



Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

An extremely rare case of thyroid malignancy from the non-Alpine region: Angiosarcoma



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ARTICLE INFO

Article history:

Received 27 September 2015

Received in revised form

16 December 2015

Accepted 17 December 2015

Available online 23 December 2015

Keywords:

Thyroid gland

Primary angiosarcoma

Head and neck malignancy

Surgery

Hematoma

ABSTRACT

INTRODUCTION: Thyroid angiosarcoma is a rather rare malignancy featuring a poor prognosis, and which may interfere with other aggressive thyroid tumors; it is usually seen in the Alpine region.

CASE PRESENTATION: A 74-year-old male was referred to our center with complaints of progressive neck swelling and dyspnea. He had multiple nodules featuring cystic degeneration and calcifications in the thyroid gland, together with multiple lymphadenopathies of the neck region. Fine-needle aspiration cytology (FNAC) confirmed the presence of anaplastic carcinoma. A total thyroidectomy was performed. During the postoperative period, multiple drainage were performed for recurrent hematomas, but hematoma development could not be prevented. On postoperative day 7, the patient died due to multiple-system failure. Histopathological investigation of the thyroidectomy specimen indicated that the lesion was an angiosarcoma.

DISCUSSION: The cytological diagnosis of thyroid angiosarcoma is quite difficult. Extracapsular invasion and distant organ metastasis during surgery are known as strong and negative prognostic factors for thyroid angiosarcoma. Treatment is quite difficult, since this tumor is locally aggressive, destructive, and features a high recurrence rate. In this case, since extracapsular invasion, as well as lymph node and lung metastasis were present at the time of surgery; the expected survival time was quite short.

CONCLUSION: This case shows that during differential diagnosis, patients initially diagnosed with anaplastic carcinoma via FNAC may actually present with angiosarcoma. It may be helpful to review the treatment modalities for this cancer type, which has a rather poor prognosis and features severe bleeding, as well as local and distant metastasis.

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1. Introduction

Thyroid angiosarcomas are rare and very aggressive malignancies [1]. Most thyroid angiosarcoma cases are reported from the Alpine region; only a few cases are reported from the areas beyond this region. This cancer, which is reported in advanced ages, generally develops as a multinodular goiter [2,3]. This tumor originates from the vascular structures of the thyroid gland and is recognized histopathologically by its atypical endothelial cells; it is also associated with the presence of vascular canals microscopically. In addition to its resemblance to anaplastic cancer based on the presence of atypical cells, its aggressive and destructive nature

can result in misdiagnosis [1]. Patients commonly present with compression symptoms including a lesion on the neck, dyspnea, hoarseness, and dysphagia due to the rapid growth of the tumor. In many cases, systemic metastasis is present at the time of diagnosis and thyroid angiosarcoma commonly has a tendency of metastasizing to local regional lymph nodes and the lungs [2–4]. In this paper, a 74-year-old male patient who underwent fine-needle aspiration cytology (FNAC), who was initially diagnosed with anaplastic carcinoma, and who was later diagnosed with angiosarcoma following total thyroidectomy is presented. Appropriate treatment modalities are subsequently discussed.

2. Case presentation

A 74-year-old male patient complaining of dysphagia, moderate dyspnea, hoarseness, and neck pain for 1 month was admitted to our tertiary center. Neck ultrasound (US) revealed a conglomerated isoechoic nodule that almost totally filled the right lobe; the nodule

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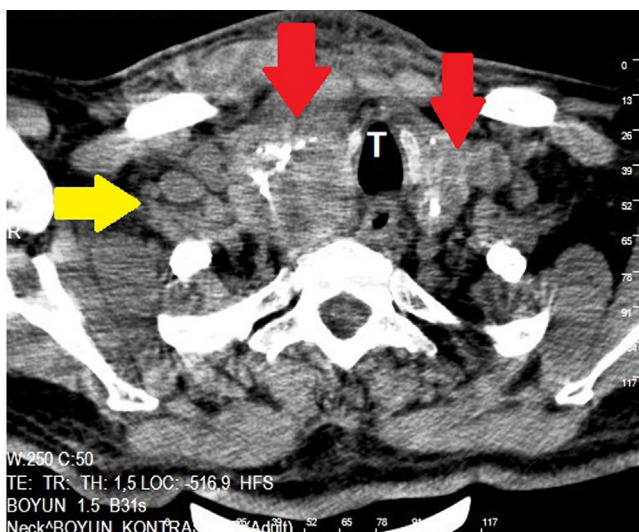


Fig. 1. Preoperative neck CT images of the patient. The trachea is seen to be deviated to the left. Red arrow: thyroid gland featuring calcifications and extending into the retrosternal area, which cannot be clearly differentiated from the surrounding tissues. Yellow arrow: lymphadenopathies.



