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High grade transformation of adenoid cystic carcinoma in the palate: Case report with review of literature

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ABSTRACT

INTRODUCTION: Adenoid cystic carcinoma (ACC) is a rare tumor developed in minor salivary glands, the palate being the most common site.

CASE PRESENTATION: Here, we report a case of a 58-year-old man with a 3-year-growing swelling in the right palate diagnosed with high grade transformation adenoid cystic carcinoma. The exam revealed a 4 cm large mass. A tumor resection with a radical neck dissection was performed.

DISCUSSION: High grade transformation in adenoid cystic carcinoma is recently described by Cheuk et al. in 1999. This transformation has more aggressive behavior than conventional solid ACC and has usually been associated with recurrences, early distant metastasis, and greater mortality.

CONCLUSION: The aim here is to highlight clinical, histopathological, therapeutic and prognostic aspects of high-grade transformation in ACC with literature review.

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1. Introduction

Adenoid cystic carcinoma (ACC) is an extremely rare epithelial tumor that mainly affects minor salivary gland, especially in oral cavity but may also occur in sinonasal tract, nasopharynx, oropharynx, and trachea. This tumor arises also in major salivary gland; the most common site is the parotid gland [1]. It rarely appears in other location such as vulva, external auditory canal, cervix, lachrymal glands, esophagus, breast and Cowper glands [2].

This tumor represents 1% of all malignant tumors of oral and maxillofacial region and 22% of all salivary gland epithelial malignancies [1].

ACC is an indolent tumor, characterized by a slow progression with local and distant recurrences and decreased survival rate [3].

ACC with high grade transformation is a very rare variant. It is defined as the transformation of a low-grade malignant neoplasm into a high-grade carcinoma which is more aggressive and has more local recurrences and metastasis [4]. We present a rare case of ACC of the minor salivary glands of the hard palate composed only of

high grade areas with low grade component identified in lymph node metastasis and a literature review on its clinical, histopathological, immunohistochemical, therapeutic and prognostic aspects. This work is in line with the SCARE criteria [5].

2. Case report

A 58-year-old man presented with an oral cavity swelling that had been growing slowly for three years. There were no familiar or personal histories. Otorhinolaryngological examination revealed a 4 cm firm; immobile mass in the right palate. The right submandibular gland had a 1 cm firm and painless swelling. Multiple right jugular lymph nodes were observed.

An ultrasound examination showed two cervical lymph nodes in IA and IB section, suspecting thus tuberculosis, lymphoma, or metastatic carcinoma.

A fine needle aspiration of the palatal tumor showed monomorphic population of basaloid cells in clumps, clusters, and as single cells. The tumor cells showed mild atypia. They were round to oval with scanty cytoplasm and hyperchromatic nuclei. Most areas showed tumor cells surrounding hyaline globules. Based on these features diagnosis of adenoid cystic carcinoma was retained.

A resection of the tumor and a right functional lymph node dissection were performed followed by a resection of right submandibular gland without any complications. The operation was practiced by a professor of Otolaryngology with 15 years of experi-

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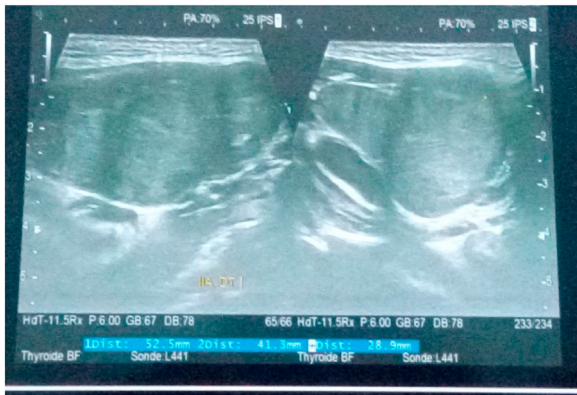


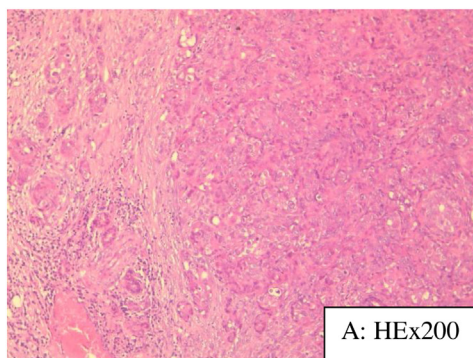
Fig. 1. Ultrasound examination showing cervical lymph nodes in IA and IB section, suspecting tuberculosis, lymphoma or metastatic carcinoma.

ence. The tumor was received in three fragments. These fragments were solid with white or gray-tan appearance and measured respectively 3, 1.7 and 1 cm. The right submandibular gland measured 4 cm.

