CASE REPORT

Synchronous multiple unilateral parotid gland tumors of benign and malignant histological types: case report and literature review

Múltiplos tumores síncronos unilaterais de glândula parótida de tipos histológicos benignos e malignos: relato de caso e revisão da literatura

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Received 6 October 2015; accepted 8 March 2016
Available online 22 April 2016

Introduction

Salivary gland tumors are a very heterogeneous group of lesions. According to the histological classification published by WHO in 2005, 10 types of benign and 24 types of malignant tumors of the salivary glands can be distinguished. All of these lesions are relatively rare, and represent only 3–4% of head and neck tumors. 80% of them are located within the parotid gland, and they usually present as a single parotid lesion. Unilateral parotid neoplasms are very uncommon, and they usually have the same histological type. The most common type of such a lesion is Warthin tumor (6–12% of all adenolymphomas). The coexistence of tumors of different histological types in the same parotid gland constitutes less than 0.3% of all salivary gland neoplasms. The most common histological combination is Warthin tumor and pleomorphic adenoma. Two different unilateral parotid neoplasms can be metachronous or synchronous. However, even when more than one tumor occur at the same time, they must be distinguished from hybrid tumors, in which we can find two or more distinct histological types of neoplasms having an identical origin in the same tissue.

Synchronous benign and malignant ipsilateral parotid tumors are an extremely rare phenomenon. It was described for the first time by Tanaka in 1953 as mucopidermoid carcinoma associated with Warthin tumor. To our knowledge no case in the literature mentioned the occurrence of a tumor consisting of carcinoma ex pleomorphic adenoma and Warthin tumor, which is reported in the present paper.

Case report

61 year-old man presented with a 10 year history of a non-tender, growing, left parotid mass. On clinical examination a firm, mobile mass was evident, with no overlying skin changes. The diameter of the lesion was 4 cm. No facial nerve palsy or lymphadenopathy was detected (Fig. 1).

A CT scan revealed a 57 mm × 40 mm × 27 mm heterogeneously enhanced left parotid mass, involving both lobes of the gland (Fig. 2). There was no evidence of osteolytic changes in mandibular bones. Moreover, no invasions of the masseter muscle or of the parapharyngeal space were showed. A few 15–19 mm lymph nodes in the retro- and submandibular space were described. Fine needle aspiration biopsy confirmed pleomorphic adenoma. The
The synchronous occurrence of tumor adenoma posed with parotidectomy. En bloc removal of the tumor was achieved with the excision of the superficial lobe. The facial nerve was preserved. Macroscopically, the mass was enveloped, solid and yellowish, with one cyst (1.5 cm in diameter) on the marginal part. Microscopically, the tumor mass included three different morphological patterns (Fig. 3). Pleomorphic adenoma was the dominant component. Within its tissue atypical cells of carcinoma ex pleomorphic adenoma were found. The marginal part of the solid mass included Warthin tumor cells. Surgical margins were free from neoplasm.

Due to the postoperative histopathological finding of malignant components of the tumor the patient was proposed a re-operation, involving the removal of the deep lobe of the parotid gland and elective neck dissection of I and II cervical lymph node groups. The patient did not give consent to surgical re-treatment. Therefore, even though CT scans did not indicate the presence of positive lymph nodes, the patient was referred for radiation treatment. No signs of recurrence were revealed during a follow-up after 5 years.

**Discussion**

Multiple salivary gland tumors are occasionally seen, and account for 1.7-5% of parotid lesions. The vast majority of this phenomenon belongs to the same histological type of tumors, with Warthin tumor being the most common. Multifocal pleomorphic adenoma occurs rather infrequently. Synchronous parotid tumors of different histology account for less than 0.3% of all salivary gland neoplasms. The most common combination is Warthin tumor and pleomorphic adenoma. Benign and malignant tumors in the ipsilateral parotid gland are extremely rare. Since Tanaka first reported the case of coexisting bilateral Warthin tumor and mucopeidermoid carcinoma, only 25 papers have reported the incidence of synchronous unilateral tumors of the parotid or periparotid region.