Fig. 2. The image of the total thyroidectomy specimen of the patient.

contained micro-calcifications without clearly delineated borders, separating it from parenchyma. There were also multiple nodules featuring similar characteristics on the left lobe. Moreover, levels 2 and 3 of the right neck, as well as multiple lymphadenopathies (the largest of which was $14 \times 17 \times 24$ mm in dimension) exhibiting the same characteristics as thyroid nodules were observed. Afterwards, FNAC was performed for both the right and left thyroid lobes, as well as for the lymphadenopathies on the neck region. The pathological results of the biopsies of both lobes and neck levels 2 and 3 were reported to be “compatible with thyroid anaplastic carcinoma”. However, a widespread hematoma had developed on the right side of the patient’s neck. The hematoma of the patient, who had a normal bleeding profile, as well as the patient’s bleeding time and the thrombocyte functions regressed upon follow up. At that time, computed neck tomography (CT) was performed, and bilaterally increased heterogeneity featuring calcifications on the thyroid gland, an increase in the dimensions of the right sternocleidomastoid muscle (SCM), and multiple lymph nodes (the largest of which had a diameter of 3 cm) at the bilateral neck levels were reported. Moreover, increased densities were also found on the right supraclavicular adipose areas and on the skin due to edema. An increase in soft tissue density narrowing in the right paralaryngeal area and depletion of the larynx to the left were observed (Fig. 1). Upon physical examination, bilateral painless diffuse stiffness was palpated across the entire neck region. On endoscopic examination, the larynx was edematous and deviated to the left side with right vocal cord paralysis. Regarding his medical history, it was learned that he had a multinodular goiter for 10 years. In biochemical examination, thyroid stimulating hormone (1.63 uIU/mL), freeT₃ (3.26 pg/mL), freeT₄ (1.13 ng/dL), anti-thyroperoxidase antibody (5.04 IU/mL) and calcitonin (1.05 pg/mL) were normal but thyroglobulin antibody was high (619.4 IU/mL). Thorax CT revealed multiple nodules featuring a metastatic appearance in both lungs. Lung fiberoptic bronchoscopy revealed active hemorrhage originating from the right upper main bronchi, and brush and lavage samples were obtained. Upon pathological evaluation of these samples, malignancy findings were not present. Afterwards, the patient was evaluated by our tumor board. To overcome respiratory deficiencies and to obtain an actual diagnosis, it was decided that surgery would be performed (a total thyroidectomy, if possible), versus biopsy and tracheotomy.

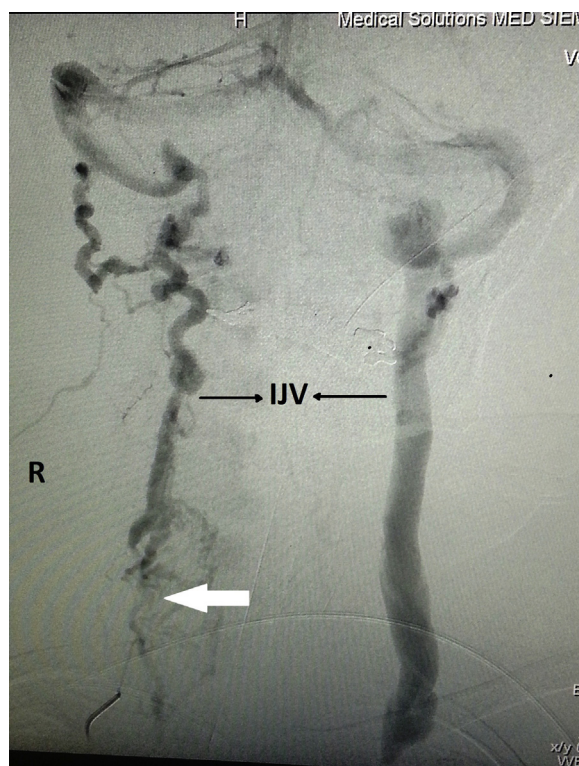


Fig. 3. The venography image of the patient performed after the development of the third hematoma. The right IJV is observed to be obliterated in inferior parts (r: right; white arrow: the obliterated area of the IJV).

