Primary malignant fibrous histiocytoma on the thyroid

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ABSTRACT

A 42-year old white female with a primary Malignant Fibrous Histiocytoma (MFH) is described. The patient was examined for a “cold” nodule of the thyroid diagnosed five years previously. The patient had been on L-thyroxine therapy for three years which was discontinued by the patient 18 months prior to the present visit. Fine needle aspiration of the thyroid nodule indicated a low differentiated neoplasm with some mucous production. The patient underwent total thyroidectomy and excision of the infiltrated part of the anterior cervical muscles. The histology showed MFH on the thyroid, an extremely rare primary localization of this neoplasm. For the subsequent 8 years, the patient was well with no evidence of recurrence or metastasis. Afterwards, she developed a fast growing nodal structure on the mitral valve, leading to its surgical replacement. This operation was followed by several thromboembolic episodes (pulmonary and cerebral) which led to her death 10 years after thyroidectomy.

Key words: Malignant Fibrous Histiocytoma, Thyroid gland, Krukenberg tumor

INTRODUCTION

Malignant Fibrous Histiocytoma (MFH) was first described by O’Brien and Stout in 1964¹. The histologic origin of this tumor remains controversial. Initially it was considered as originating from a histioyte exhibiting fibroblastic activity²⁴. Later on, it was proposed that the tumor derives from a primitive mesenchymal cell which gives rise to two types of cells, namely, fibroblasts and histioocytes⁵⁻⁷. MFH consists both of spindle fibroblast-like cells and of plump, histioyte-like cells, arranged in a fascicular or storiform pattern, accompanied by polymorphic giant cells and inflammatory elements. Many varieties of this classic form have been described, with variable representation of fibroblasts or histioocytes, a fact leading to the existence of the broad morphologic spectrum of MFH which also explains the variable terminology. On one side of the spectrum, fibroblastic cells predominate (pleomorphic fibrosarcoma)⁸, while on the other, extreme histioytic cells are the main cell type (reticulocytic sarcoma of smooth tissue, malignant histioctyma)⁹⁻¹⁰. Intermediate forms of the neoplasm have also been described, named after their predominant cell population¹¹⁻¹⁷.

Because of the broad histologic variation of MFH, this neoplasm is often confused with other types of
sarcomas, such as pleomorphic rhabdomyosarcoma and liposarcoma and hence its true frequency and biologic behavior have not been precisely defined.\(^{18,19}\) MFH affecting the thyroid gland (primary or metastatic) is quite rare.\(^{20-24}\) In the present communication we describe a case of MFH affecting the thyroid gland and its surrounding tissues. In the same patient a Krukenberg tumor had also been detected. This coexistence is not easily interpreted and it is most likely fortuitous.

**CASE REPORT**

A 42-year old white female was examined at the outpatients' department of "St. Savvas" Endocrine Clinic for evaluation of her thyroid. A single “cold” nodule of the right thyroid lobe had been diagnosed 5 years earlier and the patient had been treated with L-thyroxine (0.1 mg/day) for a total of three years. The patient discontinued L-thyroxine, without notifying her physician, 18 months prior to her visit to our clinic. It must be noted here that 3 months previously, the patient underwent total hysterectomy and adnexectomy for a Krukenberg tumor of the right ovary.

Physical examination revealed an obese female (weight: 79 kg; height: 152 cm). An abdominal scar, due to the previously performed hysterectomy, was observed. There was a palpable, firm nodule on the lower part of the right thyroid lobe, about 2.5 cm in diameter, giving the impression of adhesion posteriorly and being slightly painful on palpation. Cervical lymph nodes were not palpable. The remainder of the physical examination was unremarkable.

The general laboratory screening tests were within the normal range. The thyroid hormones and the thyroglobulin values were normal. Both antimicrosomal and antithyroglobulin antibodies were negative.

