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A Rare Cutaneous Presentation of Metastatic Orbital Adenocarcinoma

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Primary ductal adenocarcinoma of the lacrimal gland (PDALG) is a rare tumor accounting for less than 2% of all tumors arising within the orbit. It is classified as a high-grade malignant epithelial tumor due to its variable biologic behavior and aggressive clinical course. Due to its rare incidence, the clinicopathologic profile is poorly identified and generally dependent on the few available reports and case series. Metastatic lesion of PDALG presenting as a skin lesion is very rare with only one previously reported case. We report here a case of metastatic PDALG that presented with cutaneous features. This case illustrates that such a rare malignant tumor may present to dermatologists, requiring prompt diagnosis and management with a multidisciplinary approach. **(Korean J Dermatol 2016; 54(3):206～209)**

Key Words: Primary ductal adenocarcinoma of the lacrimal gland, Metastatic adenocarcinoma, Orbital adenocarcinoma

INTRODUCTION

Primary ductal adenocarcinoma of the lacrimal gland (PDALG) is a rare, high-grade epithelial malignant tumor with variable clinical presentations and biologic behaviors. It accounts for less than 2% of all malignant tumors arising in the orbit[1]. Due to its rare incidence, the clinicopathologic profile is poorly defined are there are few case reports or case series available.

PDALG occurs as a rapidly growing palpable mass, usually exceeding the limits of adequate surgical excision at the time of presentation[2]. Histopathologic examination of the primary tumor shows pleomorphic cells with numerous mitotic figures arranged in cords along with lumen formation[3,4].

Cutaneous metastasis of a lacrimal gland epithelial tumor is very rare with only a single case previously reported. Metastatic skin lesions of an adenocarcinoma usually occur as nonspecific firm nodules, mimicking other common disorders[5]. Therefore, immunohistochemical study is necessary to determine the primary sites of metastatic lesions. The aim of this case report is to raise dermatologist awareness that rare malignant tumors may present with cutaneous features.

CASE REPORT

A 51-year-old Korean male patient was referred to the dermatology department with a solitary plaque located on the cheek. The size and erythema of the lesion had been increasing over the previous four months, however, there were no other associated symptoms.

Two years prior, the patient had been diagnosed with colorectal adenocarcinoma on routine health examination and an endoscopic mucosal resection was performed. No lymphovascular invasion was noted and colonoscopic evaluation showed no recurrence or remnant lesions. After 6 months, the patient presented to the ophthalmology department with an indurated mass on his left eyelid. The mass had been present for 1 month and swelling of the eyelid and pain gradually intensified. A computed tomography (CT) scan showed a mass involving the left orbital cavity and the ethmoidal and frontal sinuses with enlarged lymph nodes. An excisional biopsy was performed on the medial orbital wall and found infiltration of clustered, atypical cells. These cells had prominent nucleoli with fine and granular cytoplasm filled with mucin. Neoplastic cells were positive for

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pan-keratin markers (CK AE1/3) and CEA but were negative for CD68, suggesting primary ductal adenocarcinoma of the lacrimal gland (PDALG). Magnetic resonance imaging (MRI) and $^{[18F]}$Fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) revealed hypermetabolic uptake in the surrounding sphenoid sinus and level I, II, and III lymph nodes; indicating regional infiltration. Due to the extent of the infiltration, left orbital exenteration and postoperative radiotherapy was recommended. However, the patient insisted on globe-sparing treatment despite the consequent poor prognosis and underwent concurrent chemoradiotherapy in place of the operation. The patient received a total of 10 cycles of weekly fluorouracil and cisplatin-based chemotherapy with tomotherapy (69.96 Gy) for the gross tumor and surrounding lymph nodes for a period of 2 months. The treatment was well-tolerated with no significant adverse reactions, aside from mild general weakness. Follow up imaging studies after 3 and 6 months showed that the main mass had significantly decreased in size as well as a positive number of lymph nodes, indicating near-total or total response to therapy.

