

# ANGIOSARCOMA OF THE PAROTID GLAND

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## Summary

Angiosarcomas of the major salivary glands are rare tumours. The authors describe a case of the tumour located in the right parotid gland of a 77-year-old woman. Histological examination revealed a poorly differentiated tumour made up of epithelioid and spindle cells. These two types of cells intermingled. In some parts, primitive mutually anastomosing irregularly shaped vascular spaces with atypical endothelial cells were found. The tumour cells were positive for CD31, CD34, EMA and FVIII (focally). Due to the relatively short follow-up period the prognosis of the disease is difficult to estimate.

**Key words:** angiosarcoma – parotid gland – immunohistochemistry

## Souhrn

### Angiosarkom příušní žlázy

Angiosarkom velkých slinných žláz patří ke vzácně se vyskytujícím nádorům. Autoři uvádějí jeden takový nádor lokalizovaný v pravé příušní žláze 77leté ženy. Histologické vyšetření ukázalo, že šlo o nediferencovaný nádor tvořený epitelioidními strukturami a protáhlými nádorovými buňkami. Oba buněčné typy v sebe vzájemně přecházejí. Místa byly zjištěny i primitivní, vzájemně anastomozující nepravidelné cévní prostory s atypickými endoteliemi. Nádor pozitivně reagoval s protilátkami proti CD31, CD34, EMA a FVIII (ložiskovitě) antigenům. K prognóze onemocnění je zatím obtížné se vyslovit vzhledem ke klinicky relativně krátké době sledování pacientky.

**Klíčová slova:** angiosarkom – parotis – imunohistologie

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Angiosarcomas of the major salivary glands are rare. They were described either as isolated or together with the same tumours in the oral region (2, 4, 6, 7, 10, 11). Besides primary angiosarcomas of the salivary glands, secondary tumours were observed. Fanburg-Smith et al. (3) found that angiosarcomas of the oral cavity and salivary glands included 7 secondary angiosarcomas of which 3 involved the parotid gland. In some cases, angiosarcoma is linked to a benign vascular tumour such as congenital haemangioma (2).

## CASE REPORT

A 77-year-old woman presented with an enlarged right parotid gland. Clinical examination revealed a tumour which was surgically removed. Macroscopically, the mass was relatively well-defined, solid, grey-white, sized 2 x 1.5 x 2 cm. The patient was treated with radiotherapy. One year postoperatively, the patient was without clinical signs of recurrence. Detailed clinical examination did not reveal any other primary tumour.

Histologically, the tumour was made up mostly of spindle cells, with a gradual transition into areas composed of large epithelioid cells (Figs. 1, 2). These cells had abundant, eosin-stained cytoplasm, vesicular nuclei and distinct nucleoli. Some areas were less cellular, made of connective tissue, with irregular narrow, mutually anastomosing vascular spaces. These spaces were lined by atypical endothelial cells (Fig. 3). The tumour contained necrotic areas. Numerous mitoses were noted.

For immunohistochemistry paraffin embedded tissues were examined. Sections were deparaffinized and the

following primary antibodies were used (dilution in parenthesis): CD34 – clone QBEnd-10 (1:50), von Willebrand factor (factor VIII; 1:100), vimentin – clone Vim3B4 (1:50), AE1-AE3 (1:50), S-100 protein (1:100), SMA – clone 1A4 (smooth muscle actin; 1:50), Ki-67 – clone MIB-1 (1:100) all from DAKO, Glostrup; CD31 (1:40), EMA – clone GP1.4 (epithelial membrane antigen; 1:50), produced by Novocastra, Newcastle. We used an avidin-biotin conjugate (ABC) method. The colour was developed with diaminobenzidine, supplemented with hydrogen peroxide. Immunohistological examination showed positive results with antibodies against vimentin, CD31, CD34, epithelial membrane antigen (EMA) (Figs. 4-6) and von Willebrand factor (factor VIII). Negative results were obtained in tests with antibodies against cytokeratins AE1/AE3, S-100 protein and smooth muscle actin (SMA). The proliferation marker Ki-67 was positive in “hot spots” of 60-80 % of cells.

## DISCUSSION

Malignant mesenchymal tumours of the major salivary glands are uncommon findings. As of 1986, sixty-seven sarcomas or sarcomatoid lesions were recorded in the AFIP registry of salivary glands, including 4 primary angiosarcomas or malignant haemangioendotheliomas, 11 malignant schwannomas, 9 fibrosarcomas and 4 malignant fibrous histiocytomas (1). Most frequently, the parotid glands are affected; angiosarcomas of the submandibular glands are rare (3, 10, 11). According to some authors (3), angiosarcomas localized in the oral cavity and major salivary glands account for 2% of all angiosarcomas. Most frequently, they develop in

