OLGU SUNUMU CASE REPORT

Salivary Duct Carcinoma Ex Pleomorphic Adenoma of the Parotid Gland: A Case Report

Parotis Glandı Pleomorfik Adenomundan Gelişen Tükürük Kanalı Karsinomu

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ABSTRACT Salivary duct carcinoma is a highly malignant salivary gland tumor with aggressive clinical behavior that has similar histological features with invasive ductal carcinoma of the breast. Malignant salivary gland tumors are rarely derived from preexisting pleomorphic adenoma (PA). Carcinoma ex PA is defined as a malignant epithelial neoplasm arising in association with a primary or recurrent PA and it accounts for approximately 2-5% of all PAs. Most of these tumors are located in the major salivary glands, particularly in the parotid gland. Fine-needle aspiration (FNA) biopsy is widely used as a diagnostic tool for the initial evaluation of parotid gland masses. The cytologic appearance of most PAs are characteristic. Although it is not difficult to recognize a PA, malignant tumors originating from PA may present a diagnostic problem. We report here a case of salivary ductal carcinoma ex PA of the parotid gland diagnosed by FNA biopsy and discuss the possible problems in diagnosis.

Key Words: Adenoma, pleomorphic; salivary gland neoplasms; biopsy, fine-needle

ÖZET Tükürük kanalı karsinomu memenin invaziv duktal karsinomuna benzer histolojik özelliklere sahip agresif klinik davranış gösteren malign tükrük bezi tümörüdür. Malign tükrük bezi tümörleri mevcut pleomorfik adenom zemininden oldukça nadir olarak gelişir. Primer veya rekürren pleomorfik adenom zemininden gelişen malign epitelyal neoplaziler tüm pleomorfik adenomların %2-5'ini oluşturur. Bu tümörlerin çoğu majör tükrük bezlerinde, sıklıkla parotisde lokalize olur. Parotis kitlelerinin ilk değerlendirilmesinde ince iğne aspirasyon biyopsisi sıklıkla kullanılan bir diagnostik işlemdir. Birçok pleomorfik adenomun sitolojik görüntüsü karakteristik olmasına rağmen pleomorfik adenom zemininde gelişen malign tümörler tanıda sorun yaratabilir.

Anahtar Kelimeler: Pleomorfik adenoma; tükrük bezi neoplazileri; ince iğne aspirasyon biyopsisi

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Salivary duct carcinomas (SDCs) of salivary gland origin are uncommon neoplasms and were first described by Kleinsasser et al. in 1968.[1,2] Only about 20-23% of SDCs had pre-existing PA. In carcinoma ex pleomorphic adenoma (CXPA) epithelial malignancy may develop from a primary or a recurrent PA. Most of these tumors are located in the major salivary glands, particularly in the parotid gland.

Epithelial malignancies reported as carcinoma arising from PA have a wide spectrum of histological patterns such as adenocarcinomas not otherwise specified, poorly differentiated adenocarcinomas, SDCs, adenoid cystic carcinomas, polymorphous low-grade adenocarcinomas and myoepithelial

carcinomas.[1] Frequently only one of these histological patterns are observed in CXPA.

FNA biopsy is widely used as a diagnostic procedure in the initial evaluation of parotid gland masses. Although the cytologic appearance of most PAs are characteristic, malignant tumors originating from PA may cause a problem in diagnosis. We report here a case of salivary duct carcinoma ex pleomorphic adenoma of parotid gland.

CASE REPORT

A 62-year old man presented with a 10 years history of a left parotid mass. The gland had slowly increased in size and it was asymptomatic until one month before when it started to grow rapidly. Clinical examination revealed a firm, immobile 4 x 3 x 2 cm mass of the left parotid gland. Head and neck CT revealed a mass of 4 cm in its longest dimension with irregular contours of the superficial lobe of the left parotid gland. Based on these findings FNA biopsy was performed.

The FNA biopsy revealed a hypercellular smear composed of sheets of epithelial cells, which have big, ovoid nuclei and mostly uniform chromatin pattern. Spindle shaped mesenchymal cells and large amount of myxoid background were also observed. There were some epithelial cells showing nuclear enlargement and hyperchromasia to a worrying degree (Figure 1). Epithelial cells forming cohesive sheets, groups and papillary structures were also seen. In addition to these groups, there were many single cells in the myxoid background. Therefore, PA diagnosis was made. However, due to the bizarre neoplastic cells seen in the FNA biopsy material, a carcinoma in PA was suspected, surgical excision was offered and the tumor was completely excised. As the intraoperative pathologic examination revealed malignancy, complete resection of the tumor and parotid gland, a part of the external auditory canal and left neck dissection were performed.

