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Case report

Thyroid angiosarcoma: A case report and review of literature

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ABSTRACT

Introduction: Thyroid angiosarcoma is a very aggressive and rare malignancy that is mostly seen in elderly of Alpine regions, related to high prevalence of iodine deficient goiter. The major diagnostic challenge is to distinguish between this entity and anaplastic carcinoma and to specify whether it is a primary or metastatic angiosarcoma. The objective of this work is to clarify this distinction through our case report and a revue of literature.

Case report: We report the case of a 55 years-old female patient, with no medical history, admitted to the General Surgery Department of Ibn Sina Hospital in Rabat for the management of a cervical mass classified sonographically TI-RADS 6. It was also noted a lesion of the skin next to the thyroid lodge. The patient underwent total thyroidectomy with simple post-operative course. A third tumor location was discovered in the stomach during Oesophago-Gastro-Duodenoscopy (OGD).

Results: Microscopically, the thyroid, cutaneous and gastric tumors showed rows of oval to spindle-shaped cells, with marked cytonuclear atypia and high mitotic activity. The stroma was richly vascularized and fibro-inflammatory. Immunohistochemical studies demonstrated that the tumor cells showed positive staining for cytokeratin (AE1/AE3), CK7, ERG and CD31, while they exhibited no immunoreactivity for CK20, thyroglobulin or CD34.

Discussion: The first diagnostic challenge is to rule out anaplastic carcinoma. Using and the classification proposed by Cutlan et al. and a large immunohistochemical panel the diagnosis of epithelioid angiosarcoma was retained. Based on epidemiological and clinical criteria, the primary site in our case was more likely to be cutaneous.

Conclusion: In summary, thyroid angiosarcoma is an uncommon thyroid neoplasm which poses a problem of differential diagnosis with anaplastic carcinoma and metastatic angiosarcoma. The use of a large panel of antibodies as well as the epidemiological and clinical data can solves the problem in the most difficult cases.

1. Introduction

Thyroid angiosarcoma is a very rare malignancy that is mostly seen in elderly of Alpine regions, related to high prevalence of iodine deficient goiter. It is a very aggressive tumor due to persistent local disease and distant metastases [1].

The major diagnostic challenge is to distinguish between this entity and anaplastic carcinoma and to specify whether it is a primary or metastatic angiosarcoma.

The objective of this work is to clarify this distinction through our case report and a revue of literature. This case report has been reported in line with the SCARE Criteria [2].

2. Case report

We report the case of a 55 years-old female patient, with no medical or family history including irradiation, born and resident in a mountainous region of northern Morocco. The patient had no history of smoking or alcohol and drug use. She was referred by family physician to the General Surgery Department of Ibn Sina Hospital in Rabat for the management of a painless cervical mass. Clinical examination of the thyroid gland showed a remarkable enlargement of the left lobe in which a nodular lesion was seen. It was also noted a lesion of the skin next to the thyroid lodge. Thyroid gland ultrasonography showed a multinodular, plunging and compressive goiter classified TI-RADS 6, at the

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expense of the left lobe. Computed tomography (CT) of the chest confirmed the diagnostic and showed multiple pulmonary nodules evoking a secondary localization. The results of thyroid function tests were within the normal range. The patient underwent total thyroidectomy 2 weeks after presentation and had simple post-operative course. The surgery was performed by a professor specialized in general surgery with a background of 20 years of experience in this field. A biopsy of the cutaneous lesion was also performed. The surgical specimen as well as the cutaneous sample were sent to the pathological anatomy department and were fixed in 10 % formalin (Fig. 1).

Two weeks after surgery, the patient was admitted in the emergency room for moderately abundant melena and hematemesis. After hemodynamic stabilization, she benefited from an Oesophago-Gastro-Duodenoscopy (OGD) that showed an ulcerated, bleeding, budding lesion in the fundus. This lesion was biopsied and addressed to our department for examination.

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 Editor-in-Chief of this journal on request.

3. Results

Gross examination of the surgical thyroid specimen showed a whitish firm tumor, poorly limited and measuring 4 × 4 × 5 cm, at the expense of the right lobe (Fig. 2).