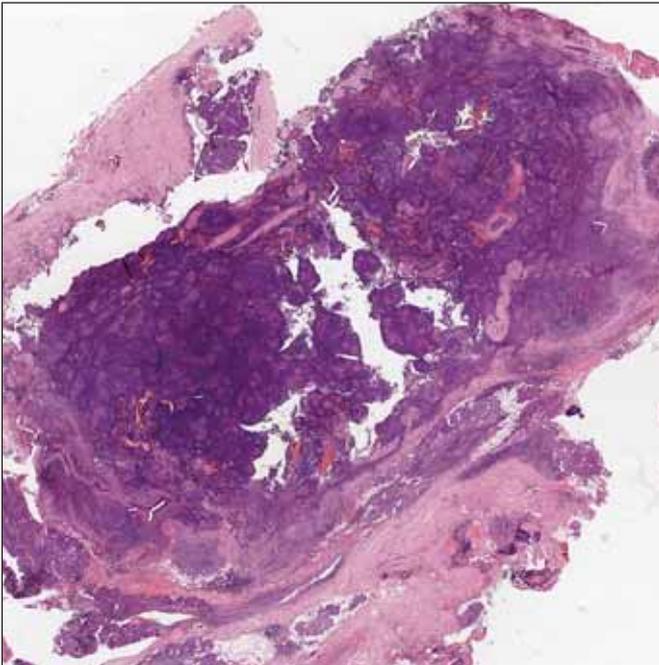


Fig. 1. General appearance of the tumour. (HE, 2.5x)

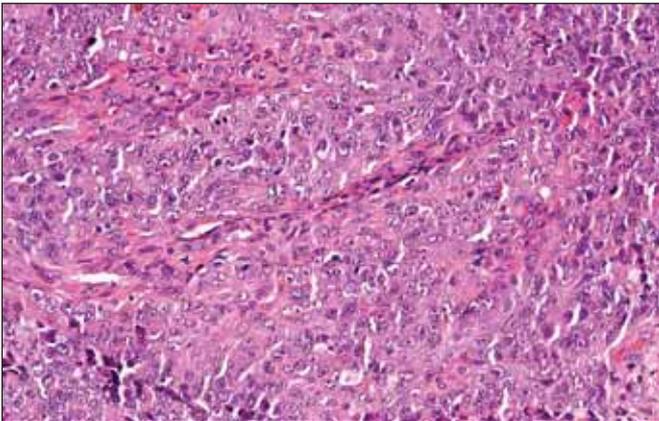


Fig. 2. Angiosarcoma with epithelioid structures. Spindle cells around. (HE, 400x)

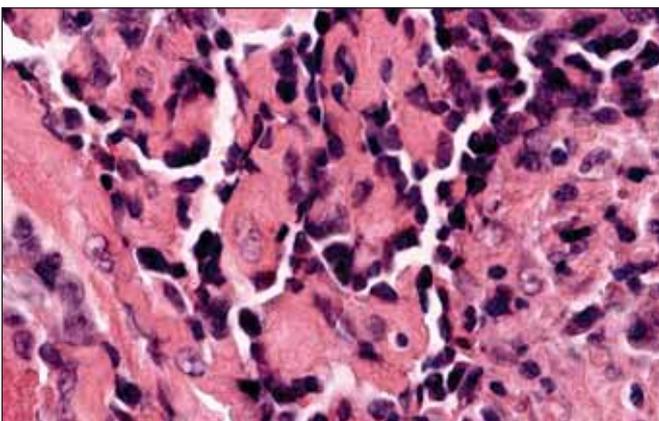


Fig. 3. Primitive mutually anastomosing vascular spaces with atypical endothelial cells. (HE, 400x)

older patients, in their 50s and 60s. Most angiosarcomas arise de novo. Some may develop following radiation therapy to treat malignant tumours in various locations (5, 8, 12). Radiation-induced angiosarcomas have been described in the

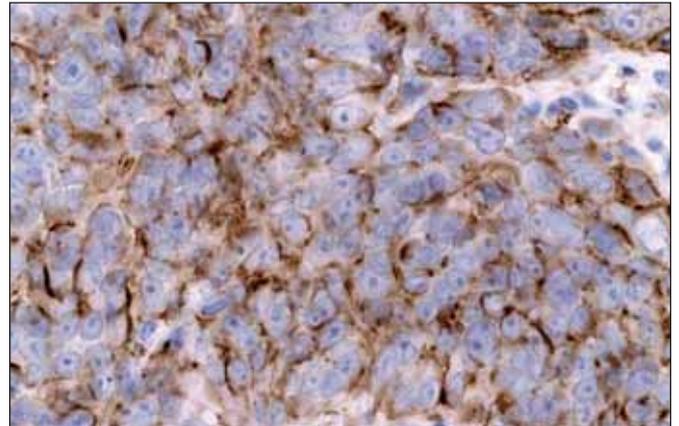


Fig. 4. Tumour cells positive with antibody against CD31 antigen. (400x)

