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CASE REPORT

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Histopathological case report of high grade salivary duct carcinoma

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Abstract

The case of a 39-year-old man with slowly growing mass in the superior part of left parotid region is described. Patient presented neurological symptoms including hypomobility of lower left eyelid and inability of complete closure of left side eyelids resulting in conjunctivitis and hyperlacrimation. Routine physical examination supported by image and laboratory tests was performed. Pathomorphological results of hematoxylin and eosin staining as well immunohistochemical examination in view of clinical presentation pointed to diagnosis of high grade salivary duct carcinoma. Rare incidence, histological view similar to breast cancer and body localization are sufficient reasons for further analyses and descriptions of this type of lesions. *(Folia Histochemica et Cytobiologica 2015, Vol. 53, No. 4, 342–345)*

Key words: salivary duct carcinoma; salivary gland; parotid malignancy

Introduction

The salivary duct carcinoma (SDC) is an uncommon aggressive malignancy localized in the head and neck region most commonly involving parotid gland. It was described for the first time by Kleinsasser *et al.* in 1968 and due to rather rare incidence insufficient descriptions of SDC can be found in literature [1, 2]. Clinical symptoms may not be present, while if they occur, mostly often pain, swelling and paresis are reported. Histopathologically it resembles high grade ductal breast carcinoma structure with frequently observed perineural spread, lymphovascular invasion with intraductal emboli. Surgery is a common treatment of choice followed by adjuvant radiotherapy, supplemented by chemotherapy in advanced cases. Prognosis is rather poor and is strongly associated with clinical course [1]. Due to many similarities with breast cancer as well still incoherent diagnostic and therapeutic procedures we present our case study.

Case report

The 39-year-old man complaining of decreased mobility of lower left eyelid and painless swelling of the left preauricular area was admitted to the surgical department. Within the last three months, the patient was diagnosed and treated for sialoadenitis whereas present symptoms occurred within three weeks. The physical examination revealed left eye lagophtalmus (inability of complete closure of eyelids) and lower eyelid hypomobility resulting in conjunctivitis and

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hyperlacrimation. The eye movement inability, neither diplopia were not present. The left parotid gland fulfilled the parotideomasseterical region of the same side in a form of solid, firm mass. Cervical lymphadenopathy was absent. Problems with mouth opening, mastication and local tenderness as well as intraoral pathology were not observed. Overall patient's condition was good, chronic diseases and pharmacotherapy were not reported, family medical history (including breast cancer) was irrelevant. Magnetic resonance image examination revealed tumor of lobular structure (22 × 21 × 27 mm) in dorsocranial area of the left parotid glad adjacent to the left mandibular condyle and the ear canal. Margins were clearly defined, without any infiltration and centrally located necrosis. The unaffected salivary gland neighboring the tumor revealed slightly higher density in computed tomography (CT) scans whereas in the central part of parotid gland showed incorporated hypodensity area (diameter 6 mm) what finally was diagnosed by radiologists as an active or metastatic lymph node. Other lymph nodes in CT examination didn't reveal any features of pathology. The chest X-ray image was normal. Radical parotidectomy was selected as a treatment of choice due to signs and symptoms of malignant process (partial facial nerve paralysis, tumorous mass with central necrosis and suspicious lymph node metastasis). The location of the tumor enabled to save buccal, mandibular and cervical branches of the left facial nerve, whereas temporal and zygomatic were resected with neoplastically changed masses. Specimen consisted of lipomesenchymal masses with a visible structures of parotid salivary gland and several yellow-white solid bearings from 0.3–1.3 cm in diameter. The dissected material was sent for histopathological examination while soft tissue defect was closed locally.

