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CASE REPORT

Bilateral Basal Cell Adenocarcinoma of the Parotid Gland: In a Recipient of Kidney Transplant

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Abstract: We report a rare case of bilateral basal cell adenocarcinoma (BcAC) of the parotid gland in a male patient 30 years after kidney transplantation and continuous administration of immunosuppressive therapy. BcAC is a salivary gland malignancy first recognized as a distinct neoplastic entity in WHO classification of salivary gland tumours in 1991. Over 90% of BcACs are detected in the parotid gland. The most important differential diagnosis is basal cell adenoma. Infiltrative growth is the distinguishing feature of BcAC. Administration of immunosuppressive medication to this patient for three decades may have contributed to development of this rare neoplasia. To our knowledge, similar cases of BcAC have not been reported previously.

Keywords: post transplantation malignancy, basal cell adenocarcinoma, salivary gland cancer, immunohistochemistry

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Introduction

Histopathology of BcAC is characterized by two cell types: small basaloid epithelial cells at the periphery of tumour clusters and larger epithelial cells situated centrally in tumour clusters. Different histological growth patterns are seen, i.e. solid, trabecular, tubular and membranous types. In general, BcAC possesses a good prognosis. It metastasizes seldom, but may recur locally.[1,2] Although BcAC may develop from a primary basal cell adenoma, it often grows *de novo*. The differential diagnosis includes other neoplasms containing basal cells. Chondromyxoid stroma seen in pleomorphic adenoma is absent from basal cell adenomas and BcACs.[2,3] Differential diagnosis with high grade malignancies, e.g. adenocystic carcinoma (ACC), is important because of the low malignant behaviour and good prognosis of BcAC. However, the main differential diagnosis of BcAC is a benign basal cell adenoma. The two may share virtually similar histologic appearances. Criteria for the diagnosis of BcAC include infiltrative growth with possible perineural or vascular invasion. Other features may include nuclear pleomorphism, necrosis and mitotic activity. The differential diagnosis of ACC must also be considered. BcAC lacks the architectural pattern of pseudocysts and true glands within the same tumour islets that is typical for ACC.[2,4,5] Immunohistochemistry with basal cell markers, e.g. p63 and CK14, may be helpful in differential diagnosis of BcAC suggesting basal cell derivation of tumour cells. Cell proliferation markers, such as Ki67, are often suggestive in the differentiation of BcAC from basal cell adenomas and pleomorphic adenomas. However, invasive growth remains the only decisive criteria of malignancy.[1,2]

Renal transplantation is known to raise the life-long incidence of malignancies.[6] A recent Finnish study showed a 0.8% overall incidence for non-cutaneous head and neck cancer during 10 years of follow-up after renal transplantation.[7] We describe a rare case of bilateral BcAC arising in the parotid glands of a kidney recipient 30 years after transplantation.

Case Report

A male patient aged 60 years had a history of chronic glomerulonephritis, which finally evolved into terminal uremia. Renal transplantation from a cadaver source was successfully performed in 1977. The anti-rejection drug regimen for the first post transplantation decade was azathioprine and methylprednisolone, then azathioprine combined with cyclosporine for 15 years and finally from 2005 onwards only cyclosporine as monotherapy.

In 2003, he was operated for a malignant melanoma of the skin of chest (Clark IV, Breslow 2,3 mm with clean sentinel nodes). No signs of recurrence were seen during follow-up.

He presented in 2007 for a midline neck pain in the thyroid region after having a common cold 2 months previously. Ultrasonography revealed an asymptomatic lesion of 10 mm in the right and 6 mm in the left parotid gland (Figs. 1 and 2). Fine needle aspiration of the right side showed a slight suspicion of malignancy, while the lesion of the left parotid was interpreted as a basal cell adenoma.

