

Pharyngeal squamous cell carcinoma with osteoclast-like giant cells: a case report and review of the literature

Osteoklast benzeri dev hücreler içeren faringeal skuamöz hücreli karsinom:
Olgu sunumu ve literatürün gözden geçirilmesi

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Benign osteoclast-like multinuclear giant cells are rarely found in tumors other than bone and soft tissue neoplasms, and they are even rarer in squamous cell carcinomas. We examined a nasopharyngeal tumor from a 52-year-old female who had undergone surgery one year earlier for hypopharyngeal squamous cell carcinoma. Histopathologically, in addition to tumor infiltration by atypical epithelial cells with squamoid differentiation, giant cells with 10-20 nuclei and a large amount of eosinophilic cytoplasm were seen infiltrating the tumor. The giant cells did not show atypia or mitosis. Immunohistochemically, the tumor cells stained for pan-keratin and epithelial membrane antigen, and the giant cells were positive for leukocyte common antigen, CD68, and Mac 387. This case was diagnosed as moderately differentiated squamous cell carcinoma with multinuclear giant cells. In this case, the giant cells infiltrating the tumor were benign and of monocytic/histiocytic origin. Studies including large case series are needed to obtain reliable information on the clinical and prognostic importance of this histological feature.

Key words: Nasopharynx; osteoclast-like giant cells; squamous cell carcinoma.

Benign osteoklast benzeri multinükleer dev hücrelerin, kemik ve yumuşak doku tümörleri dışındaki tümörlere eşlik etmesi nadir bir histopatolojik bulgudur. Skuamöz hücreli karsinomlarda ise çok daha nadiren saptanmaktadır. Bir yıl önce hipofaringeal skuamöz hücreli karsinom nedeniyle opere olan 52 yaşındaki kadın hastada, nazofarinkste saptanan tümöre biyopsi yapıldı. Histopatolojik olarak skuamoid diferansiyasyon gösteren atipik epitelyal hücrelerin oluşturduğu tümöral infiltrasyonun yanı sıra tümör dokusunu infiltre eden, geniş eozinofilik sitoplazmalı ve ortalama 10-20 nükleus içeren dev hücreler dikkati çekti. Dev hücrelerde atipi ve mitoz izlenmedi. İmmünohistokimyasal olarak tümör hücrelerinde pan-keratin ve EMA ile dev hücrelerde ise LCA, CD68 ve Mac 387 ile reaksiyon gözlemlendi. Olguya, multinükleer dev hücrelerin eşlik ettiği orta derecede diferansiye skuamöz hücreli karsinom tanısı verildi. Olgumuzda tümörü infiltre eden dev hücrelerin benign karakterde ve monositik/histiyoitik kökenli olduğu saptandı. Geniş olgu serilerinde yapılacak çalışmalar, bu histolojik özelliğin klinik ve prognostik önemine yönelik güvenilir bilgiler sağlayacaktır.

Anahtar sözcükler: Nazofarenks; osteoklast benzeri dev hücre; skuamöz hücreli karsinom.

Benign osteoclast-like multinuclear giant cells are rarely found in tumors other than bone and soft tissue neoplasms, and they are even rarer in squamous cell carcinomas. As these giant cells are similar to osteoclasts morphologically, they are referred to as osteoclast-like giant cells (OLGCs). There is no widely accepted theory on the histo-

genesis of these cells. They might originate from undifferentiated mesenchymal cells, histiocytic cells, epithelial cells, or endothelial or reticuloendothelial cells. Recently, several investigators have proposed that carcinomas that contain OLGCs are different clinicopathological entities and that the presence of these cells indicates a

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good prognosis.^[1-3] However, the clinical importance of this phenomenon is not clear due to the small number of cases.

This article presents a patient with nasopharyngeal squamous cell carcinoma with OLGs. The histopathological and immunohistochemical results are discussed along with the literature on the origin, constitutional mechanisms, and clinical importance of these cells.