Grossly, there was an encapsulated, solid tumor measuring 4 cm in the longest diameter. However, on sections we observed an irregular, solid, gray-white tumoral mass, which had indistinctive

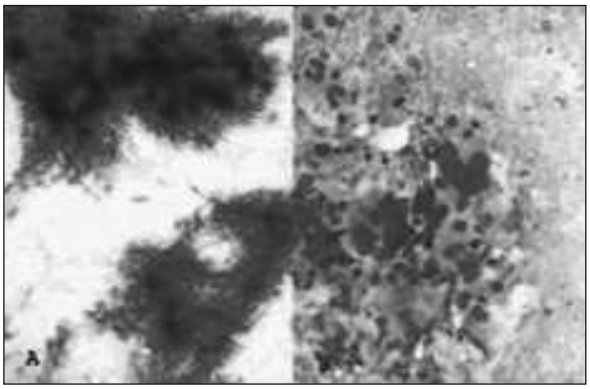

FIGURE 1: A. Hypercellular smear composed of sheets of epithelial cells which have big, ovoid nuclei and mostly uniform chromatin pattern in a myxoid background. (X10, May Grunwald-Giemsa) **B.** There were some epithelial cells representing nuclear enlargement and hyperchromasia. (X40, May Grunwald-Giemsa).

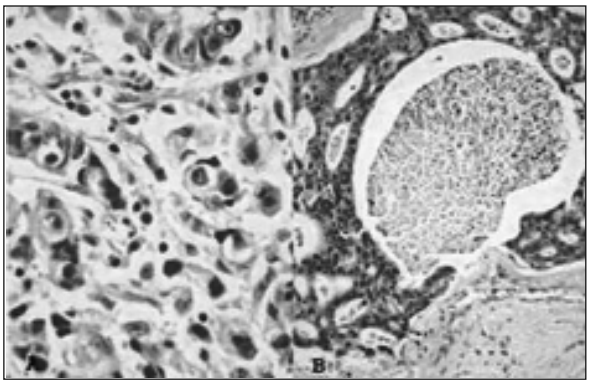

FIGURE 2: A. There were small glands and cords infiltrating prominent desmoplastic stroma (X100, H&E) **B.** Cribriform growth patterns and areas of comedocarcinoma were also observed. (X20, H&E).

borders around the encapsulated tumor. Microscopic examination revealed that the encapsulated tumor was a typical PA. There were small glands and cords infiltrating prominent desmoplastic stroma in wide areas neighboring this typical PA. In some areas, solid and cribriform growth patterns were seen and areas of comedocarcinoma were also observed (Figure 2). Histologically the tumor reminded a breast carcinoma and both invasive and intraductal components were detected. The adjacent parotid gland and striated muscle were invaded. Extensive perineural spread and vascular invasion were also observed. Individually, tumor cells were polygonal with enlarged nuclei and abundant cytoplasm, and they presented occasional mitoses and cellular pleomorphism. The nuclei appeared vesicular and highly pleomorphic and of-

ten contained prominent or inclusion-like nucleoli. Immunhistochemically high molecular weight cytokeratin and carcinoembryonic antigen (CEA) were positive; actin, vimentin, S-100 protein, prostat-specific antigen, estrogen and progesteron receptors were negative.

DISCUSSION

Malignant mixed tumors of the parotid gland are rare and include three subtypes. CXPA is the most common, whereas carcinosarcoma and metastasizing PA are less frequent.[3] SDC is an uncommon adenocarcinoma of the salivary gland first described by Kleinsasser et al. in 1968.[1,2] It is thought to be a distinct malignancy because of its highly aggressive behavior, high rate of recurrence, and nodal and distant metastases.[1,2,4,5] This tumor was seen more often in elderly men and mostly in the parotid gland. Histologically it demonstrates many similarities to breast carcinoma of the ductal type, which presents intraductal and invasive components. The intraductal component is described as a papillary or solid growth pattern, often with central necrosis. The invasive pattern is characterized by small glands and cords associated with a marked desmoplastic stroma.[1,2,4,6]

CXPA is a mixed tumor, with a second malignant neoplasm developing from the epithelial component of a pre-existing PA. Carcinomatous element displays both cytological abnormalities and infiltration of the surrounding tissue. Histological evidence for carcinomatous transformation in PA is as follows:

1- Unusual destructive and infiltrative growth

2- Abnormal nuclear changes with mitoses

3- Necrosis

4- Hemorrhage

5- Dystrophic calcification

6- Vascular and/or neural invasion; and

7- Local and distant metastasis.[6]