According to previous reports, this type of lesions was more commonly observed in male patients, with the male-to-female ratio 1.3:1. The median patient’s age was 66 years, and the average age – 64.1 years, which is almost 1 decade later than the incidence of malignancies in salivary glands in general. Warthin tumor was the most commonly described benign neoplasm (22 of 38 cases), pleomorphic adenoma was described less frequently (11 of 38 cases). There were solitary cases of other benign tumors, such as sebaceous lymphadenoma, oncocystoma and myoepithelioma. The most frequently observed malignant component was mucopeidermoid carcinoma (11 of 38 cases) and acinic cell carcinoma (8 of 38 cases). Hence, the most popular histological combination of neoplasms was Warthin tumor and mucopeidermoid carcinoma (9 of 38 cases) (Table 1).

This paper is the first one to present an in-depth study of a rare case of Warthin tumor coexisting with carcinoma ex pleomorphic adenoma in the same salivary gland. Only one occurrence of this kind has been just sparingly mentioned, without any study or analysis, in the English language literature in the 1960s. The occurrence of carcinoma ex pleomorphic adenoma in our patient is typical for this type...
of malignancy (6th–7th decade of life), which may suggest that the synchronous concomitance of Warthin tumor was coincidental, and the initial state was the most popular combination of histologically different tumors – pleomorphic adenoma and Warthin tumor. The etiology of carcinoma ex pleomorphic adenoma is associated with the accumulation of genetic instabilities in long-standing pleomorphic adenomas, hence in the present case, the primary tumor was present for many years, what is important for process of malignization.1,2,3 Although there are some data about the incidence of multiple parotid tumors after radiotherapy, our patient had no history of radiation before.2,3

Clinical examination, imaging investigation and fine needle biopsy proved inefficient in this case. Although no particular type of radiological investigation has been defined in the detection of unilateral parotid tumors, the combination of ultrasound and MRI seems to have the best effectiveness rates in differentiating malignant lesions from benign ones.2,3 Fine needle aspiration cytology is crucial in the evaluation of parotid tumors. However, its role in case of unilateral synchronous tumor is controversial.3,4

Previous studies implied that the treatment and anticipated survival rate should be analogous to the cases of malignant neoplasms of the same histological type. Surgery

Table 1 Summary of papers concerning synchronous benign and malignant unilateral parotid gland tumors.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Benign tumor</th>
<th>Malignant tumor</th>
<th>Age</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our case</td>
<td>2015</td>
<td>Warthin tumor</td>
<td>Carcinoma ex pleomorphic adenoma</td>
<td>61</td>
<td>M</td>
</tr>
<tr>
<td>Jin J2</td>
<td>2011</td>
<td>Pleomorphic adenoma</td>
<td>Lymphoepithelial carcinoma</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Srivastava S9</td>
<td>2009</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>52</td>
<td>M</td>
</tr>
<tr>
<td>Roh JL10</td>
<td>2007</td>
<td>Warthin tumor</td>
<td>Adenocarcinoma</td>
<td>71</td>
<td>M</td>
</tr>
<tr>
<td>Tanaka S11</td>
<td>2007</td>
<td>Warthin tumor + pleomorphic adenoma</td>
<td>Salivary duct carcinoma</td>
<td>67</td>
<td>M</td>
</tr>
<tr>
<td>Ethunandan M6</td>
<td>2006</td>
<td>Warthin tumor</td>
<td>Acinic cell carcinoma</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Bień S12</td>
<td>2006</td>
<td>Pleomorphic adenoma</td>
<td>Adenocarcinoma</td>
<td>51</td>
<td>M</td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td></td>
<td>Adenocarcinoma</td>
<td></td>
<td>66</td>
<td>M</td>
</tr>
<tr>
<td>Shukla M14</td>
<td>2003</td>
<td>Sebaceous lymphadenoma</td>
<td>Squamous cell carcinoma</td>
<td>68</td>
<td>F</td>
</tr>
<tr>
<td>Curry JL15</td>
<td>2002</td>
<td>Pleomorphic adenoma</td>
<td>Salivary duct carcinoma</td>
<td>67</td>
<td>F</td>
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<tr>
<td>Mayorga M16</td>
<td>1999</td>
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<td>Acinic cell carcinoma</td>
<td>78</td>
<td>F</td>
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<tr>
<td>Misselevich L17</td>
<td>1997</td>
<td>Pleomorphic adenoma</td>
<td>Acinic cell carcinoma</td>
<td>44</td>
<td>F</td>
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<tr>
<td>Seifert C18</td>
<td>1997</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>73</td>
<td>M</td>
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<tr>
<td>Hanada T19</td>
<td>1995</td>
<td>Myoepithelioma</td>
<td>Adenoid cystic carcinoma</td>
<td>71</td>
<td>F</td>
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<td>Gneppe DR13</td>
<td>1989</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>60</td>
<td>M</td>
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<td>Janecka IP20</td>
<td>1983</td>
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<td>Adenocarcinoma</td>
<td>84</td>
<td>M</td>
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<tr>
<td>Volmer J21</td>
<td>1982</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>56</td>
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<tr>
<td>Pontilena N22</td>
<td>1979</td>
<td>Pleomorphic adenoma</td>
<td>Ductal adenocarcinoma</td>
<td>69</td>
<td>M</td>
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<tr>
<td>Bab IA23</td>
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<td>Sebaceous cell adenoma</td>
<td>Adenoid cystic carcinoma</td>
<td>66</td>
<td>M</td>
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<tr>
<td>Bird R24</td>
<td>1979</td>
<td>Warthin tumor</td>
<td>Carcinoma ex pleomorphic adenoma</td>
<td>45</td>
<td>F</td>
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<tr>
<td>Gadient SE25</td>
<td>1975</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>60</td>
<td>M</td>
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<tr>
<td>Iannaccone P26</td>
<td>1975</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>70</td>
<td>M</td>
</tr>
<tr>
<td>Lumerman H17</td>
<td>1975</td>
<td>Warthin tumor</td>
<td>Mucoepidermoid carcinoma</td>
<td>65</td>
<td>M</td>
</tr>
<tr>
<td>Turnbul AD28</td>
<td>1969</td>
<td>Warthin tumor</td>
<td>Carcinoma ex pleomorphic adenoma</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Tanaka N3</td>
<td>1953</td>
<td>Pleomorphic adenoma</td>
<td>Adenocarcinoma</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND, no data.
is the gold standard in treatment of this kind of lesions. The presence of a malignancy might require a more aggres-
sive approach, hence, depending on the nature and the
location of the tumor – total or subtotal parotidectomy is
indicated. Intraoperative frozen section biopsy might add
important information that could alter the management and
improve the final outcome of the treatment. Our case seems
to confirm that a routine use of this examination may have
influenced the extent of the surgical management in the
way that the total parotidectomy and the elective I and II
level lymph node removal would be performed. Thus, re-
operation would not be necessary.