CASE REPORT

Clinical History

A 52-year-old female presented to the Otolaryngology Clinic with dysphagia for five months. Indirect laryngoscopy revealed a vegetating mass filling the left sinus pyriformis and causing swelling in the posterior pharyngeal wall. An incisional biopsy was performed with a working diagnosis of a hypopharyngeal tumor. Histopathologically, the biopsy material was diagnosed as squamous cell carcinoma. Bilateral functional neck dissection and total laryngopharyngoesophagectomy with a gastric pull-up were performed. No complications occurred postoperatively, and the patient underwent radiotherapy. At her 12-month follow-up, a second primary tumor was identified in the nasopharynx. Histopathologically, this tumor was a moderately differentiated squamous cell carcinoma with OLGs. The patient underwent radiotherapy again for the second primary tumor in the nasopharynx. Unfortunately, she died 10 months later because of carotid artery erosion due to osteoradionecrosis.

Histopathological and Immunohistochemical Findings

Histologically, the initial incisional biopsy and the material obtained at the subsequent operation revealed atypical squamous cells that had abundant eosinophilic cytoplasm with enlarged, vesicular nuclei and marked nucleoli, and infiltrating stroma as solid islets of centrally forming keratin. Immunohistochemically, the tumor was positive for pan-keratin and epithelial membrane antigen. The tumor was diagnosed as well-differentiated squamous cell carcinoma. Histopathologically, the

biopsy of the nasopharyngeal tumor showed uniformly distributed infiltrating multinucleated giant cells with an osteoclast-like appearance alongside atypical squamous cells. The multinucleated giant cells had abundant eosinophilic cytoplasm each containing 10-20 oval-to-round nuclei. The cytoplasm of some of the multinucleated giant cells contained hemosiderin, indicating phagocytic activity. No mitotic activity or atypia was found in the multinucleated giant cells (Fig. 1). Immunohistochemically, the giant cells reacted strongly for vimentin, leukocyte common antigen, CD68, and Mac 387, but not for the pan-keratin, epithelial membrane antigen, P53, or Ki67 detected in the tumor cells (Fig. 2). The tumor was diagnosed as moderately differentiated squamous cell carcinoma with OLGs.

DISCUSSION

This report presents a case of nasopharyngeal squamous cell carcinoma with OLGs, an uncommon histological feature. OLGs are multinucleated cells with a monomorphic appearance and abundant eosinophilic cytoplasm. These cells are so named because they are similar to osteoclasts morphologically, immunohistochemically, and ultrastructurally.^[1-3]

OLGs may be found in various sites and in different epithelial and mesenchymal tumors. Although they are most commonly reported in breast^[4,5] and pancreas^[1] carcinomas, they can also be seen in carcinomas of the gallbladder,^[6] stomach,^[7] and urinary system,^[8] or stromal tumors of the uterus.^[9] They are extremely rare in squamous cell carcinomas^[3] and have never been reported in tumors in the nasopharynx.

There are two theories explaining the origin of OLGs. The first is the transformation of malignant cells into giant cells. Studies of pancreas carcinomas suggest that OLGs are related to precursor dysplastic ductal epithelial cells.^[2] Alternatively, it has been proposed that OLGs originate from reactive stromal cells.^[1] Because the morphological findings, including the presence of hemosiderin and cell remains, indicate phagocytic activity, and the immunoprofile (posi-