Thyroid ultrasound showed the existence of a lesion measuring 2.5 X 1.6 cm on the lower part of the right thyroid lobe, having mixed echogeneity and a morphology resembling that of an adenoma with cystic degeneration and haemorrhagic necrosis.

Cytological examination of fine needle aspiration smears revealed atypical cells consistent with a low grade neoplasm, probably with some mucus production (Figure 1). Following these findings, the patient underwent total bilateral thyroidectomy with partial coexcision of the surrounding anterior cervical muscles, which seemed infiltrated macroscopically. One parathyroid gland close to the tumor was also removed.

A 35 gr thyroid gland was excised carrying a grey-white, rather hard mass, 2.8 cm in diameter with some areas of hemorrhage and necrosis on the lower part of the right lobe. The mass disrupted the capsule and extended towards the coexcised striated muscles.

The histologic examination revealed a neoplastic tissue with a predominantly fascicular and locally storiform or diffuse growth pattern, widely infiltrating the lower part of the right thyroid lobe (Figures 2-5). The neoplastic spindle cells resembled mainly fibroblasts with a rather mild atypia and spare mitoses. Occasionally the cells were plumper and had an histioelet-like appearance with prominent nucleolus (Figures 2, 3). Scattered giant cells with multiple hyperchromatic irregular nuclei and eosinophilic cytoplasm were also identifiable (Figures 2, 3, 5). The stroma exhibited delicate collagen fibrils around the neoplastic cells and focally marked collagenisation (Figure 2). Some areas with myxoid change and areas with necrotic tumor tissue were also observed. Marked focal infiltration by lymphocytes and plasma cells was additionally present (Figures 2, 4, 5). The neoplastic tissue extensively invaded the thyroid capsule and extended to surrounding striated muscle cells, as well as to a coexcised parathyroid gland (partial replacement of the parathyroid gland by the tumor tissue).

![Figure 1. Fine needle aspiration material smears from the thyroid nodule of the present case. There are large histioelet-like cells (thick arrow) and other more elongated fibroblastic elements (fine arrow), M.G.G. 300x.](image)
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Immunohistochemically, many neoplastic cells were strongly positive for antichemotrypsin. Keratin or thyroglobulin were absent.

According to the histological and immunohistochemical findings the diagnosis of Malignant Fibrous Histiocytoma was made (storiform – pleomorphic type).

During the first postoperative day, the patient exhibited hypocalcemia and tetany, corrected by Calcium and Vitamin D supplements. The parathyroid function was restored completely to normal about five months later. Twenty days after surgery, a 24-hour $^{131}$I-uptake and scanning showed absence of any functioning thyroid tissue. Furthermore, as expected after total thyroidectomy, there were laboratory findings of hypothyroidism (low serum total T3-T4 and high serum TSH values) and substitution therapy with 0.15mg L-thyroxin daily was initiated.

Postoperatively, the patient remained in good health for about eight years with no evidence of recurrence; her C/T scans (neck, chest, abdomen), carried out every six months, being normal. The only abnormal, constant finding was a small cyst in the left adrenal, without any alterations in size during follow-up and with normal adrenal function tests. For the adrenal lesion the diagnosis of an incidentaloma was considered.

Eight years post thyroidectomy, the patient com-

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**Figure 2.** Malignant Fibrous Histiocytoma of the thyroid: Area with histioyte-like cells and pleomorphic nuclei. Invaded thyroid follicles (long arrow) and stromal collagenisation (short arrow), H.E. 125x.

**Figure 3.** Malignant Fibrous Histiocytoma of the thyroid: Thyroid follicle with colloid (black arrow) and large histioyte-like malignant cells having large nucleoli (white arrow), H.E. 300x.

**Figure 4.** Malignant Fibrous Histiocytoma of the thyroid: Storiform pattern (fine arrow) and thyroid follicle enclosed (thick arrow), H.E. 125x.