However, 5 months after treatment, the patient returned to the clinic with complaints of upper eyelid induration and edema with an accompanying skin lesion on the ipsilateral cheek (Fig. 1A). A physical examination revealed a coin-sized erythematous plaque with induration. There was no palpable cervical lymphadenopathy. A skin biopsy revealed abnormal aggregates of the glandular structure in the epidermis and lower dermis with an infiltrative pattern (Fig. 2A). On high power view, well-formed glandular and ductal structures showed malignant epithelial cells with prominent nuclei (Fig. 2B). Immunohistochemical staining was performed

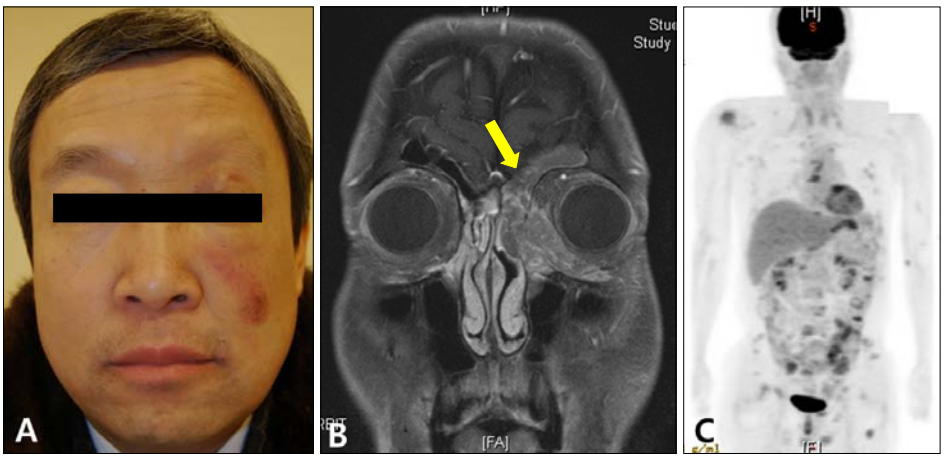

Fig. 1. Photograph, magnetic resonance (MRI) and positron emission tomography-computed tomography (PET-CT) scan of the patient. (A) Solitary coin sized erythematous to purple plaque on Lt. cheek. (B) MRI scan demonstrating local recurrence on the left medial orbital wall. (C) PET-CT scan revealed newly developed numerous osteolytic lesions.

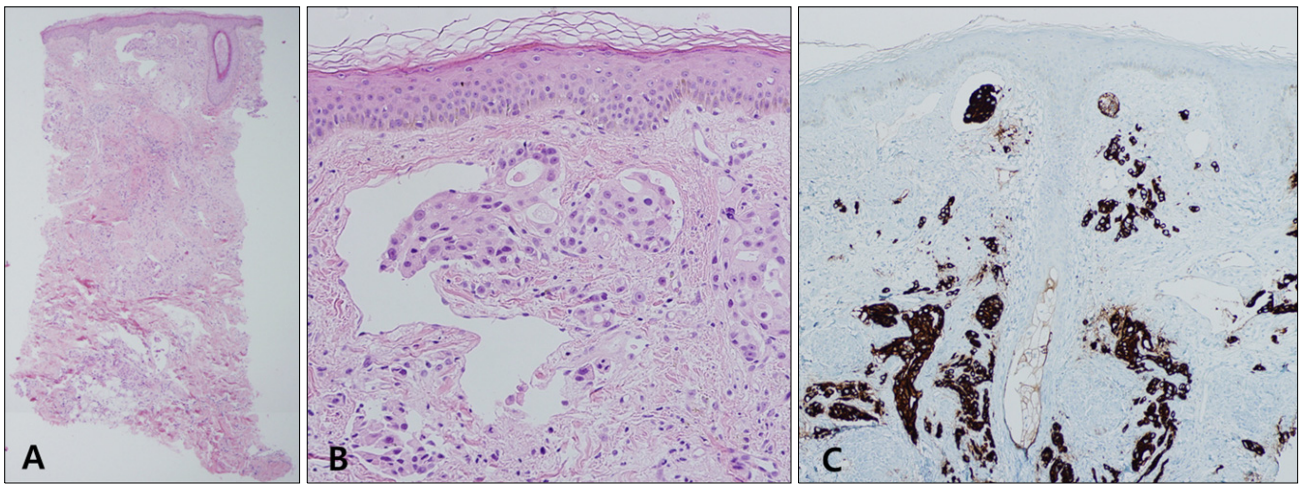

Fig. 2. (A) Abnormal aggregates of glandular structure in epidermis and lower dermis with infiltrative growth (H&E, ×40). (B) Well-formed glandular and ductal structures composed of malignant epithelial cells with prominent nuclei (H&E, ×200). (C) The neoplastic cells showed positive for CK7 and negative for CK20 or CDX-2 (CK7, ×100).

to exclude the possibility of metastatic colon adenocarcinoma. Neoplastic cells stained positive for CK7 and negative for CK20 and CDX-2, suggesting a metastatic lesion originating from a ductal adenocarcinoma of the lacrimal gland (Fig. 2C). An MRI scan revealed recurrence of the primary orbital tumor on the left medial orbital wall. Subsequent imaging study for the purposes of systemic evaluation revealed numerous newly- developed osteolytic lesions in the axial skeleton and proximal appendicular bones (Fig. 1B, C). The patient was treated again with a regimen of etoposide and cisplatin. He concomitantly received radiotherapy under a palliative setting and is under close observation.