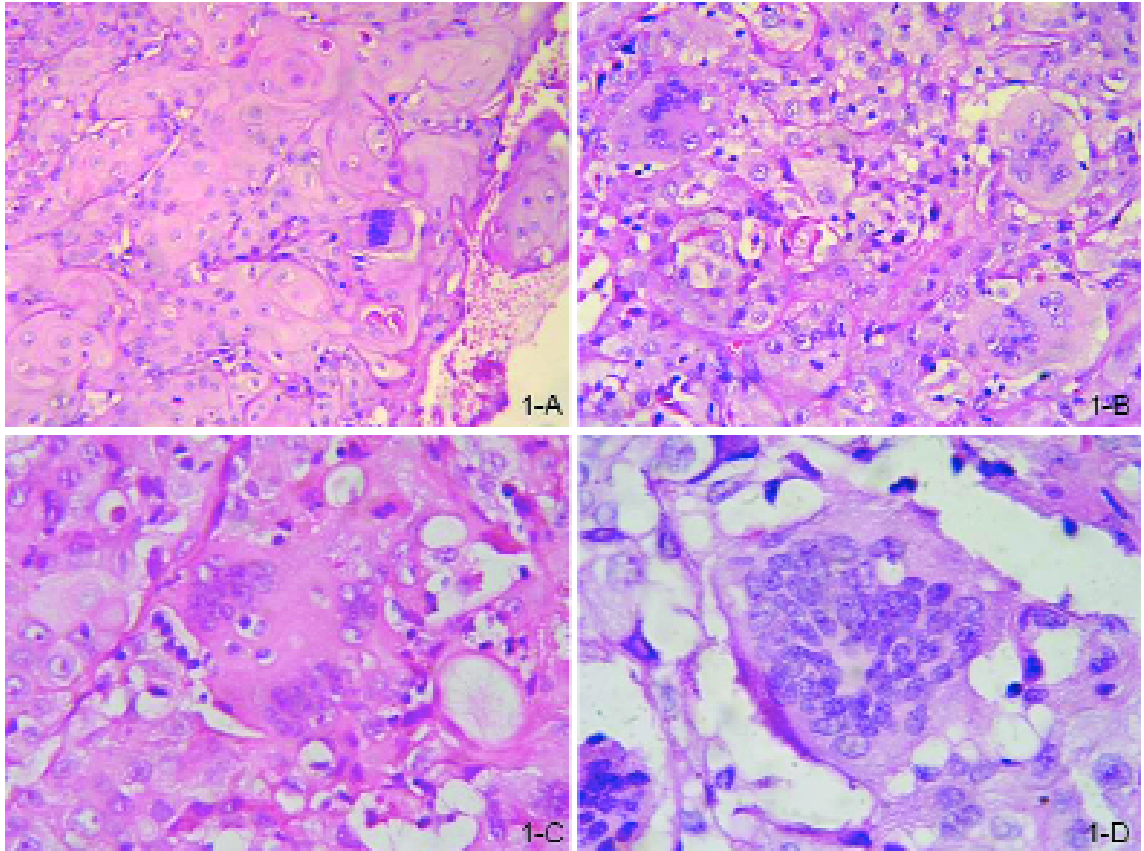


Fig. 1. Osteoclast-like giant cells intermingled with atypical squamous cells (A, x60; B, x80). Cellular debris engulfed by osteoclast-like giant cells (C, x100; D, x120); hematoxylin and eosin.

tive for CD68, leukocyte common antigen, and Mac 387) is consistent with a monocytic/histiocytic origin, the theory suggesting that OLGs are a subtype of macrophages is more widely accepted.

Recently, studies have examined the similarities between osteoclasts and OLGs found in extraskeletal tumors. The two cell types cannot be distinguished from each other under light microscope. They are also similar ultrastructurally in terms of their cellular surface structures, Golgi apparatus, and lysosomes. Immunophenotypically, OLGs contain alpha-1 antitrypsin, CD68, and acid phosphate activity, indicative of a monocyte/macrophage origin. Both cell types have the ability to resorb bone, although the activity of OLGs is not influenced by parathormone or calcitonin levels. Based on the findings, OLGs found in extraskeletal tumors appear to be specif-

ic macrophage subtypes different from osteoclasts and foreign-body-type giant cells.^[1-9] Sakai et al.^[1] studied pancreas carcinomas containing OLGs and reported that the giant cells expressed histiocytic markers and did not include the ki-ras mutation. The morphologic attributes and immunoprofiles of the giant cells found in the current patient are both suggestive of the benign, monocytic/histiocytic nature of these cells. These cells are thought to be histiocytes that had migrated into the tumor tissue as a result of chemotactic factors released from the tumor cells and that coalesced there to form giant cells. However, further studies are required to clarify the specific mechanism involved.

Squamous cell carcinomas with sarcomatous differentiation may contain multinuclear giant cells. However, the morphological and immunohistochemical characteristics of those cells differ