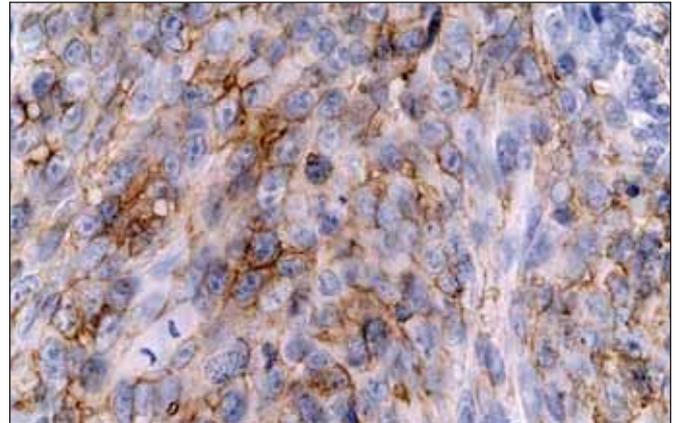


Fig. 5. Positive reaction with antibody against CD34 antigen. (400x)

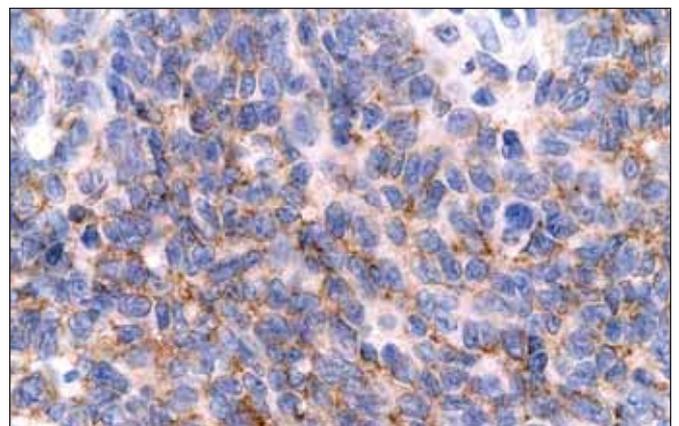


Fig. 6. Epithelioid cells of the angiosarcoma positively react with antibody against EMA. (400x)

parotid glands as well (7). In other cases, the tumours are secondary to benign vascular lesions such as congenital haemangiomas or vascular malformations. These may develop also in young adults (2).

According to Fanburg-Smith et al. (3), the histological picture shows that the most common pattern is made up of spindle cells. In our case, the tumour consisted of spindle cells mixed with epithelioid cells. In some regions, these cellular areas were interspersed with less cellular ones made up of connective tissue with primitive irregular vascular spaces lined by atypical endothelial cells.

Differential diagnostic considerations in angiosarcomas

are relatively broad. Well-differentiated tumours must be distinguished from various types of haemangiomas. Our case was that of a poorly differentiated angiosarcoma. Such tumours, especially those in uncommon locations such as the parotid glands, must be distinguished from a wide range of other tumours, for example malignant myoepitheliomas, melanomas, undifferentiated carcinomas, fibrosarcomas and metastatic tumours. Sampling is important. Even poorly differentiated angiosarcomas may show regions with transition to more differentiated areas, such as in our case. Differential diagnostic considerations must be based on immunohistological assessment.

Histologically, angiosarcomas express the CD31 and CD34 antigens. The two markers are considered relatively specific and sensitive. Von Willebrand factor (factor VIII) is the most specific but only poorly sensitive. Also in our case, positivity was only focal. Angiosarcomas may react with cytokeratins (4) and EMA antibodies as well, as often seen in the epithelioid form. Whereas most cells were found to be positive for antibody against EMA in our case, the results were negative using antibodies against cytokeratins AE1/AE3.

In our case, tumour cells reacted immunohistologically with antibody against vimentin. Focal positivity with antibody against von Willebrand factor was mostly in the primitive vascular spaces. Most cells of the tumour were positive with antibody against CD31. When using antibody against the CD34 antigen, positive results were mainly in lighter areas around the primitive vascular spaces.

Due to the low number of angiosarcomas found in the oral cavity and major salivary glands, there is only little experience with their prognosis. However, prognostic data on the most common angiosarcomas of the skin, subcutaneous and deep soft tissues suggest that these are highly aggressive tumours. Half of the patients die within one year after diagnosis. In contrast to these findings, Fanburg-Smith et al. (3) reported a relatively good prognosis in the oral region and salivary glands in most cases. In 11 cases out of 14 angiosarcomas localized in these regions, regardless of grading, no recurrence or metastatic spread were observed over an average follow-up of 8.6 years. Very different are secondary tumours, though, with patients dying within 15 months after diagnosis (3). Besides surgical removal of the tumour, radiotherapy is recommended (2, 9).

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