiomyosarcoma (LMS).¹⁰ LMS is characterized by proliferation of spindle cells with blunt-ended nuclei showing nuclear pleomorphism arranged in an alternating fascicular pattern. In our case there were no features suggestive of LMS. Furthermore, the immunohistochemistry was negative smooth muscle actin and desmin immunostains.

Spindle cell lesions of the skin such as dermatofibroma (DF) and dermatofibrosarcoma protuberance (DFSP) were also included in the differential diagnosis. DFSP is a poorly circumscribed spindle cell tumour of undetermined malignant potential. It arises in the dermis and infiltrates into the subcutis. This tumour is characterized by uniform growth of spindle cells that are arranged in a monomorphous storiform pattern and is

immunoreactive to CD34 immunostain. DF shows mononuclear cells arranged in similar storiform growth pattern as DFSP but lack the infiltrative growth pattern of DFSP and is negative for CD34 and positive for factor XIIIa. In our case no storiform growth pattern was detected and both CD34 and factor XIIIa immunostain were negative.

All previous four cases showed significant sarcomatous component of the SCC, among which the OGCs were dispersed raising the controversy if this OGCs proliferation was a truly reactive phenomenon or if this was a malignant component of sarcomatous component of the SCC. Three of the four previous reports favoured OGCs for being reactive process due to absence of cytological atypia, absence of reactivity to epithelial markers of SCC and positivity for histiocyte marker CD68.

OGCs associated with squamous component of the adenosquamous carcinoma of the pancreas has also been reported.¹¹ However, the mechanism of the formation of the OGCs is unknown. Deyama et al. (2008) demonstrated that oral squamous cell carcinomas stimulate osteoclast differentiation in vitro likely via indirect osteoblast-mediated stimulation through cytokines.¹²

In conclusion, compared to the previous four cases, this case appears unique in that there was no sarcomatous component of the SCC. The masses of OGCs were distinctly separate from the foci of SCC, showed benign cytological features and an immunohistochemical profile similar to the previous reports. Therefore this case favours the notion that exuberant growth of OGCs is a reactive phenomenon rather than a true neoplastic process.

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