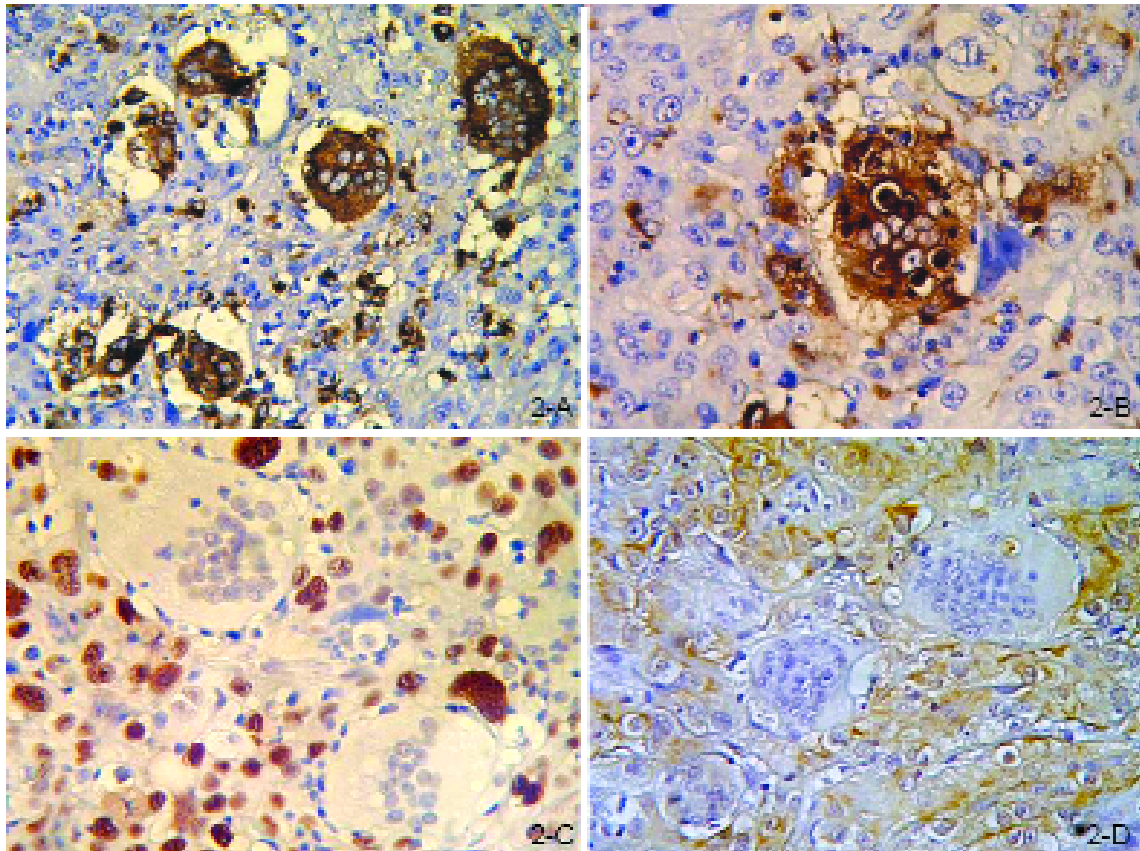


Fig. 2. Osteoclast-like giant cells expressing (A) Mac 387 and (B) CD68. (C) Keratin and (D) Ki67 immunoreactivity in atypical squamous cells (BSA-DAB).

from those of OLGs. We considered sarcomatous differentiation of squamous cell carcinoma in the differential diagnosis of our patient's nasopharyngeal tumor, as it contained giant cells. However, the benign morphology and the expression of histiocytic markers indicated the reactive nature of the giant cells and revealed the monocytic/histiocytic origin.

Although the giant cells accompanying carcinomas belong to a different morphological spectrum, the clinical and prognostic importance of the presence of these cells is not known. Studies of breast and pancreas carcinomas, which are the most common carcinomas to present with OLGs, indicate that these tumors have a better prognosis than typical carcinomas.^[4,5,10,11] However, the limited number of cases and the lack of long follow-up studies hinder the clarification of the importance of this observation. There are

also contradictions regarding the identification of the tumors associated with OLGs. Whether or not this histologic feature should be mentioned in reports remains controversial.

The presence of OLGs may cause some difficulties in reaching a diagnosis. While in some cases it may be confused with sarcomatous transformation, in others it is difficult to discern from giant cell tumors. A detailed histomorphological examination, comprehensive immunohistochemical profile analysis, and many samples are required to discriminate such cases.

To our knowledge, the presence of OLGs in nasopharyngeal tumors has not been reported previously in the English literature. In this case, the giant cells infiltrating the tumor were benign and had a monocytic/histiocytic origin. Studies including large case series should supply reliable information on the clinical and prognostic importance

of this histological feature. Denoting the presence of OLGs in pathology reports is important in terms of forming a database for future studies.

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