Case Report

Breast metastasis of salivary duct carcinoma in a patient: a case report

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Abstract: Salivary duct carcinoma (SDC) is a rare and highly aggressive cancer with a worse prognosis that has been demonstrated to exhibit invasive growth with early regional and distant metastasis. Breast metastasis of salivary duct carcinoma rarely occurs. Here, we reported a case of submandibular gland SDC metastasis to breast in a 64-year-old female patient who underwent a complete removal of a right submandibular gland and radical neck dissection in 2010 and undergo adjuvant radiotherapy and chemotherapy. Two years later, MRI identified mass in multiple regions, including bilateral cervical, bilateral breast, supraclavicular fossa, thyroid gland and the fourth thoracic vertebra. A fine-needle aspiration biopsy of the right breast was performed. SDC was confirmed by IHC analysis of the breast aspiration specimen.

Keywords: Salivary duct carcinoma, salivary gland, metastasis, breast

Case report

A 64-year-old Chinese female discovered an abnormal but painless lump (mass) in her right submandibular gland in October 2010. The size of the mass increased over one month. In November 2010, the patient was admitted to our institution for a magnetic resonance imaging (MRI). MRI of the jaw and face revealed a heterogeneous mass in her right submandibular gland, measuring 2.0 × 4.5 cm, and multiple enlarged cervical lymph nodes on the right side extending to the lymph nodes of carotid sheath. The patient subsequently underwent fine-needle aspiration of the right submandibular gland mass, cytological examination detected salivary ductal carcinoma (SDC), a highly malignant salivary gland tumor with aggressive clinical behaviors. Therefore, a complete removal of a right submandibular gland and radical neck dissection were performed. Histopathologic examination of the surgical specimen showed SDC of the submandibular gland and 100% cervical lymph nodes metastasis (8/8). The patient received adjuvant radiotherapy and chemotherapy after surgery and visited hospital regularly for follow-up. After two years, in January 2012, she noticed an enlarged lymph node in the right neck with pain that feels having a stiff neck. MRI of the neck, chest and upper abdominal identified metastasis in multiple regions, including bilateral cervical, bilateral breast, supraclavicular fossa, thyroid gland and the fourth thoracic vertebra. The patient was diagnosed a metastatic malignancy, and received palliative chemotherapy. One and a half years later (August 2013), a painless mass was found in the left breast, and the size increased gradually. In October 2013, a painless mass was also found in the right breast (Figure 1). Figure 2 shows metastasis in several regions identified by PET-CT, including bilateral cervical, bilateral breast, supraclavicular fossa, thyroid gland and the fourth thoracic vertebra (Figure 2).

Pathologic findings

A fine-needle aspiration biopsy of the right breast was performed. Micrograph of the needle aspiration revealed the presence of a monomorphic population of cells in a broad two-dimensional flat sheet, with occasional papillae and gland-like structure formation. The individual cells were large and polygonal, with abundant and finely granular cytoplasm. The nuclei were round to oval with moderate pleomor-
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Figure 1. A. Multiple enlarged lymph nodes in right neck; B, C. Markedly enlarged bilateral breast with lumps at different sizes, inducing multiple hard lumps.

Figure 2. Positron emission tomography (PET) - computed tomography (CT) scan. PET - CT showed metastasis in multiple regions, including the right side of the jaw, bilateral neck, bilateral breast and bilateral armpit.

phism and prominent nucleoli. Atypical nuclei with prominent nucleoli and scattered mitotic were shown in Figure 3. Microscopic examination of the paraffin-embedded aspirates showed tumor fragments focally, resulting in a cribriform appearance. The large-sized tumor cells were shown to have abundant finely granular cytoplasm with uniform round to oval nuclei. Their nuclei are relatively large (1-2 small nucleoli per nucleus) and showed mild pleomorphism. Immunohistochemistry (IHC) stains of the tumor cells were positive for
human epidermal growth factor receptor 2 (her-2/neu) and gross cystic disease fluid protein-15 (GCDFP-15), and negative for immunoreactivity to progesterone receptor (PR), estrogen receptor (ER) and mammaglobin receptor (Figure 4). SDC was confirmed by IHC analysis of the breast aspiration specimen.

**Discussion**

SDC is a distinctive primary neoplasm of the salivary gland first described by Kleinsasser et al. in 1968 [1]. The term was selected because of its resemblance to ductal carcinoma of the breast. However, the use of this term has been reportedly confusing to pathologists and clinicians, even though the majority of salivary duct carcinoma arises from the ductal system. The parotid gland is the most common occurrence site, accounting for over 80% of all cases. Occurrence in submandibular glands and minor salivary gland sites are involved in a minority of cases. In such cases, painless but rapidly growing parotid mass were often observed, which may be accompanied by facial nerve deficits and cervical lymphadenopathy. It comprises 5-6% of salivary gland carcinomas and affects males over 50 yr more commonly, although it may occur at any age. Therefore, SDC is regarded as a high-grade malignant tumor, and has been demonstrated to have a propensity for invasive growth with early regional metastasis.

In addition to regional metastasis, distant metastasis to different sites, such as lungs, bone, liver, thyroid adrenal gland, brain, and skin [2-5] through lymphatic and hematogenous routes have also been observed, which may contribute to an overall poor prognosis.

The cytological literature relating to SDC is confined to single cases or small case series [6, 7]. Various architectures of growth patterns have been well described, including cribriform, trabecular, acinar and papillary formations [8]. The individual polygonal-to-cuboidal tumor cells are large and monomorphic to pleomorphic, with abundant and finely granular cytoplasm. The nuclei usually exhibit marked pleomorphism with granular chromatin and small to prominent nucleoli. The presence of definitive or apparent cribriform cell groups should alert the pathologist to the possibility of a SDC [7, 8]. Therefore, cytological examination by MRI or PET may provide important evidence on diagnosis, even in the absence of palpable cervical lymphadenopathy [6].

IHC biomarker study has been widely used to distinguish primary and metastatic lesions, which may serve as important indicators of metastasis tumor, such as SDC. A positive AR and GCDF-15 protein and a negative ER and PR are suggestive of SDC [9-13], which is in line with our IHC results. Among the five biomark-
ers. Her-2, a protein found on the surface of breast ductal carcinoma cells, is a well-known biomarker associated with increased metastatic potential in breast cancer. The gene encoding this receptor is a proto-oncogene known as her-2/neu (also known as HER-2/neu or c-erbB-2), and is amplified in more than 20% of invasive breast cancers. It has been known as an indicator of prognosis in node negative breast cancer patients [11-14]. Considering of the similarity between breast ductal carcinoma and SDC, expression of her-2/neu has been examined in a previous study, showing a 20-25% incidence of her-2/neu expression in SDC [15-18]. In addition, expression level of her2-neu has been linked to early local disease recurrence, distant metastasis and poorer survival [11]. Several breast cancer studies have shown that her-2/neu gene amplification status has improved the possible responders to targeted therapy with trastuzumab (a monoclonal antibody that interferes with the HER2/neu receptor), resulting in a prolongation of survival [19-21]. Trastuzumab is now also being used to treat salivary gland cancers, with mixed results [22-27].

Conclusion

In conclusion, based on the medical treatment, cytological examination and IHC analysis, we concluded submandibular gland SDC possibly through the lymphatic route. Chemotherapy with trastuzumab and paclitaxel had been given to this patient, she has finished six systemic chemotherapy, with the continued use of trastuzumab for one year. In May 2015, the patient died of brain metastasis.

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Disclosure of conflict of interest

None.

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