MINOR SALIVARY GLAND MUCINOUS ADENOCARCINOMA OF BUCCAL MUCOSA – CASE REPORT AND REVIEW OF THE LITERATURE

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Mucinous adenocarcinoma (MAC) is commonly found in the gastrointestinal tract but head and neck localisations are very rare. This article presents the case of a 67-year-old patient suffering from a minor salivary gland MAC of the left buccal mucosa, who was treated in the Department of Cranio-Maxillofacial Surgery in Krakow due to multiple recurrences of the tumour. The results of immunohistochemical staining, the course of surgical treatment and follow-up, as well as a review of literature are also discussed.

Key words: mucinous adenocarcinoma, minor salivary glands, immunohistochemistry, radiography.

Introduction

Mucinous adenocarcinoma (MAC) is most frequently observed in the digestive organs. The most common localisation is the large intestine (colon), and it is estimated that MAC constitutes 10-20% of colorectal cancers, followed by the pancreas, ovary, lung, prostate, and breast [1]. The primary head and neck localisation of MAC is very rare and accounts for about 3% of salivary gland tumours. Salivary gland MACs are characterised by high aggressiveness due to a high rate of local recurrences and nodal metastasis [1-3].

The tumour is composed of large extracellular mucin pools and irregular-shaped neoplastic epithelial cells surrounded by numerous cystic cavities, separated by fibrous strands. The cancer cells have clear cytoplasm and small, round, darkly-stained nuclei. The tumour cells form nests embedded in the extracellular mucin pools [3-7]. According to some authors the histological features are so characteristic that differential diagnosis from other malignant salivary gland tumours is straightforward [5]. On the other hand, there are authors who regard MAC’s recognition criteria as controversial and inconclusive [3, 6, 8]. According to the WHO, the microscopic image is dominated by small foci of cancer cells or even single cells surrounded by large areas of extracellular mucin separated by connective fibrous strands. In addition, at least half of the tumour cells should produce mucus [8]. Histologically, MAC may be confusingly similar to the mucinous eccrine carcinoma of the skin, mucinous carcinoma of the breast and colloid carcinoma of the bowel [7]. An important feature of MAC are mucus-producing cells which show positive staining for mucicarmine and Alcian blue. However, these cells are also characteristic for other salivary gland tumours; hence immunohistochemical (IHC) staining is helpful in differential diagnosis. Typical for MAC is a strongly positive reaction for cytokeratins (CK) AE1/AE3,7, intermediate or strong reaction for CK 8, 18, 19, positive reaction for epithelial membrane antigen (EMA), vimentin, carcinoembryonic antigen (CEA), and varied reaction with α-SMA (smooth muscle actin), α-amylase and calcitonin. Cytokeratins, vimentin, S-100 protein, and α-SMA pos-
itive staining is characteristic for most salivary gland tu-
mours [3, 4, 6]. Some authors believe that the positive
reaction for neuron specific enolase (NSE), calcitonin and
somatostatin may be the evidence of neuroendocrine dif-
ferentiation, but the exact significance of this expres-
sion is unknown [8]. Primary minor salivary gland MAC
requires exclusion of metastatic nature of the tumour.
An important feature of salivary gland MACs is a clear
difference in the number of chromosomal aberrations
in comparison with MAC of digestive organs [1].

Case report

A 67-year-old patient reported to the Outpatient
Unit of the Department of Cranio-Maxillofacial Sur-
gery due to a large tumour involving the left half of
the face. The lesion had been observed by the patient
for about 12 years, originally removed as an epidermal
cyst of the left cheek in the regional hospital. Three years
later a recurrent tumour in the postoperative scar was
removed. The histological examination revealed geomet-
lous adenocarcinoma, most likely arising from a mi-
nor salivary gland of the oral mucosa; the lesion was
excised without adequate margins. The patient was con-
sulted in the Department of Oncology but due to the
radioresistance of the tumour he was disqualified from
adjuvant radiotherapy and was admitted to our de-
partment in order to extend the surgical resection. In
1997 the excision of the tumour of the left infraorbital
area with resection of the underlying bone was per-
formed; the defect was reconstructed by the frontal flap.
The margins of resection were positive; thus an addi-
tional extended excision of the postoperative scar was
performed. This time there were no signs of the tu-
mour in the histopathological examination. In 1999 the
next excision of the local recurrence was carried out,
and the histological examination indicated radical ex-
cision. In 2007 the patient reported again to our de-
partment with the suspicion of local recurrence in the
left cheek but did not consent to the proposed surgery
and avoided follow-up examination until 2012, when
the patient reappeared, presenting an extensive tumour
involving the whole left half of the face infiltrating the
orbit, infraorbital area, left cheek as well as masseteric
area and submandibular region on the left side (Fig.
1, 2). The range of the tumour was confirmed in CT
of the facial part of the skull (Fig. 3, 4). Diagnostic bi-
opsy was performed. During collection of the diagnostic
material, a jelly-like consistency of the tumour could
be observed with an abundant outflow of mucus. The
results of basic blood tests revealed no abnormalities.
The ultrasound examination of the abdomen and