The operation began with a preoperative modified Kocher incision of 10 cm in length, but it was observed that the strap muscles were quite coherent with the thyroid. The results of the frozen section obtained from this region were “compatible with anaplastic carcinoma”. Later, the operation was continued with inclusion of the strap muscles to the surgery. Although left lobe dissection was uneventful, during the right lobe dissection, the thyroid was

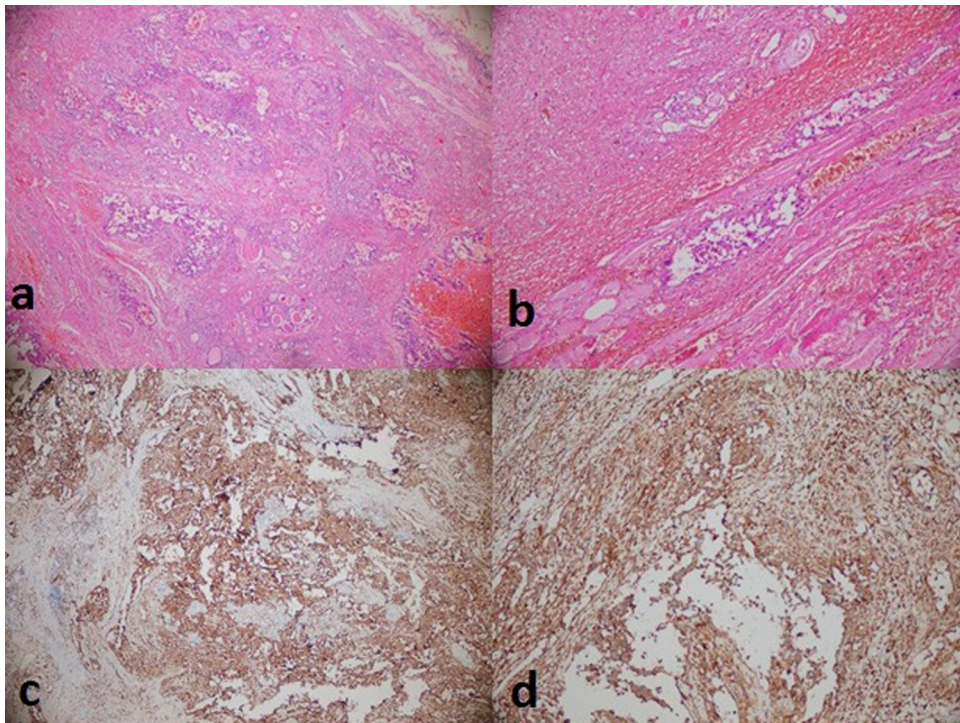


Fig. 4. Histopathological and immunohistochemical images of the patient: (a) vascular tumoral structures between thyroid follicles (H&E $\times 40$). (b) Vascular tumoral structures in the muscle tissues around the thyroid gland (H&E $\times 40$). (c) CD31 positivity ($\times 40$). (d) CD34 positivity ($\times 40$).