A right partial parotidectomy was performed and a preoperative frozen section was interpreted as a pleomorphic adenoma. However, in paraffin sections of the resected tissue invasive tumour growth into connective tissues surrounding parotid gland was seen confirming BcAC as the final diagnosis. Consequently, a total parotidectomy was performed one week later. The superficial lobe of the left parotid gland was operated two months later. In histological examination of the left superior lobe, three foci of BcAC were also seen displaying invasive growth into surrounding tissues.

Neck ultrasonography and plain chest x-ray indicated no signs of metastasis to locoregional lymph nodes or distant sites. In histologic examination, both tumours showed appearance of basal cell adenocarcinomas with a mainly tubular growth pattern (Figs. 3A, E). The tumours in both parotid glands occurred multifocally, and were only partly encapsulated. Distinct invasive growth into adipose tissue was detected (Fig. 3B). Cellular and nuclear pleomorphism was only slight. Immunohistochemistry for Ki-67 antigen (Mib-1 antibody) showed cell proliferation of 5% in the left (Fig. 3H), and 10% in the right side (Fig. 3D), respectively.

Discussion

The basaloid parotid tumours in our case showed features of invasive growth that are a hallmark of basal cell adenocarcinomas. In our patient the differential diagnoses of basal cell adenocarcinoma, basal cell

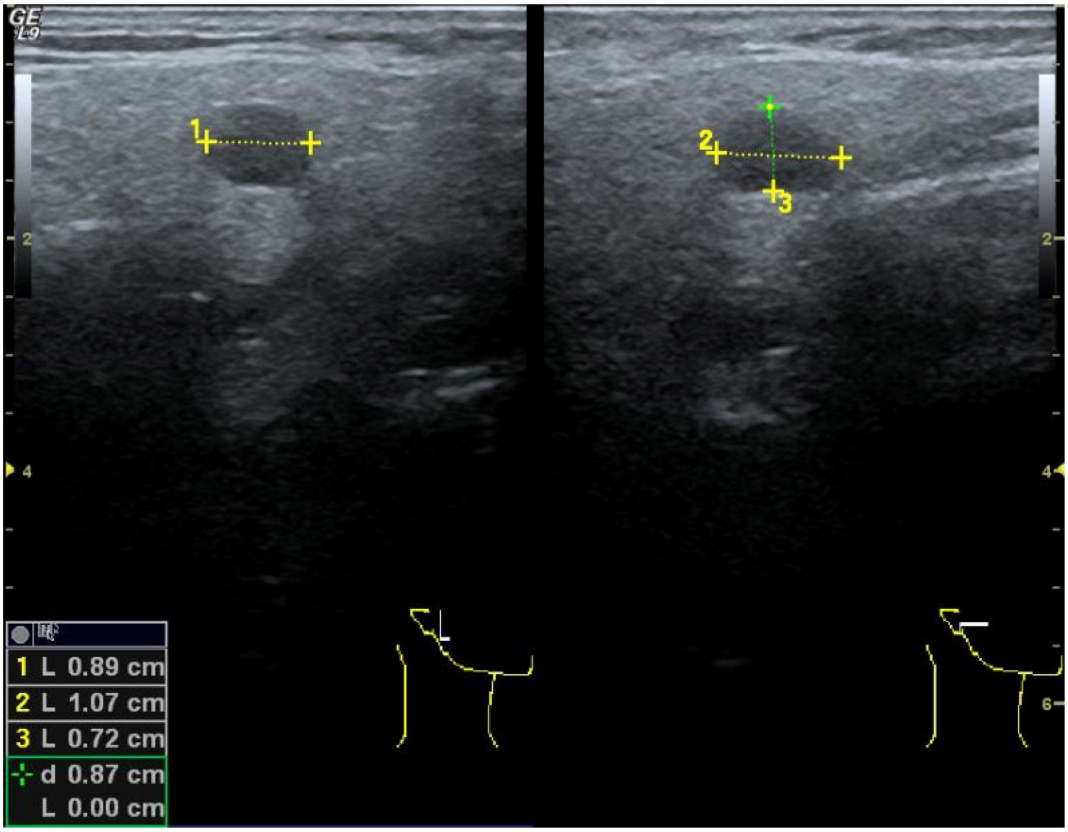

Figure 1. Ultrasonography imaging of the right parotid gland tumour.