Fig. 1. The patient with minor salivary gland MAC of the
buccal mucosa infiltrating the left half of the face

Fig. 2. The same patient – lateral view
X-ray image of the chest revealed no distant metastases. The histological result of the biopsy of the tumour of the left cheek revealed recurrent mucinous adenocarcinoma G1 with cancer cells of medium size, with a slightly basophilic cytoplasm and oval nuclei. The cancer cells were arranged in small concentrations and patches embedded in mucus, divided into small cavities (Fig. 5, 6). The cells presented the following pattern of IHC reactivity: CK: AE1/AE3, CK19 positive reactions in the cancer cells; in contrast, CK5/6, CK5/6/18, and SMA were negative. Histochemical reactions – PAS, Alcian blue, mucicarmine – were positive in the cancer stroma (Fig. 7, 8). The tumour originated from a small salivary gland. Due to the severity and advancement of the disease the patient was disqualified from surgical treatment, reconsulted in the Department of Oncology and qualified for palliative chemotherapy.

**Discussion**

As a rare tumour, MAC causes difficulties in diagnosis [3, 5, 6, 8]. Clinical symptoms of the head and neck MAC are uncharacteristic and diagnosis is based on the histopathological and immunohistochemical examination. In the available literature (PubMed 1973-2012) we have found 21 published cases of MAC arising from minor salivary glands localised in the palate (9 cases), buccal mucosa (4 cases), floor of the mouth (3 cases), lips (3 cases) and tongue (2 cases) [3, 6, 7, 9].
Fig. 7. MAC cells embedded in mucus – in Alcian blue staining, magnification 50×

Fig. 8. PAS staining (mucus in pink, cell structures of the cancer in blue), magnification 100×

Table I. Reported cases of MAC arising from minor salivary glands

<table>
<thead>
<tr>
<th>REFERENCES</th>
<th>LOCAL APPEARANCE</th>
<th>AGE</th>
<th>SEX</th>
<th>LOCALISATION</th>
<th>CERVICAL LYMPH NODE METASTASIS</th>
<th>TREATMENT</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shumway</td>
<td>greyish tumour</td>
<td>72</td>
<td>male</td>
<td>palate</td>
<td>no</td>
<td>excision + RT</td>
<td>8 months</td>
</tr>
<tr>
<td>Notani</td>
<td>ulcerated tumour</td>
<td>64</td>
<td>male</td>
<td>palate</td>
<td>yes</td>
<td>RT + maxillectomy + ND</td>
<td>6 months</td>
</tr>
<tr>
<td>Gao</td>
<td>ulcerated tumour</td>
<td>50</td>
<td>male</td>
<td>palate</td>
<td>yes</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Gao</td>
<td>ulcerated tumour</td>
<td>51</td>
<td>male</td>
<td>palate</td>
<td>yes</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Gao</td>
<td>exophytic tumour</td>
<td>58</td>
<td>female</td>
<td>palate</td>
<td>no</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Gao</td>
<td>ulcerated tumour</td>
<td>48</td>
<td>female</td>
<td>palate</td>
<td>yes</td>
<td>not mentioned</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Gao</td>
<td>tumour</td>
<td>70</td>
<td>male</td>
<td>floor of the mouth</td>
<td>not mentioned</td>
<td>excision + ND + chemotherapy</td>
<td>cervical lymph node metastasis after 9 months, cervical skin metastasis after 20 months</td>
</tr>
<tr>
<td>Mano</td>
<td>ulcerated tumour</td>
<td>70</td>
<td>male</td>
<td>palate</td>
<td>yes</td>
<td>excision + ND</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Seoane</td>
<td>exophytic fibroma-like tumour</td>
<td>47</td>
<td>male</td>
<td>palate</td>
<td>no</td>
<td>excision</td>
<td>not mentioned</td>
</tr>
<tr>
<td>Aydin</td>
<td>tumour</td>
<td>80</td>
<td>male</td>
<td>lip</td>
<td>not mentioned</td>
<td>excision</td>
<td>6 months</td>
</tr>
<tr>
<td>Uchida</td>
<td>tumour</td>
<td>65</td>
<td>male</td>
<td>ventral part of the tongue</td>
<td>no</td>
<td>glossectomy</td>
<td>6 years</td>
</tr>
<tr>
<td>Ide</td>
<td>tumour 1 cm</td>
<td>76</td>
<td>female</td>
<td>lower lip</td>
<td>no</td>
<td>excision</td>
<td>distant metastasis after 6 years</td>
</tr>
<tr>
<td>Ide</td>
<td>tumour 1.4 cm</td>
<td>82</td>
<td>female</td>
<td>upper lip</td>
<td>no</td>
<td>excision</td>
<td>local and nodal recurrence after 3 years</td>
</tr>
<tr>
<td>Barbosa</td>
<td>tumour</td>
<td>52</td>
<td>male</td>
<td>floor of the mouth</td>
<td>no</td>
<td>RTGTH + excision + ND</td>
<td>11 months</td>
</tr>
<tr>
<td>Current case</td>
<td>primarily tumour of the cheek</td>
<td>67 (43)</td>
<td>male</td>
<td>cheek</td>
<td>yes</td>
<td>multiple excision</td>
<td>24 years</td>
</tr>
</tbody>
</table>