Routine hematoxylin and eosin (H & E) staining performed on paraffin embedded material revealed lipomatous salivary gland structure infiltrated by high grade carcinoma with an extensive perineural spreading and invasion into lymphatic vessels. The presence of an intraductal component with comedonecrosis (Figure 1) was observed in approximately 10% of tumor mass. A desmoplastic reaction was present in the vicinity of the neoplasm. Out of the three identified/resected lymph nodes, two were metastatic. The neoplastically changed tissue was composed of a population of polygonal elements with a fine glandular and/or a homogenous eosinophilic cytoplasm. The nuclei were mostly anisomorphic within prominent nucleoli (focally multiplied). A rich mitotic activity (including atypical mitoses) was evident (10–20 *per* 10 high power fields). For set up a final diagnosis in view of above described results the panel of 11 markers was used. All procedures were conducted according to running immunohistochemical protocols. Direct monoclonal antibodies against Ki-67 (clone MIB-1, 1:100), cytokeratin (CK, clone AE1/AE3, 1:100), CK 7 (clone OV-TL12/30, 1:100), carcinoembrionic antigen (CEA, clone II-7, 1:50), estrogen receptor (ER, clone 1D5, 1:50), progesterone receptor (PR, clone PgR636, 1:200), prostatic specific antigen (PSA, clone ER-PR8, 1:50), p63 (clone 4A4, 1:50), calponin-1 (clone EP789Y, 1:100) and polyclonal against S100 protein (1:600) and HER-2 (1:400) were used. All reagents and antibodies except anti-p63 and anti-calponin (Zytomed, Berlin, Germany) were obtained from DakoCytomation, Glostrup, Denmark. The proliferation activity index measured by Ki-67 expression was 50%. The evident positive reaction was observed for CK, CK 7 and CEA while for HER-2 it was intermediate. No expression of ER, PR, PSA, p63, s100 and calponin-1 was observed. Final diagnosis was salivary duct carcinoma with pathological advancement classification pT2, pN2, pMx and grade of histological malignancy G3.

During the postoperative recovery period the patient underwent adjuvant four field simultaneous integrated boost radiotherapy with a modulated intensity of the beam. The total dose was counted as 54–60–66 Gy in 30 fractions. A complete left facial nerve paralysis with good response to the rehabilitation procedures was observed. During 12 months of follow-up period muscles innervated by unresected branches of the left facial nerve restored their function. A permanent left eye lagophtalmos causes a reasonable discomfort for the patient.

State of the art

SDC is an uncommon aggressive malignancy localized in the head and neck region. Up to 80% of cases occurs in parotid, in which they are mostly located in lateral (superficial) lobe. It comprises approx. 15–23% of tumors located in parotid. Annual incidence of malignant tumors varies from 0.4 to 2.6 cases/100,000 population *per* year with visible geographic variations in frequency of tumor type. It is observed 4 times often in men occurring after fifth decade of life and it represents approximately 9% of all salivary malignancies [1]. It has been suggested that approximately 25% of SDC arose from pre-existing pleomorphic adenoma [3]. Development of salivary duct tumors was assessed in view of viral infections (mostly Epstein-Barr virus, cytomegalovirus and SV40) but results are equivocal [1, 4]. Whereas involvement of ionizing radiation and increased expression of hormone receptors (ER, PR and AR; androgen receptor) in