The mechanism of malignant transformation of PAs were discussed by a number of authors. Malignancy may appear in either long-standing or recurrent PAs.[3] Felix et al. reported that the basement membrane components like laminin, type IV collagen and tenascin deposition in the extracellular matrix were associated with malignant transformation of PAs as well as with their biological progression.[7] Pre-existence of a PA were noted in 20% and 23% of the cases reported by Delgado et al and Lewis et al, respectively.[8]

In this case, evaluation of FNA biopsy slides revealed a hypercellular smear that was composed of sheets of epithelial cells, which had large, ovoid nuclei and mostly uniform chromatin pattern. Spindle shaped mesenchymal cells and a large amount of myxoid background were also observed. Since we observed only the benign counterpart of the tumor in most areas, it was hard to relate this tumor with a SDC. However, some epithelial cells had nuclear enlargement and hyperchromasia enough to cause suspicion. Epithelial cells forming cohesive sheets, groups and papillary structures were also seen. Although PA diagnosis was made based on these findings, the tumor was suspected to be carcinoma in PA due to the bizarre neoplastic cells seen in the FNA biopsy material.

The nuclear features of all cell types in usual PA a are small or absent, and mitoses are few. However, very occasional examples of PA are densely cellular and display marked cytological atypia.[9] This is reflected in FNA biopsy specimens in which the epithelial cells demonstrate loss of cohesion and nuclear enlargement and hyperchromasia to a worrying degree. Takeda reported that these bizarre cells seen in benign PA were neoplastic myoepithelial cells in nature and they were scattered in solid-proliferating areas and myxoid areas.[9] It is important not to over diagnose such changes. However, if PA with bizarre neoplastic cells and hypercellularity were included in a biopsy specimen the correct diagnosis would have been missed.

Another rare but confusing situation is infarction of PA. Although spontaneous infarction of PA is uncommon, post-FNA infarction in PA of the parotid gland is well documented. Individual and clusters of small cells with dark, degenerated nuc-

lei in a necrotic background were seen in FNA biopsy specimens in such cases. These features may cause major diagnostic problems in cytologic materials due to necrosis and atypical squamous metaplastic cells.[10] Although there were epithelial cells forming cohesive sheets, groups and papillary structures showing slight nuclear atypia, no necrotic background or atypical squamous metaplastic cells were seen in our slides. Thus, we excluded the diagnosis of infarction of PA.

The histological diagnosis of CXPA depends on the recognition of elements of a benign PA admixed with a carcinomatous cell population.[11] Reliable separation of non-invasive CXPA is difficult and not always possible on FNA biopsy materials. The cellularity, degree of nuclear atypia and presence of necrosis may be helpful features in distinguishing between the two entities. Necrosis of the neoplastic tissue should be considered as an alarming sign that indicates malignant transformation.[10]

Immunohistochemistry was believed to be of potential assistance in the diagnosis of salivary gland tumors and in the prediction of histogenesis. In our case, immunohistochemical staining in carcinoma areas showed negative reaction for actin, vimentin, S-100 protein, prostate-specific antigen, estrogen and progesteron receptors. High molecular weight cytokeratin and CEA staining were positive. Therefore, immunhistochemistry proved the disappearance of myoepithelial cells in carcinoma areas. In one study, Araujo et al. suggested that the presence of CK14 positive basal cells surrounding tumor islands might be important to identify the in-situ intraductal growth pattern.[12] In another study, Skalova et al. reported that over expression of HER2/neu protein was a useful marker of malignant transformation in PAs.[13] Thus, when obvious invasion was not detected in a PA, CK14 and/or HER2/neu protein would be helpful to identify the malignant transformation.

Cytological features of SDC described by investigators included relatively monomorphic tumor cells forming cohesive clusters and sheets, a cribriform pattern, hyperchromatic and eccentrically located nuclei, large and prominent nucleoli, intranuclear holes and a necrotic background.[1] Since in most areas we observed only the benign counterpart of the tumor, only a few of these criteria were seen in our FNA biopsy slides. After making a diagnosis of CXPA mucoepidermoid carcinoma, oncocytic neoplasms, acinic-cell carcinoma, terminal duct carcinoma and adenoid cystic carcinoma should be considered in the cytological differential diagnosis of SDC.[1]

In our case, obvious elements of PA could still be identified in the aspirate. Besides sheets of epithelial cells, which hah large, ovoid nuclei and uniform chromatin pattern were observed; some epithelial cells showed nuclear enlargement and hyperchromasia. Although it is known that in some benign PAs, neoplastic bizarre cells are seen and these cells can be misdiagnosed as malignant change; the degree of cellularity and nuclear atypia should be alarming for malignancy

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