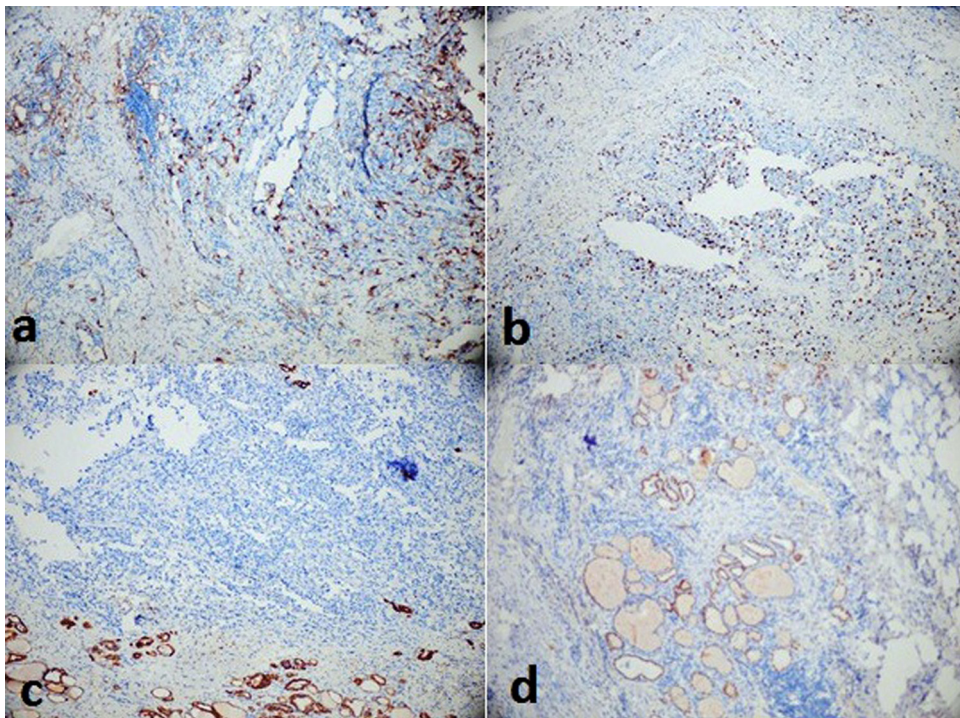


Fig. 5. Immunohistochemical images of the patient. (a) Vimentin positivity ($\times 40$). (b) Ki67 positivity ($\times 40$). (c) Thyroglobulin negativity ($\times 40$). (d) TTF-1 negativity ($\times 40$).

observed to be adherent to the SCM, but the thyroid tissue was dissected from this muscle by blunt dissection. On the left side, the parathyroid glands were preserved, but they were included in the specimen on right side. Both recurrent laryngeal nerves were defined and preserved. Once bleeding control was achieved, the surgery was completed (Fig. 2).

On postoperative day 1, the patient was re-operated due to a hematoma on the neck; any foci other than the bleedings around the right SCM muscle could not be found. Electro-cauterization was performed and absorbable hemostatic materials were applied; the operation was finished after achieving control of the hemorrhage. Based on the suspicion of bleeding profile abnormalities, the patient's bleeding profile, bleeding time, and thrombocyte acti-

vation tests were performed and all their results were normal. Following this bleeding, the patient was evaluated in the operation room 3 more times. Intraoperative angiography and venography were performed; no bleeding foci could be determined (Fig. 3). The patient was followed, intubated, and pressured dressings were applied. In the following periods, the patient's hematoma continued to progress. During all these procedures, massive transfusions were performed. However, the patient died on postoperative day 7 due to multi-organ failure. The day he died, the histopathological investigation was completed and reported as "angiosarcoma" based on the lesion's histomorphologic and immunohistochemical features. The histopathological sections revealed that there were diffuse hemorrhage areas and a vascular tumor dispersed between the thyroid follicles, producing a mass in some areas of the thyroid tissue. Tumor cells were characterized by large, spherical nuclei, and they were lining irregular vascular splits. The surrounding adipose tissue and muscle tissue were infiltrated by the tumor. Immunohistochemical studies revealed that the tumor cells were positively reacting with CD31, CD34, and vimentin, while they were negatively reacting with CK7, CK20, chromogranin, EMA, thyroglobulin, TTF-1, and calcitonin (Figs. 4 and 5).

3. Discussion

Angiosarcoma is a rather rare and highly hostile mesenchymal neoplasm with its destructive and aggressive features, as they show many morphological characteristics [5]. In the etiopathogenesis of angiosarcoma, chronic lymphedema and radiation exposure are the most commonly known predisposing factors. Angiosarcoma is frequently reported on the skin and superficial soft tissues. However, lesions of the chest, liver, bone, spleen, and heart are also frequently reported. The most common reason for skin and superficial soft tissue involvement is the presence of chronic lymphedema. Furthermore, frequent involvement of the chest region is associated with mastectomy and radiation exposure due to radiotherapy, particularly in cases of breast cancer. Cutaneous angiosarcoma is reported in the head and neck region, and especially on the scalp. However, thyroid angiosarcomas are extremely rare [5].