DISCUSSION

Space occupying lacrimal gland lesions are generally inflammatory and lymphocytic, while epithelial tumors account for just 20 to 30% of all cases. Primary epithelial tumors arising in the orbit include benign mixed tumors or pleomorphic adenoma, adenoid cystic carcinoma, and adenocarcinoma; and the latter is the rarest subtype with an aggressive behavior[6]. PDALG was first documented by Katz et al.[7] in 1996 and since then, there have been few reported cases. There is a slight male predominance with a tendency to occur in the older population, however, its clinicopathologic profile is still poorly understood. The tumor often manifests as a rapidly-growing mass causing a wide range of visual symptoms including diplopia, ptosis, globe displacement, and visual loss. The clinical course shows early infiltration to the surrounding nasal cavity, paranasal sinuses, and other soft tissue structures[8]. Due to its aggressive nature, the recommended treatment for PDALG involves exenteration or en bloc resection of the tumor mass with regional lymph node dissection, followed by radiation therapy as soon as histological confirmation is achieved.

Cutaneous metastasis has not yet been reported in Korean patients with PDALG. Metastatic lesions most commonly involve the lungs and other internal organs. There has been one previous report of cutaneous metastasis of PDALG presenting as an erythematous patch on the chest[9]. In patients with adenocarcinoma of the internal organs, cutaneous metastasis develops in 0.7～10% of cases, with varying incidence depending on the primary tumor subtype[10]. The prevalence of cutaneous metastasis of the visceral tumor amounts to 2% of all skin tumors. This usually presents as solitary, discrete, painless, and freely-movable plaques or nodules with sudden onset, preferentially occurring on surfaces located close to the site of the primary tumor. The most frequent primary origins in order of frequency are: the lungs, the colon and rectum, the breast, and the kidneys[11]. As an adenocarcinoma is the basic malignant neoplasm which can arise from all glandular structures, diagnosis is almost entirely dependent on histopathologic features, and immunohistochemical evaluation is mandatory for accurate assignment.

As our patient had a history of colorectal adenocarcinoma; immunohistochemistry was performed for CK7, CK20, and CDX-2; with positive staining obtained for CK7. Metastatic adenocarcinoma of colorectal origin is known to express CDX-2 and stain negative for CK7 with very high sensitivity and specificity[12-14]. Based on the patient's clinical course and immunohistochemical profile, the possibility of metastatic adenocarcinoma originating from the colon was excluded.

Given the infrequent incidence of malignant lacrimal gland tumors, their immunohistochemical features are yet to be elucidated. Of the lacrimal gland epithelial tumors, PDALG shows more prominent mucin content during specimen examination, which can be demonstrated with mucicarmine and alcian blue stains. There exists a similarity between salivary and lacrimal gland tumors, with similar classification according to histologic features. Both tumors show pleomorphic cells with many mitotic figures arranged in sheets and cords with variable amounts of mucin production[15]. Immunohistochemical studies of salivary duct carcinomas have shown that approximately 93% of tumors express androgen receptors, while expression of estrogen and progesterone receptors is rare. A recent case series of five patients reviewed the clinicopathologic profiles and found that PDALG was positive for androgen receptors in all cases, with negative expression for estrogen and progesterone[16]. Thus, further understanding of the histopathological and immunohistochemical characteristics may help to define this tumor's pathogenesis and lead to successful treatment outcomes.

In summary, our case illustrates the first Korean case of an orbital adenocarcinoma presenting as a metastatic skin lesion, after showing a significant clinical response to concurrent chemoradiotherapy. Metastatic spread to the skin is rare and may suggest widespread metastatic disease, resulting in a poor prognosis. Immunohistochemical findings are essential to the diagnosis and further understanding of its pathogenesis can be postulated with supporting characteristic biomarkers.

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