Microscopically, the tumor was composed of rows of oval to spindle-shaped cells, with marked cytonuclear atypia. The cytoplasm was scanty eosinophilic and the nuclei was hyperchromatic. Several mitotic figures and vascular emboli were noted. The tumor was partly necrotic and showed hemorrhagic changes. The stroma was richly vascularized and fibro-inflammatory (Fig. 3).

Immunohistochemical studies demonstrated that the tumor cells showed positive staining for cytokeratin (AE1/AE3), CK7, ERG and CD31. The tumor cells exhibited no immunoreactivity for CK20, thyroglobulin or CD34 (Fig. 4).

Microscopic examination of the cutaneous and gastric samples showed the same proliferation described above and the tumor cells exhibited the same immunohistochemical characters (Figs. 5, 6).

4. Discussion

Thyroid angiosarcoma is a very uncommon tumor that is highly seen in European Alpine regions where it represents 10 % of all thyroid neoplasms [3]. This predilection for mountainous regions has been explained by iodine deficiency leading to thyroid goiters. In the English literature, few non-alpine thyroid angiosarcoma have been reported, suggesting the presence of other etiological factors not yet known, involved in the pathogenesis of this disease [4]. The patients' ages ranged from 50 to 88 years, with a female predominance (Female male ratio, 9:3) [5]. Clinical and radiological features are nonspecific and include thyroid mass with compression symptoms or signs related to distant metastasis. On gross examination, the tumor is usually a single nodule commonly filled with bloody fluid and compressing thyroid.

Microscopically, thyroid angiosarcoma is a pleomorphic tumor, usually poorly differentiated, with irregular slit vascular spaces and anastomosing channels lined by large, atypical cells of endothelial lineage. The first diagnostic challenge is to rule out anaplastic carcinoma. In fact, clear-cut separation between the angiosarcoma and angiomatoid anaplastic thyroid carcinoma is difficult because they yield

Fig. 2. Gross image of the tumor.

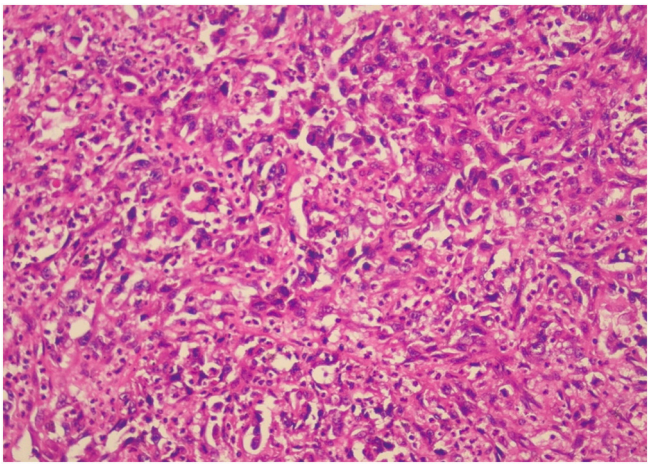

Fig. 3. Histological image of the thyroid tumor (HE × 40).

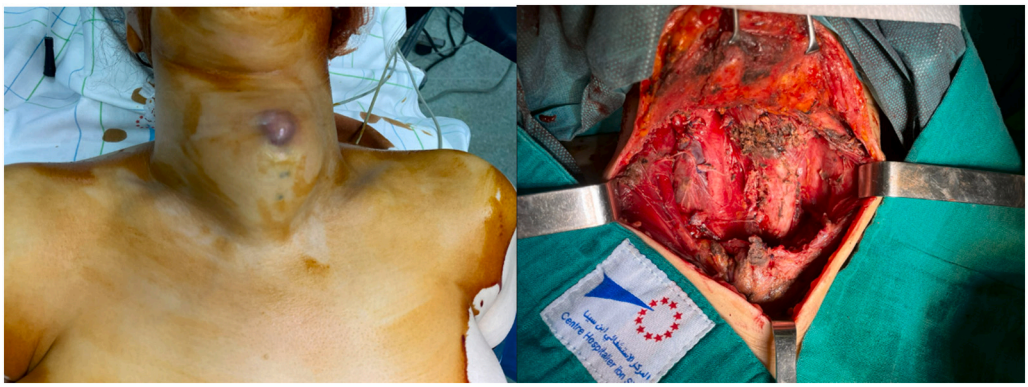

Fig. 1. Clinical (left) and intraoperative (right) image.