Although the incidence of thyroid angiosarcoma is high in the Alpine regions, such as in Switzerland and Northern Italy, it is very low in rest of the world. There are only a few case reports from Turkey [6]. This tumor is predominantly reported in elderly patients with a history of nodular goiter for many years. Although some alterations, such as Hashimoto thyroiditis and intranodular hemorrhage, were reported as potential etiological factors in the development of a vascular endothelial tumor (such as thyroid angiosarcoma), the developmental etiopathogenesis of thyroid angiosarcoma was still not determined [7].

The cytological diagnosis of thyroid angiosarcoma is quite difficult. The FNAC results of this disease may be confused with those of many other diseases such as anaplastic cancer, epitheloid sarcoma, alveolar rhabdomyosarcoma, and alveolar soft part sarcoma. Therefore, these tumors should be excluded during differential diagnosis [1,8]. In the diagnosis of angiosarcoma, different staining patterns of many samples, as well as an investigation of different slices, may take a long time, resulting in delays in treatment. In this case, preoperative FNAC samples and preoperative frozen section samples were reported as anaplastic carcinoma, and angiosarcoma could not be determined. In fact, during retrospective evaluations, the fact that a hematoma developed on the patient's neck during the postoperative period following FNAC may be a sign that angiosarcoma is present, as it is an aggressive thyroid tumor. However, the exact diagnosis could only be reached with reports of the histopathological evaluation of the total thyroidectomy material following the death of the patient.

The treatment of thyroid angiosarcoma is quite difficult since this tumor is locally aggressive, destructive, and highly recurrent. The first-line treatment modality of choice is radical surgery, even though surgical treatment and adjuvant chemoradiotherapy should be selected as additional treatments [1–5]. Although the prognosis of patients operated on after a diagnosis of angiosarcoma (if restricted only in the thyroid gland) is not poor, these patients are reported to have a 5-year survival rate of 33.3%, as they generally admit to hospital in advanced stages [4]. In these patients, extracapsular invasion and distant organ metastasis during surgery are known as strong negative prognostic factors [1,4].

In this case, since extracapsular invasion, as well as lymph node and lung metastasis were present at the time of surgery, the patient's expected survival time was quite short. This was especially enhanced given that extracapsular invasion of this highly vascular tumor to the SCM and the tissues surrounding it resulted in hemorrhages and hematoma development during the postoperative period. Hemorrhage stability could not be achieved in this case, and chemoradiotherapy could not be performed during the postoperative period. Radical neck dissection may stop bleeding, even if with a low probability, in the postoperative period after the development of recurrent hematomas; however, since the patient's general condition was not well, this operation could not be performed. If this operation could be performed, the patient may have died early on in the postoperative period, since the patient's prognosis was already quite poor.

4. Conclusion

In conclusion, thyroid angiosarcoma, which is a rather aggressive malignancy, should be kept in mind during the differential diagnosis of cases that are prediagnosed or predicted to be anaplastic carcinoma (as determined by FNAB). We suggest that in cases of prediagnosed and aggressive thyroid malignancies, hemorrhage development following FNAC may serve as a clue that can be used to diagnose the patient with angiosarcoma. In the presence of extracapsular invasion of this poor-prognosis tumor, patients may expire due to severe hemorrhages following surgical treatments.

Conflict of interest

None.

Funding

None.

Ethical approval

Ethical approval is not necessary for this case report.

Consent

Ethics committee approval is not necessary for this case report.

Authors contribution

Ömer Bayır: study design, data collection, data interpretation, writing the paper.

Demet Yilmazer: study design, data collection, data interpretation, writing the paper.

Reyhan Ersoy: endocrinological data collection, writing the paper.

Yasemin Akca: histopathological data collection, writing the paper.

Güleser Saylam: study design, writing the paper.
Ünsal Han: histopathological data collection.
Ali Özdek: writing the paper.
Bekir Çakır: endocrinological data collection, editing the paper.
Mehmet Hakan Korkmaz: editing the paper.

Guarantor

None.

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