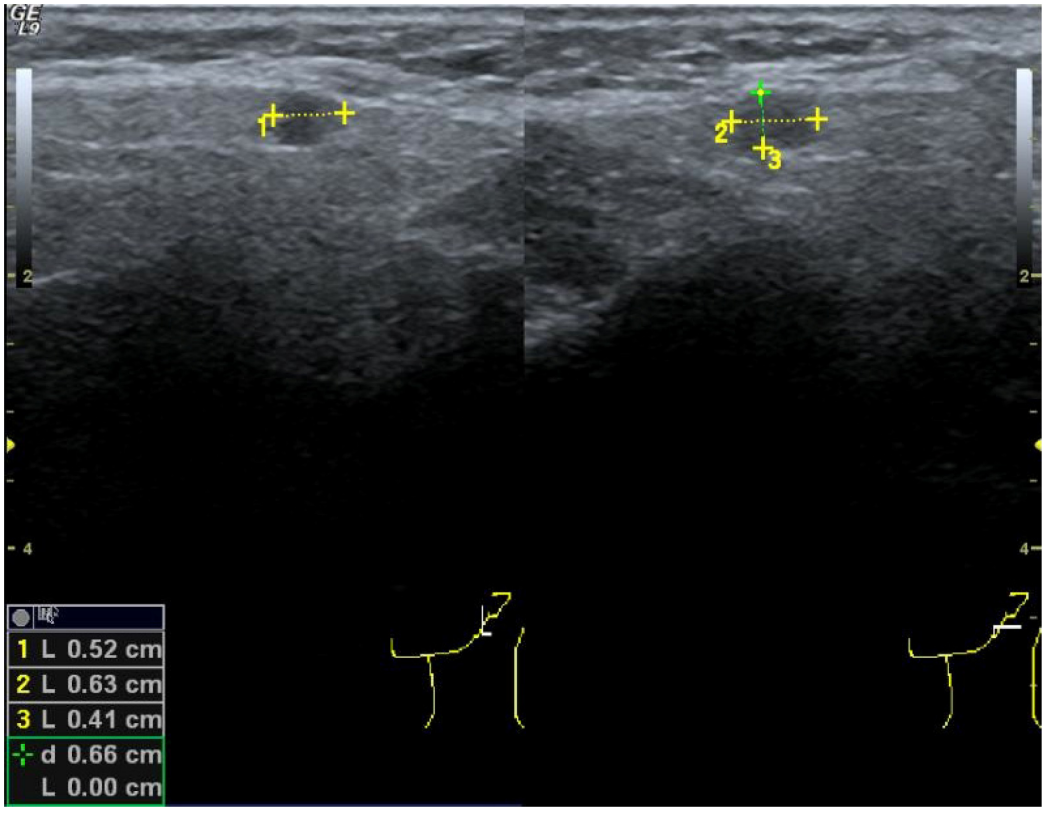

Figure 2. Ultrasonography imaging of the left parotid gland tumour.