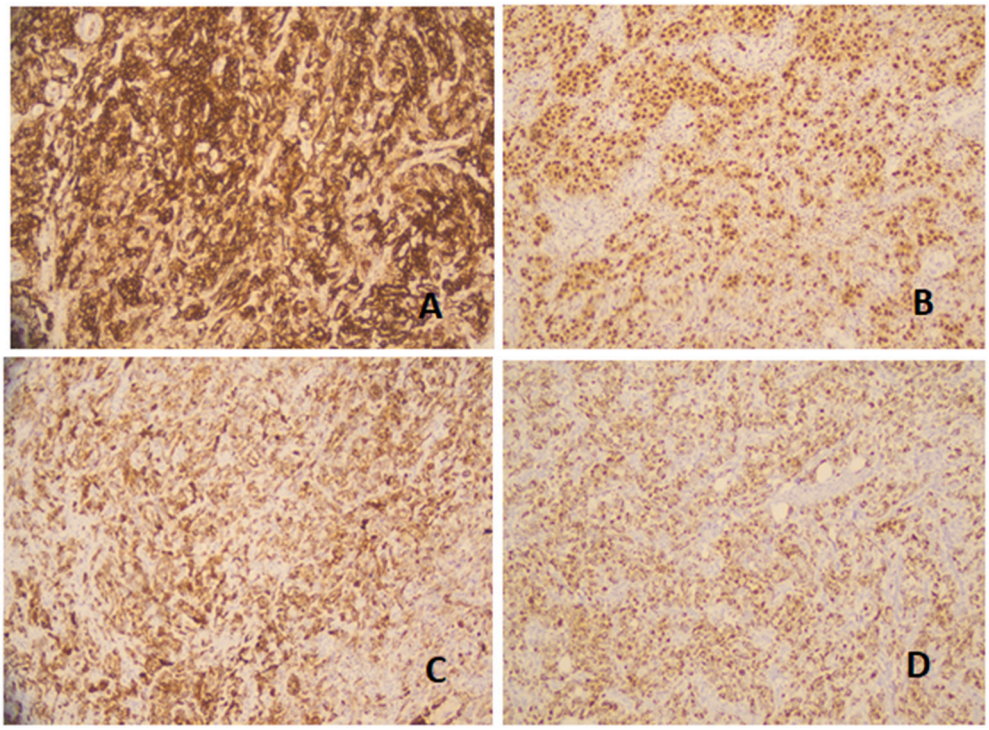

Fig. 4. Positive staining of tumor cells for CD31 (A), ERG (B), AE1/AE3 (C) and CK7 (D).

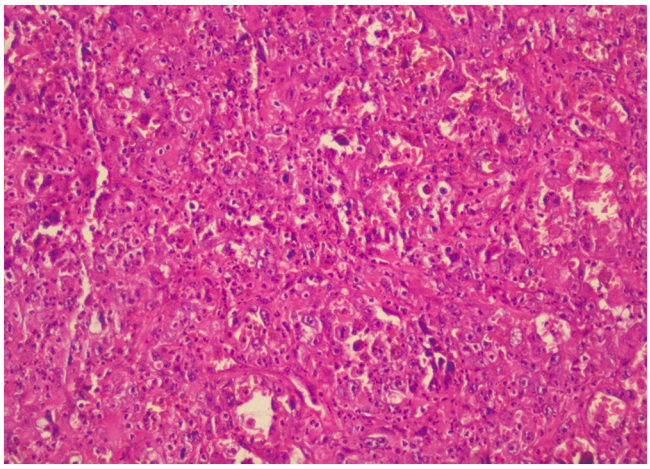

Fig. 5. Histological image of the gastric tumor (HE × 20).