RT – radiotherapy, NP – neck dissection
The data of 13 patients (reported in English-language literature only) are presented in Table 1. In the oral cavity MAC appears as an exophytic, painless tumour of various morphology which clinically may imitate adenoma, fibroma or pyogenic granuloma. MAC of the floor of the mouth resembles calculus of the salivary duct. In differential diagnosis all neoplasms with cells producing mucus should be taken into consideration, e.g. mucoepidermoid carcinoma, mucinous cystadenocarcinoma, mucin-rich salivary duct carcinoma and signet-ring cell adenocarcinoma. An analysis of the reported cases of MAC arising from minor salivary glands revealed that the disease was characteristic for older adults (average age 57 years) with male to female ratio 2 : 1. Cervical lymph node involvement at the time of initial diagnosis of MAC was observed in 12 patients (57.1%).

Major salivary gland MAC was reported in 9 to 14 patients (some cases might be doubled). In 5 cases the primary tumour was localised in the submandibular gland, in 3 to 8 cases in the parotid gland and in 1 in the sublingual gland. The data concerning the frequency of MAC occurrence in minor and major salivary glands are ambiguous and indicate predominance of MAC arising from minor salivary glands (2 : 1) [3-8]. Other atypical localisations of MAC include the nasal cavity, paranasal sinuses and one case of a tumour of the mandibular ramus [8].

In the currently reported case, we believe that the tumour arising from the minor salivary gland of the buccal mucosa was initially misdiagnosed as an epidermal cyst. In our patient immunohistochemical staining revealed positive reaction for CK AE1/AE3 as well as CK19, and negative for CK5/6, CK5/6/18 and SMA. Also positive staining for PAS, Alcian blue and mucicarmine was obtained in mucin stroma of the cancer. These findings correspond with the results presented by other authors [4, 5, 7, 8].

In commonly observed cases of MAC of the digestive organs well-established algorithms of therapy are available. In the treatment of patients in stage I surgery is the method of choice, in stages II and III surgery combined with chemotherapy, whereas in stage IV surgery combined with chemo/radiotherapy is indicated [10-13]. Based on the current literature, we conclude that the best treatment modality in patients with MAC of the head and neck region is surgery, comprising wide excision of the tumour with concomitant neck dissection. Some authors stress the necessity of adjuvant radiotherapy in these patients. As limited clinical data are not sufficient for establishing clear indications for chemotherapy, in patients with head and neck MAC, the decision should be taken after an analysis of each individual case [3, 4, 6, 7].

Conclusions

In the cases reported so far, the aggressive character of salivary gland MAC is proved by a high rate of cervical lymph node metastases (about 60%) present at the initial diagnosis of the tumour as well as a high rate of local recurrence. Such features of the tumour as well as its radioresistance suggest that extensive excision combined with neck dissection is the optimal treatment modality in patients with MAC of the head and neck region. We can hypothesize that in the presented patient exceptionally long follow-up might have been related to unique different chromosomal aberrations in the cancer cells. Appropriate immunohistochemical profiling is mandatory for the proper histopathological diagnosis of MAC.

The authors declare no conflict of interests.

References


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