Adjuvant radiotherapy is highly recommended for
high-grade malignancies like carcinoma ex pleomorphic ade
noma, due to a high risk of locoregional recurrence. Due to
the fact that the surgical treatment was not optimal in this
case, the patient was qualified for radiation therapy in order
to minimize the risk of subclinical microscopic spread of the
disease.

Conclusions

Multiple synchronous unilateral parotid tumors may cause
significant discrepancies between the preliminary and
definitive histopathological prognosis, especially when pre-
operative clinical assessment and FNAC did not indicate
the presence of two different neoplasms within one gland.
The awareness of the coexistence of benign and malignant
lesions in ipsilateral parotid gland should raise the clinical
vigilance in the process of evaluation of a parotid mass.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Eveson JW, Auclair P, Gnepp DR, El-Naggar AK. Tumours of the
salivary glands. In: Barnes L, editor. Pathology and genetics of
head and neck tumours. World Health Organization classification
2. Zeebregts CJ, Mastboom WJ, van Noort G, van Det RJ. Syn-
chronous tumours of the unilateral parotid gland: rare or
3. Gnepp DR, Schroeder W, Heffner D. Synchronous tumors arising
4. Seifert G, Donath K. Multiple tumours of the salivary glands –
terminology and nomenclature. Eur J Cancer B Oral Oncol.
1996;32B:3-7.
5. Tanaka N, Chen W. A case of bilateral papillary cystadenoma
lymphomatosum (Warthin’s tumor) of the parotid complicated
6. Ethunandan M, Pratt CA, Morrison A, Anand R, Macpherson DW,
Wilson AW. Multiple synchronous and metachronous neoplasms
of the parotid gland: the Chichester experience. Br J Oral Max-
2004;33:531-4.
8. Jin J, Chen Y. Unilateral parotid gland involvement with
synchronous pleomorphic adenoma and lymphoepithelial carci-
noma: a case report and literature review. Shanghai Kou Qiang
9. Srivastava S, Nadelman C. Synchronous ipsilateral Warthin
tumor encased by a separate mucoepidermoid carcinoma of the
parotid gland: a case report and review of the literature. Diagn
10. Roh J, Kim J, Park CI. Synchronous benign and malignant
et al. Synchronous unilateral parotid gland neoplasms of three