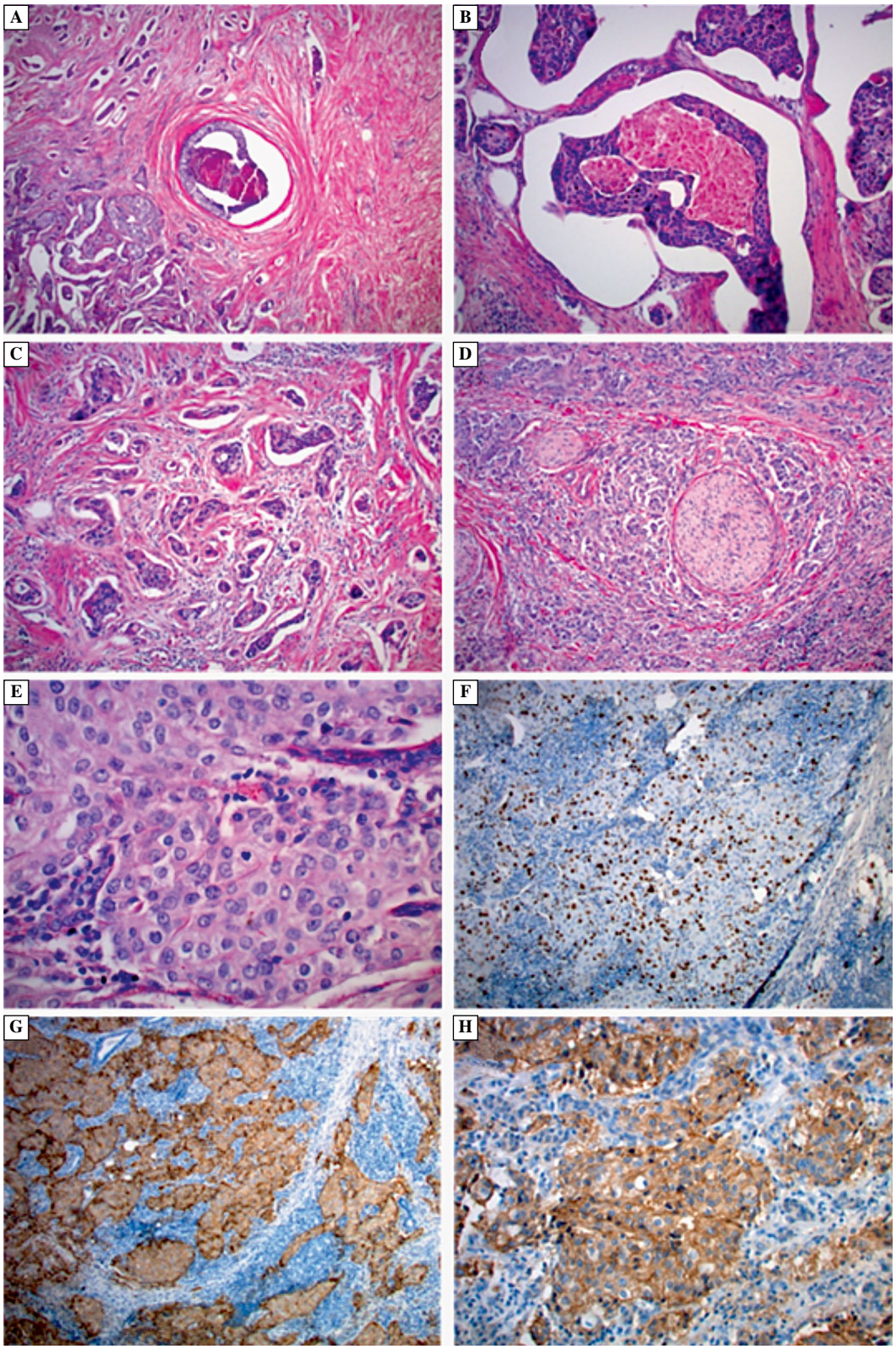

Figure 1. Microphotographs of routine hematoxylin and eosin staining (**A–E**) and immunohistochemical reactions (**F–H**) showing features of salivary duct carcinoma (SDC). A, B. Intraductal component of SDC with comedonecrosis (×40 and ×100, respectively); C. Infiltrating growth of SDC (×100); D. Perineural invasion of SDC (×100); E. High mitotic activity, cancer nest (×400). Immunohistochemical nuclear expression of Ki-67 (F; ×100) and cytoplasmic expression of carcinoembrionic antigen (G; ×40) and HER-2 (H; ×200)

salivary tissue is strongly evidenced [5, 6]. No association between tobacco use and alcohol consumption was found. Symptoms vary from massive edema, pain, inflammation, mastication and vocalization problems in aggressive forms of SDC, to even asymptomatic in slowly growing entities. Normally SDC is characterized by an invasive local growth with early distant metastases. The radiographic examination gives unspecific results and should be rather used to verify localization during diagnostics instead of setting a diagnosis. Ultrasound, CT and MRI examinations give much more precise results revealing typical features of SDC [7]. The final diagnosis is based on the regular histopathological examination, because fine needle aspiration biopsy, which sometimes is performed may not give convincing results. Instead of routine H & E stained sections analyzed by pathomorphologist who is searching for typical features *i.e.* tumor nests, perineural spread, intraductal emboli, additional immunohistochemical reactions may be performed. Due to morphologic and molecular similarity to breast cancer, histopathological as well molecular profiling should be conducted to provide effective diagnostics and treatment. Consequently, Ki-67, ER, PR, HER-2 markers should be tested, with additional set of AR, CK, p53 and epithelial growth factor receptor, as proposed by other researchers [4, 8, 9]. The classification of salivary gland tumors is rapidly evolving with description of new entities, such as mammary analogue secretory carcinoma (MASC), whereas entities, such as salivary duct carcinoma, are being increasingly recognized with improved understanding of their molecular characteristics [10]. Genetic events which might occur in SDC, *i.e.* loss of heterozygosity associated with expression of epithelial growth factor receptor family proteins (*e.g.* HER-2) and p53 genes which result in the overexpression of the protein, what potentially may be used for therapy [11, 12]. The first therapeutic step comprises the radical surgery intervention with suspicious lymph node dissection, followed by radiotherapy. The chemotherapy is reserved for metastatic stages of SDC. The results of a recent studies have suggested that HER-2 overexpression is associated with a poor prognosis. Therefore, HER-2 status should be evaluated at least in the presence of advanced SDC, and targeted therapy should be considered in the adjuvant setting [13]. During regular course of the disease as well after recommended treatment whole or partial facial nerve paralysis is very often observed, even up to 60% of cases [1, 5, 7]. Prognosis is relatively poor and most strongly correlates with clinical stage. Despite aggressive surgery and additional radiotherapy approximately one third of patients develop local recurrence and nearly 50% distant metastases. 65% of patients dies of SDC usually within 4 years after diagnosis [1, 14]. Further analyses of this neoplastic entity may be useful in diagnostic process as well in therapeutic usage.

