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A Case of Hemangiosarcoma in Thyroid with Severe Anemia due to Bone Marrow Metastasis

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Abstract. A 56-year-old woman presented with rapidly enlarging thyroid mass and deep anemia. There was no history of gastrointestinal bleeding, and endoscopic examinations of the gastrointestinal system were normal. Fine needle aspiration cytology from the thyroid nodule was suspicious. After blood transfusion, total thyroidectomy was performed. Post-operative histopathological examination of the specimen revealed hemangiosarcoma of the thyroid. After establishment of the diagnosis chemotherapy was started. But hemoglobin values decreased again and hepatosplenomegaly developed at the second month of surgery. Bone marrow aspiration cytology which was performed demonstrated the same tumoral cells infiltrating bone marrow. The patient died at 12th week after surgery. Thyroid hemangiosarcoma can metastasize to the bone marrow and anemia may be an indicator of the advanced disease. In the differential diagnosis of the anemia, bone marrow metastasis and bone marrow biopsy should be considered in suspected cases.

Key words: Hemangiosarcoma of the thyroid, Anemia, Bone marrow

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PRIMARY thyroid hemangiosarcoma is a very rare and aggressive disease. The incidence is highest in European Alpine regions and it constitutes 2–10% of all malignant thyroid tumors in Switzerland, Austria and northern Italy [1, 2]. In other parts of the world it is extremely rare. Findings develop according to the area of metastasis. Local recurrence and metastasis are frequent and patients usually die in a short time after diagnosis. Early tumor metastasis to regional lymph nodes and lungs is frequent. Bone marrow metastasis may occur in later stages. Multimodality treatment consisting of surgery, radiotherapy and chemotherapy is widely accepted [3, 4].

We present a case of primary thyroid hemangiosarcoma metastasizing to the bone marrow, thus confusing the etiology of the anemia.

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Case Report

A 56-year-old woman presented with a neck mass which she had noticed four years ago. This mass enlarged rapidly in the last two months. Physical examination revealed an enlarged thyroid gland and there was a hard, irregular and mildly tender painful nodular lesion measuring 4 × 4 × 3 cm in the right thyroid lobe. There were no evident cervical lymph nodes. The patient was anemic. Blood values were as follows: hemoglobin (Hb) 6.6 g/dl, hematocrit 22.8%, red blood cell count (RBC) 3.6×10^{12}/L, mean corpuscular volume (MCV) 63 fL, mean corpuscular hemoglobin (MCH) 18.1 pg, mean corpuscular hemoglobin concentration (MCHC) 28.9 g/dl. White blood cell, platelet counts and standard biochemistry tests were within normal limits. She did not have any other accompanying systemic disease and she had no history of gastrointestinal bleeding. Upper gastrointestinal system endoscopy and colonoscopy were normal. The results of the thyroid function tests were as follows: thyroid-stimulating hormone (TSH) 0.01 μIU/ml (normal range 0.35 to 5.50); free thyroxine (fT4) 1.50 ng/dl (normal range

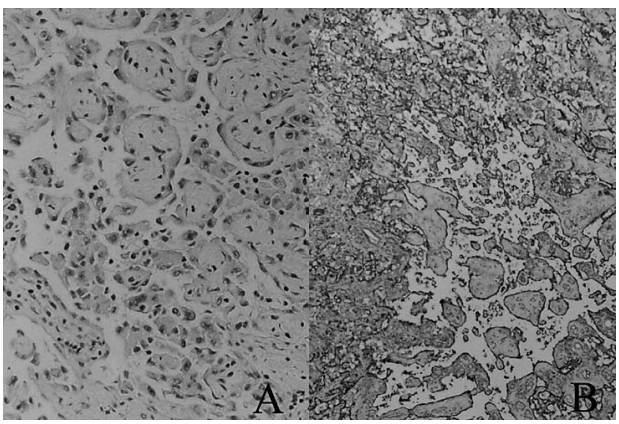

Fig. 1. A. Histopathological picture of the atypical cells in thyroid (HE ×200). B. Factor 8-related antigen positivity in the tumoral tissue (×200).

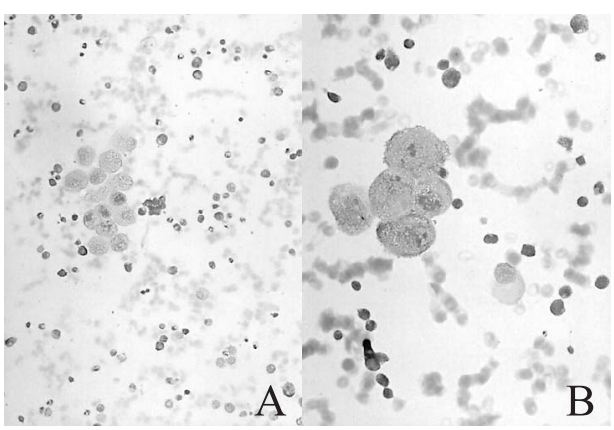

Fig. 2. Cytological examination of the bone marrow revealed oval or round shaped pleomorphic neoplastic cells (May-Grünwald-Giemsa, A ×200, B ×400).