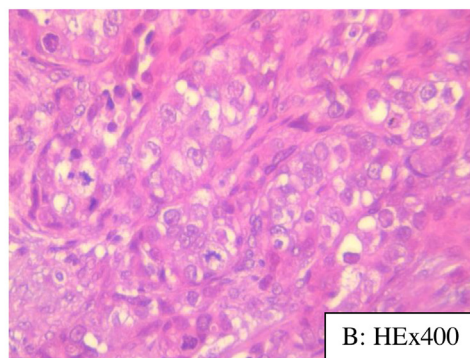
Microscopically, the tumor was composed only of sheets and nests of cells with scanty eosinophilic cytoplasm, large hyperchromatic nuclei, and prominent nucleoli. The mitosis was numerous. The stroma showed hyalinization change (Figs. 1 and 2). Areas of necrosis and extensive perineural invasion were perceived. The tumor invaded widely the adjacent skeletal muscle. Three of thirty-five lymph nodes of the right functional neck dissection were metastatic. The biggest lymph node was diffusely invaded with capsular effraction. In this lymph node, metastasis was composed of biphasic tubular and, cribriform structures containing myoepithelial and epithelial cells within a myxoid and/or hyaline matrix (Fig. 3). The tumor cells were hyperchromatic, monomorphic, small, and angulated (Fig. 3). The two other metastatic lymph nodes showed a low-grade ACC component with area of large pleomorphic cell component.

The immunohistochemical study (Table 1) showed that p53 was focally and weakly expressed (Fig. 4) and Ki67 index was 18% in the low-grade ACC component (Fig. 5), whereas, high grade component was strongly and focally positive for p53 (Fig. 6) and Ki67 index was 70% (Fig. 7). S100 protein (PS100) was positive in 30% of tumor cells in low grade ACC component (Fig. 8). However, its expression accounted for 95% in high grade ACC areas (Fig. 9). Smooth Muscle Actin (SMA) was positive in low grade component (Fig. 10) with loss of expression in high grade one (Fig. 11). In all components, C-kit (CD117) expression was observed in 90% of tumor cells (Figs. 12 and 13) and HER-2 was negative (Figs. 14 and 15).

The diagnosis of high grade transformed ACC of the palate was made.

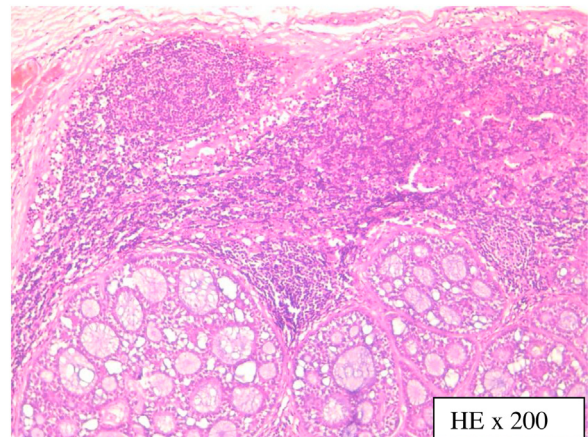


A: HEx200



B: HEx400

Fig. 2. Adenoid cystic carcinoma with high grade transformation: A: HEx200/ B: HEx400.



HE x 200

Fig. 3. lymph node invasion with low grade ACC component.