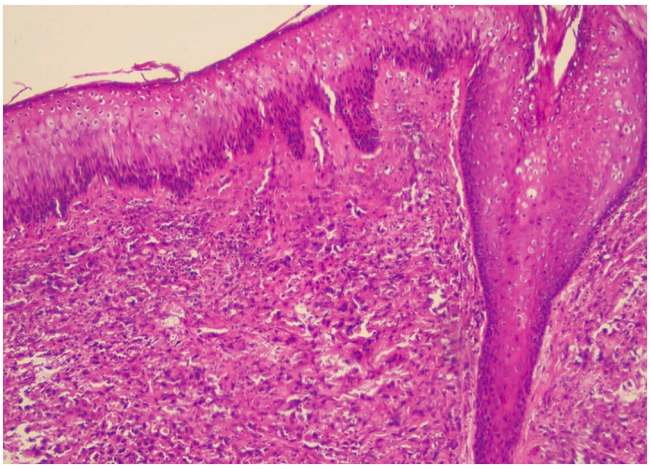

Fig. 6. Histological image of the cutaneous tumor (HE × 10).

nearly the same clinical prognosis and overlapping histological and immunohistochemical findings. Indeed, in angiosarcoma, the tumor cells always express one or more endothelial markers (factor VIII; CD31; CD34) and sometimes epithelial markers and in particular cytokeratins (CK). On the other hand, they do not express thyroglobulin or Podoplanin (D2–40). In angiomatoid anaplastic carcinoma, tumor cells express epithelial markers (CK, EMA), rarely thyroglobulin and may express certain endothelial marker [3,6–8]. PAX8 and TTF1 and podoplanin show immunopositivity in anaplastic carcinomas.

In 2000, Cutlan et al. proposed a classification to distinguish between these two entities. Thus, thyroid angiosarcoma is defined by the presence of endothelial differentiation and the positivity of vascular markers. When it additionally expresses epithelial markers, it is an epithelioid angiosarcoma. On the other hand, angiomatoid anaplastic carcinoma is defined by an expression of both endothelial and epithelial markers and thyroglobulin. If the tumor does not express any vascular marker, it is considered an anaplastic carcinoma with an angiosarcoma-like appearance [6].

In our case, the tumor cells were positive for vascular and epithelial marker and were negative for thyroglobulin. Therefore, the diagnosis of epithelioid angiosarcoma was retained.

The second challenge is to specify whether it is a primary or metastatic angiosarcoma especially when other sites are involved like in our case.

Histological and immunohistochemical data are not helpful since primary angiosarcoma is negative for thyroglobulin and the immunostaining for ck7 and ck20 is inconsistent and nonspecific.

This distinction is initially based on epidemiological criteria; In fact, the most common site of angiosarcoma is the skin of the head and neck and represents about 60 % of all the cases, while thyroid angiosarcoma is very uncommon. Secondly, the chronology of the symptoms can be helpful. Indeed, in our case, the skin lesion appeared way before the

thyroid swelling, and was neglected by the patient. Based on these facts, the primary site in our case was more likely to be cutaneous.

Thyroid angiosarcoma is a very aggressive tumor. Indeed, it can rapidly spread to the cervical lymph nodes, lungs, and brain or can metastasize to the duodenum, small bowel and large bowel and induce severe bleeding [1,9–11].

Surgical resection is associated to adjuvant chemotherapy and/or radiotherapy to obtain both systemic and local control of the disease.

Metastatic disease is associated with poor prognosis and limits the mean survival time to a few months after diagnosis and surgical treatment. Our patient past away after 2 months after surgery.

5. Conclusion

In conclusion, thyroid angiosarcoma is an uncommon thyroid neoplasm which poses a problem of differential diagnosis with anaplastic carcinoma and metastatic angiosarcoma. The use of a large panel of antibodies as well as the epidemiological and clinical data can solves the problem in the most difficult cases.

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Ethical approval

The study is exempt from ethnical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contribution

L BENBELLA, F ZOUAIDIA: Identification and write up of case.

I ELOUARITH, H EL OUAZZANI, Z BERNOUSSI: Review of pathology pertaining to the case.

M K LAHLOU: Operating surgeon.

Research registration number

Not applicable.

Guarantor

L benbella.

Declaration of competing interest

No conflict of interest is declared.

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