References

1. Barnes L, Eveson JW, Reichart P, Sidransky D (eds). *Pathology and Genetics of Head and Neck Tumours*. Lyon: IARC Press; 2005:236–237.
2. Kleinsasser O, Klein HJ, Hübner G. Salivary duct carcinoma. A group of salivary gland tumors analogous to mammary duct carcinoma. *Arch Klin Exp Ohren Nasen Kehlkopfheilkd*. 1968;192:100–105. PMID: 4301301.
3. Nishijima T, Yamamoto H, Nakano T et al. Dual gain of HER2 and EGFR gene copy numbers impacts the prognosis of carcinoma ex pleomorphic adenoma. *Hum Pathol.* 2015;46:1730–1743. doi: 10.1016/j.humpath.2015.07.014.
4. Cerilli LA, Holst VA, Brandwein MS, Stoler MH, Mills SE. Sinonasal undifferentiated carcinoma: immunohistochemical profile and lack of EBV association. *Am J Surg Pathol.* 2001;25:156–163. PMID: 11176064.
5. Williams L, Thompson LD, Seethala RR et al. Salivary duct carcinoma: the predominance of apocrine morphology, prevalence of histologic variants, and androgen receptor expression. *Am J Surg Pathol*. 2015;39:705–713. doi: 10.1097/PAS.0000000000000413.
6. Nasser SM, Faquin WC, Dayal Y. Expression of androgen, estrogen, and progesterone receptors in salivary gland tumors. Frequent expression of androgen receptor in a subset of malignant salivary gland tumors. *Am J Clin Pathol.* 2003;11:9801–9806. doi: 10.1309/RVTP1G0Q727WJUQD.
7. Fenesan DI, Lenghel M, Băciuţ G. Ultrasound and CT imaging features in a patient with salivary duct carcinoma of the parotid gland: a case report with literature review. *Med Ultrason*. 2015;17:119–122. doi: 10.11152/mu.2013.2066.171.dif.
8. Masubuchi T, Tada Y, Maruya S et al. Clinicopathological significance of androgen receptor, HER2, Ki-67 and EGFR expressions in salivary duct carcinoma. *Int J Clin Oncol.* 2015;20:35–44. doi: 10.1007/s10147-014-0674-6.
9. Simpson RH, Skálová A, Di Palma S, Leivo I. Recent advances in the diagnostic pathology of salivary carcinomas. *Virchows Arch*. 2014;465:371–384. doi: 10.1007/s00428-014-1639-x.
10. Gupta R, Balasubramanian D, Clark JR. Salivary gland lesions: recent advances and evolving concepts. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015;119:661–674. doi: 10.1016/j.oooo.2015.02.481.
11. Hunt JL. An update on molecular diagnostics of squamous and salivary gland tumors of the head and neck. *Arch Pathol Lab Med.* 2011;135:602–609. doi: 10.1043/2010-0655-RAIR.1.
12. Jaehne M, Jäkel KT, Röser K, Ussmüller J, Löning T. About the prognostic value of Her-2 gene-amplification and cell-proliferation in salivary duct carcinoma of the major salivary glands — a pilot-study. *Laryngorhinootologie*. 2001;80:525–529. PMID: 11555785.
13. Lee JS, Kwon OJ, Park JJ, Seo JH. Salivary duct carcinoma of the parotid gland: is adjuvant HER-2-targeted therapy required? *J Oral Maxillofac Surg.* 2014;72:1023–1031. doi: 10.1016/j.joms.2013.11.014
14. Han MW, Roh JL, Choi SH. Prognostic factors and outcome analysis of salivary duct carcinoma. *Auris Nasus Larynx*. 2015;42:472–477. doi: 10.1016/j.anl.2015.04.005.

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