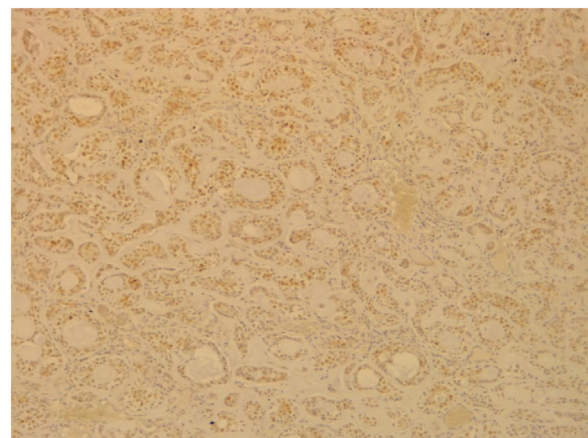


Fig. 4. p53 stain in low grade ACC component (lymph node metastasis).

The patient had an intensive chemo-radiation with the combination of cisplatin and 5-FU was subsequently undertaken, following administration of S-1, a novel oral derivative of 5-FU. After a one year of follow-up, the patient is in total remission.

3. Discussion

Adenoid cystic carcinoma (ACC) occurs most of the time in the minor salivary glands. It affects equally men and women; around the age of 50–60. It is recognized for its slow growth and indolent behavior, of late onset locoregional recurrences and silent distant

Table 1
Comparing immunohistochemical features between low grade and high-grade ACC components.

Antibody	Low grade ACC component	High grade ACC component
P53	Weakly positif (90%)	Strongly positif (90%)
Ki67	18%	70%
S100 protein (PS100)	30%	95%
Smooth Muscle Actin (SMA)	Positif (+)	Negative (–)
C-kit (CD117)	Positif (+) (90%)	Positif (+) (90%)
Her-2	Negative (–)	Negative (–)

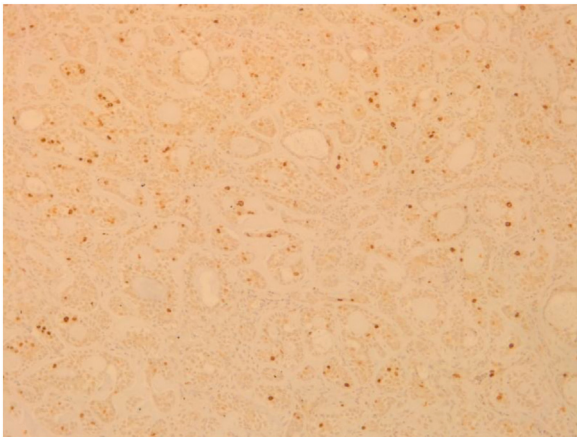


Fig. 5. Ki67 index in low grade ACC component (lymph node metastasis).

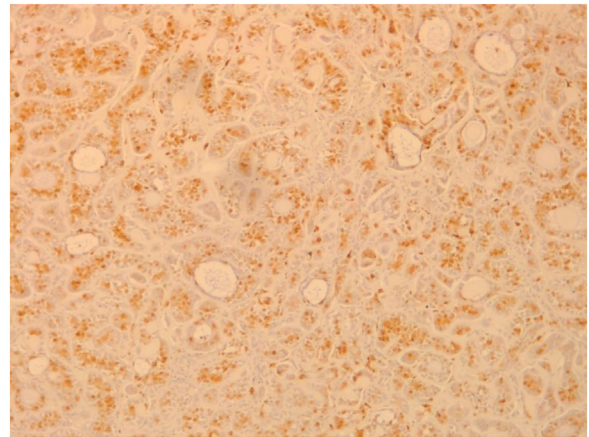


Fig. 8. PS 100 stain in low grade ACC component (lymph node metastasis).

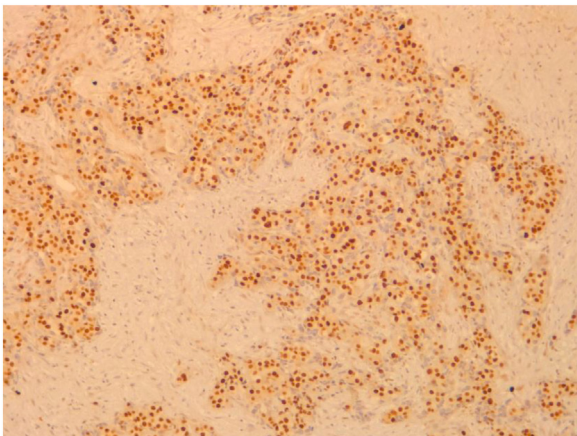


Fig. 6. p53 stain in adenoid cystic carcinoma with high grade transformation.