0.89 to 1.8); free triiodotyronine (fT3) 2.73 pg/ml (normal range 2.30 to 4.20); thyroglobulin (TG) 75.5 ng/ml (normal range 1.0 to 55.0). A technetium 99m (99m Tc) scintigraphy revealed that the nodule in the right lobe was hyperfunctioning, while the rest of the gland was suppressed. Cytological examination by fine-needle aspirate on nodule was reported as suspicious.

Computerized tomography showed bilateral multiple small lung nodules resembling metastatic lesions and also mild splenomegaly. But histopathologic confirmation could not be done. After packed red cell transfusion, total thyroidectomy was performed. Intraoperative examination of frozen section sample of the nodule was inconclusive. Right thyroid lobe was 8 × 4 × 3.5 cm and left lobe 6 × 3 × 2.5 cm in size. A region of cells showing color exchange into gray-white-brown with irregular limits of size 2.5 × 2 × 2.5 cm was determined. Microscopic examination of this region showed tumoral tissue consisting of atypical cells (Fig. 1A). In the other regions of the thyroid gland, nodular hyperplasia was seen and in the same lobe a small focus of tumoral cells in another adjacent nodule in the same lobe was determined.

On immunohistological examination, specimen was studied by immunoperoxidase technique using diaminobenzidine (DAB) chromogen for primary antibodies; factor 8-related antigen (F8, DAKO, 1:200 dilution), pancytokeratine (CK; NeoMarkers, 1:100 dilution) and CD34 (CD34, DAKO; 2:100 dilution). Tumoral cells were stained positively with F8 (Fig. 1B) and CD34, but negatively with CK, immunohistochemically.

After the diagnosis of primary thyroid hemangiosarcoma, adjuvant chemotherapy was started at the third week postoperatively and she was treated with ifosfamide and doxorubicin. Meanwhile, Hb value (6.6 g/dl) got worse again. Evident hepatosplenomegaly developed at the postoperative second month, and there were erythroblasts in the peripheral blood smear. At the 10th week following surgery, bone marrow aspiration biopsy was performed and the same tumoral cells of angiosarcoma infiltrating bone marrow were demonstrated (Fig. 2). Two weeks after the diagnosis of bone marrow infiltration the patient died.

Discussion

Primary hemangiosarcoma is one of the rare tumors of the thyroid gland. The highest prevalance is in Switzerland and the Alpine regions [1]. This is the first case reported from Turkey according to MEDLİNE search.

Angiosarcoma of the thyroid in association with hyperthyroidism is a rare condition and is reported in the literature [5]. The present case had also concurrent hyperthyroidism. In addition to angiosarcoma, pathological examination of the specimen revealed that widespread nodular hyperplasia had existed. Nodules that were very near to the tumoral tissue were probably hyperfunctioning, and so on scintigraphic image it looked as if tumoral tissue was hyperfunctioning.

Aggressive tumors can rapidly spread to the lungs, lymph nodes and the brain [1, 6–8]. Tumors can also metastasize to the duodenum, small and large bowel and can cause severe bleeding [6]. In the present case, anemia and mild splenomegaly was determined pre-

operatively. But we did not consider bone marrow metastasis. After thyroidectomy hemoglobin level decreased gradually and hepatosplenomegaly developed at the postoperative second month. Peripheral blood smears revealed erythroblasts. Bone marrow aspiration biopsy, which was then performed, demonstrated the same tumoral cells infiltrating bone marrow. We retrospectively realized that bone marrow metastasis must have existed in our patient preoperatively.

While aggressive surgical resection to achieve local control of cancer remains the cornerstone of primary treatment [3], most patients develop postoperative early systemic metastasis; this observation leads to the hypothesis that undetected systemic micrometastases are present at the time of diagnosis. So the proposal to use adjuvant chemotherapy for systemic control and radiotherapy for local control in the treatment of angiosarcoma has been widely accepted [3, 4, 7, 9]. In spite of chemotherapy the present patient did not get much benefit from this therapy.

Metastatic disease is associated with poor prognosis and limits the mean survival time to a few months after diagnosis and surgical treatment [1, 6, 8, 10, 11]. Recently, better survival rates have been reported in the literature [7, 12]. Good prognosis seems to be related mainly to the absence of extraglandular tumour spread at the time of surgery [12]. In the present case, there was extraglandular tumor spread, and the patient died three months after diagnosis.

In conclusion, primary hemangiosarcoma of the thyroid is a very rare and aggressive disease. If anemia is associated with the primary disease, it should be considered that tumoral cells may have infiltrated the bone marrow, and that deep anemia may develop. Being aware of this possibility, careful attention should be paid to bone marrow metastasis, for which bone marrow biopsy is helpful to obtain a differential diagnosis in suspected cases.

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