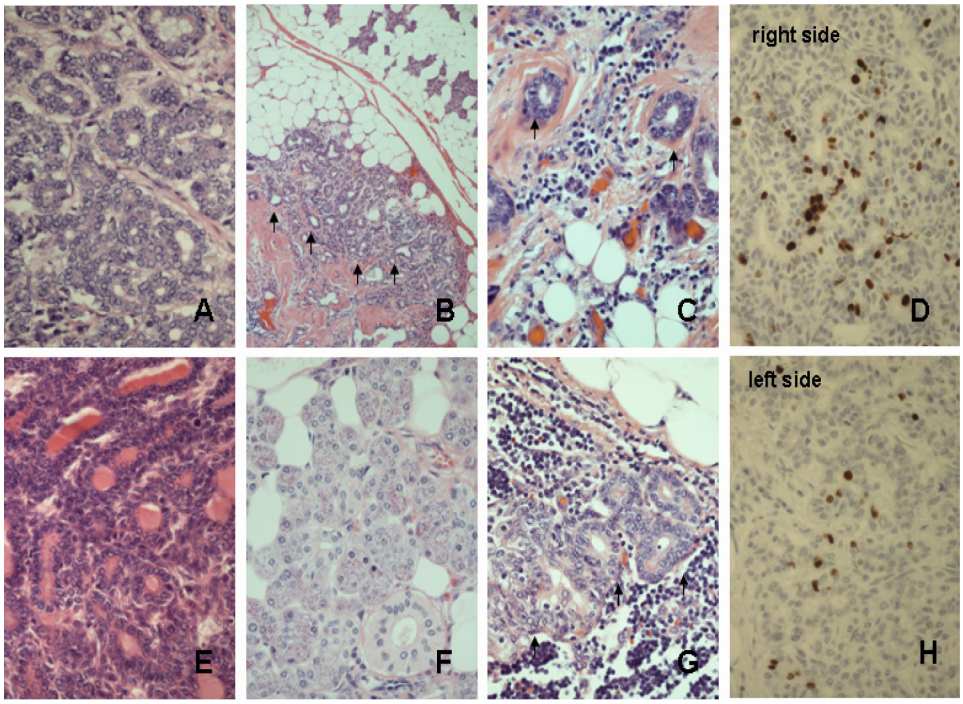

Figure 3. Bilateral Basel cell adenocarcinoma in parotid: Tubular tumour growth seen (**A**) in right side and (**E**) in left side parotid cell adenocarcinoma. (**B, C**) Infiltrative growth and (**G**) lymph node infiltration within parotid tissue marked with arrows. (**D, H**) Increased proliferation detected by Mib-1(Ki-67) immunohisto chemistry. Normal parotid tissue (**F**). Magnification ×400, except B ×100.

adenoma and pleomorphic adenoma were taken into consideration. The differential diagnosis of BcAC and basal cell adenoma can be difficult as the level of cytological atypia in many cases of BcAC is not significantly different from that seen in basal cell adenomas. However, in such cases invasive growth is the main distinguishing feature. In FNAC, BcAC often cannot be distinguished from basal cell adenoma and pleomorphic adenoma, especially if there is lack of cellular atypia.[8,9]

The proliferation index (Mib-1, Ki-67) being over 5% is a statistical marker predicting malignancy[10] and in our case it was over 5% in both parotid tumours. Development of skin cancer 2 to 3 decades after organ transplantation and immunosuppressive therapy is not unusual.[7,11,12] The majority of such cutaneous malignancies appear in the head and neck region. However, transplantation and immunosuppressive therapy raise the risk of non-cutaneous head and neck malignancies four-fold.[7] Our patient had presented with a malignant melanoma of the skin 26 years after kidney transplantation. The medical history of the patient does not include irradiation which is the only known risk factor for salivary gland malignancies.[2] Interestingly BcAC has been reported in connection with cylindroma and other adnexal tumours.[13] Cases of bilateral basal cell adenoma have been reported before but to our knowledge cases of bilateral BcAC have not been reported.[14]

Conclusion

Immunosuppressive therapy after kidney transplantation clearly increases the incidence of neoplastic conditions. We suggest a connection between the bilaterality and multifocality of the present parotid BcAC, and immunosuppression following the renal transplantation. Minimizing or even interrupting this medication should be carefully considered in such patients if cancer is diagnosed. The nefrologists in charge of the present patient are working on the options to minimize the immunosuppressive medications of the patient. No concensus prevails concerning the guidelines of what kind of changes ought to be made to the anti-rejection treatment after a transplantation patient having been developed a cancer.

Disclosures

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been

published elsewhere. The authors report no conflicts of interest.

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