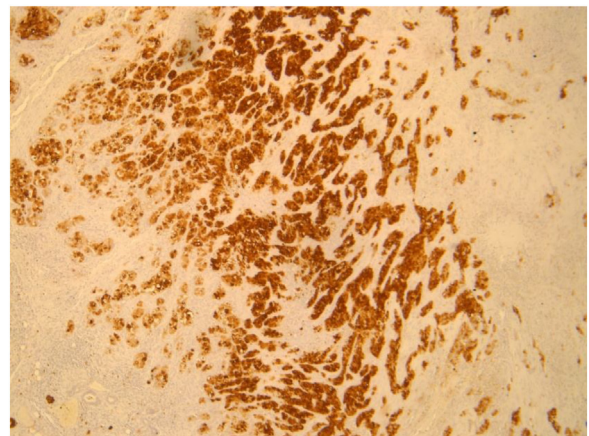


Fig. 9. PS100 stain in adenoid cystic carcinoma with high grade transformation.

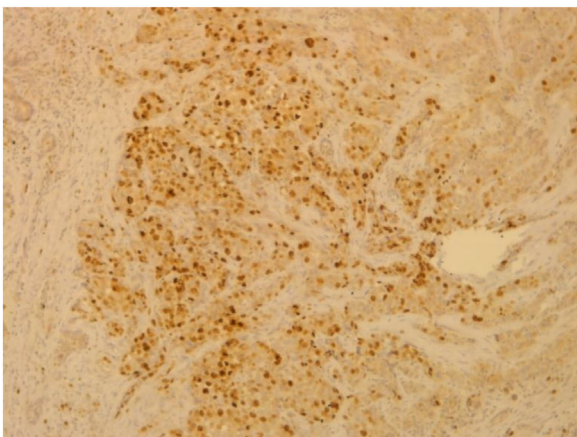


Fig. 7. Ki67 index in adenoid cystic carcinoma with high grade transformation.

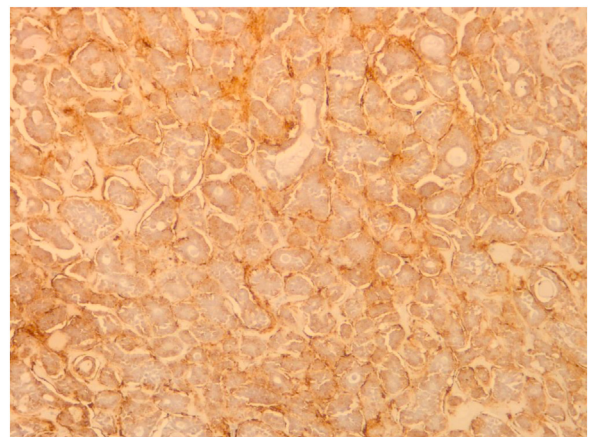


Fig. 10. AML stain in low grade ACC component (lymph node metastasis).

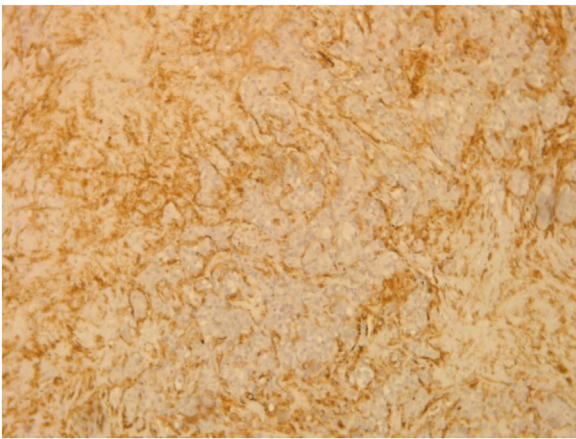


Fig. 11. AML stain in adenoid cystic carcinoma with high grade transformation.

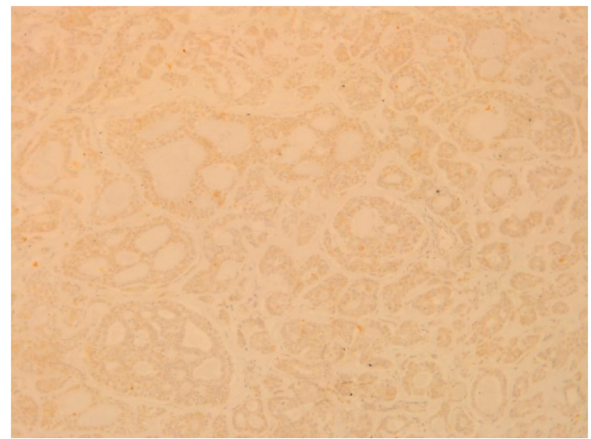


Fig. 14. Her2 stain in low grade ACC component (lymph node metastasis).

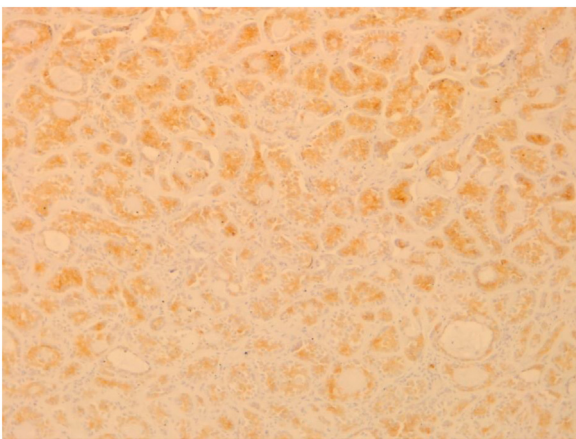


Fig. 12. CD117 stain in low grade ACC component (lymph node metastasis).

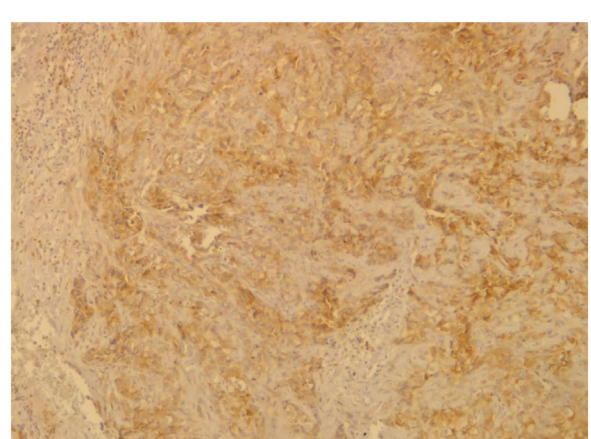


Fig. 15. Her2 stain in adenoid cystic carcinoma with high grade transformation.

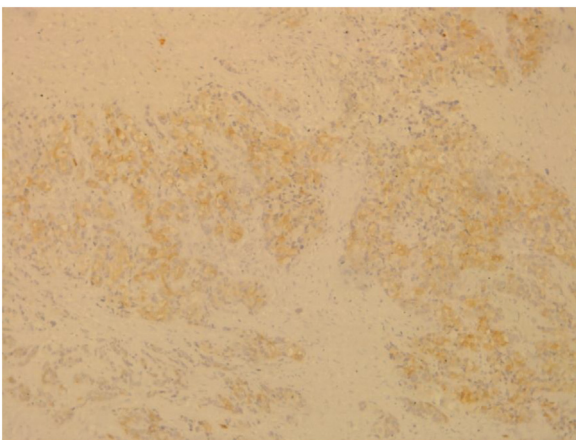


Fig. 13. CD117 stain in adenoid cystic carcinoma with high grade transformation.

metastases. This tumor is characterized by a poor long-term prognosis [6].

Microscopically, the tumor has cribriform, tubular, or solid architecture. It is composed of uniform cells with globules of hyaline material [4].

Van Weert [7], Zhang [8] and Xu have proposed two grades. This grading has been considered an important prognostic factor. Grade 1 ACCs are well differentiated and characterized by tubular and cribriform patterns without solid components; Grade 2 ACCs are composed with solid areas.

ACC with high grade transformation is defined as a high-grade transformation for low-grade areas [4], in which the high-grade component is often juxtaposed to the original lesion or the original line of differentiation is lost.

Cheuk et al. [9] firstly used the term adenoid cystic carcinoma with high grade transformation to describe areas with pleomorphic tumor cell next to areas of conventional adenoid cystic carcinoma. The transition between the two areas was mostly abrupt. And others consider this transformation as an untreated, low-grade salivary gland tumor, in a recurrent lesion or sometimes after postoperative radiotherapy [9].

Adenoid cystic carcinoma with high grade transformation occurs essentially in the submandibular gland and the minor salivary glands in the sinonasal tract or palate [6].

The age of patients ranges from 32 to 74-year-old with a mean age of 58 years with male predominance [9]. For our case, the patient's age and the site of the tumor are comparable to the cases reported in literature.

The median size of ACC with high grade transformation is about 3 cm. This tumor is very aggressive. It usually extends beyond submandibular gland and affects bone at sinonasal or palatine sites with mostly positive surgical margins.

Our case had the same histopathologic aspect described by Cheuk et al. [9]. The transformed component demonstrated marked nuclear atypia conforming to the criteria established by

Seethala et al. [6,10]. Micropapillary and squamoid components have been observed, but these areas hadn't been in our case [10].

The high-grade transformed component in ACC ranges from 10% to 100% [10]. In our case report, the whole tumor was composed of high-grade areas. The distinction of ACC with high grade transformation from ACC, mainly from the solid pattern, is sometimes hard. Nuclear enlargement was been frequently reported in the solid component. Additionally, the transition between the conventional ACC and high grade transformed ACC were sometimes difficult.

However, ACC with high grade transformation was characterized by confluent sheets, large comedonecrosis, pronounced nuclear atypia and significantly higher mitotic labeling. The stroma is desmoplastic.

On immunohistochemical examination, tumor cells showed a loss expression of myoepithelial and Her-2/Neu in the high-grade component. Her-2/Neu negativity has been helpful to eliminate the diagnostic differential of a hybrid ACC-salivary duct carcinoma [10]. The transformed component revealed a p53 overexpression in 60% of tumor cells and high Ki-67 labeling index [10].

However, the tumor cells expressed C-kit (CD117) and E-Cadherin in both conventional and high-grade components [10].

The most comment differential diagnosis of adenoid cystic carcinoma are adenocarcinoma (not otherwise specified), undifferentiated carcinoma, salivary duct carcinoma, basaloid adenocarcinoma, and carcinoma ex pleomorphic adenoma.

The prognostic depends on several parameters including the tumor stage, perineural invasion, lymphatic metastasis, and surgical margins.

Advanced tumor stage, the presence of cervical lymphatic metastasis and affected surgical margins are considered bad prognostic factors with frequent local recurrence, distant metastasis and greater mortality [4].

Treatment for adenoid cystic carcinoma with high grade transformation is principally wide local resection. Radiotherapy and chemotherapy as an adjunct to surgery has been shown to improve local control.

4. Conclusion

In conclusion, adenoid cystic carcinoma with high grade transformation is a very rare aggressive variant of adenoid cystic carcinoma. It seems to have a high predisposition for lymph node metastases and distant metastasis. On microscopic examination, adenoid cystic carcinoma with high grade transformation is characterized by nuclear enlargement and chromatin irregularities beyond those of conventional grade 2 adenoid cystic carcinoma, higher mitotic rates and Ki-67 indices, and loss of biphasic morphology.

Declaration of Competing Interest

The authors have no conflict of interest to disclose.

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Ethical approval

This study is exempt from ethical approval at our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ahlem Bchir: Conceptualization, Investigation.
Manel Njima, Nouha Ben Abdeljalil: Writing - original draft.
Seifeddine Ben Hammouda: Writing, Reviewing and Editing.
Leila Njim and Khelifa Mighri: Investigation, Visualization.
Abdelfatteh Zakhama: Visualization.

Registration of research studies

Not applicable.

Guarantor

Dr. Manel Njima.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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