**Figure 5.** Higher magnification of Figure 4: Thyroid follicle (white arrow), storiform pattern and mixed cell population. H.E. 200x.
plained of dyspnoea after exercise, shortness of breath and fatigue. On clinical examination, a systolic murmur was heard at the lower left sternal border. Cardiologic ultrasound examination revealed a small lesion on the mitral valve characterized as a “rheumatoid nodule”. The patient’s symptoms along with her clinical findings were deteriorating and the lesion was growing rapidly, leading to mitral stenosis to a degree necessitating surgical replacement of the mitral valve. Unfortunately, histologic examination of the excised tissue was not carried out so that the nature of this lesion remains unknown. After the cardiac surgery, her condition deteriorated further and several thromboembolic episodes (pulmonary and cerebral) were observed leading to her death ten years after thyroidectomy. Autopsy was not performed.

DISCUSSION

Malignant Fibrous Histiocytoma usually localizes in the extremities with a frequency of 49% for the lower – especially the thigh – and 19% for the upper18. It has also been described, at a frequency of about 16%, in the abdomen and the retroperitoneum cavities18.

The present case constitutes the second literature report of MFH primarily affecting the thyroid gland21, the other analogous cases representing metastasis of this neoplasm to the thyroid20,22-24. It should be underlined that, in the present case, there was no evidence of any other localization of the tumor at presentation and eight years following thyroidectomy, a fact which favors the possibility of a primary localization of the tumor on the thyroid.

According to the predominant histogeneity theory, suggesting a mesenchymal origin for this type of neoplasm5,6,18, this tumor may arise from deep fasciae or skeletal muscles. Thus, we should assume that in our patient the thyroid Malignant Fibrous Histiocytoma had arisen from the fasciae surrounding the thyroid, having spread to one parathyroid, close to the inferior right thyroid lobe and to a certain extent to the anterior cervical muscles.

Another possibly interesting point of the present case is the history of a Krukenberg tumor of the ovary, whose primary site was never identified despite a thorough search throughout the 10 years following the initial identification of the Krukenberg tumor. In a review by Weiss and Enzinger18, Malignant Fibrous Histiocytoma has been found to coexist with a second neoplasm in about 13% of the published cases; in none of these cases, however, was the second tumor a Krukenberg tumor of the ovary.

Malignant Fibrous Histiocytoma may also be accompanied by haemopoietic malignancies such as leukemia, Hodgkin and non-Hodgkin lymphomas, multiple myeloma and malignant histiocytosis. A case of Malignant Histiocytoma has been reported in which, as the tumor grew in size, marked eosinophilia was noted23. In another case, MFH developed on the trachea of a patient 11 years after irradiation of the neck for an infiltrating papillary carcinoma of the thyroid26. Generally, in previously irradiated areas, this tumor has been reported to develop mainly from subcutaneous tissue18. It is quite possible that skin irradiation constitutes a predisposing factor for the development of a typical fibroxanthoma of the skin27.

Hence, the coexistence of Krukenberg tumor with Malignant Fibrous Histiocytoma of the thyroid in our patient is not easily interpreted and most likely is coincidental.

Contrary to the usual biologic behavior of MFH, which is aggressive and presents with a two-year survival rate in 60% of the cases18, our patient had a long survival considering the fact that the thyroid nodule had been noted 5 years prior to the initial examination in our clinic. Furthermore, it should be mentioned that the incidence of local recurrence or metastases – mainly to the lung and regional lymph nodes – is about 44% and 42% respectively, within 3.5 years of diagnosis18,22.

In conclusion, the case of Malignant Fibrous Histiocytoma, described in this report presents the following interesting points. 1) Its rarity, constituting the second reported case primarily localized on the thyroid. 2) The coexistence of a Krukenberg tumor of the ovary most likely coincidental. 3) The slow development of the tumor, preoperatively as well as postoperatively, which could be attributed to the somewhat superficial localization, the relatively small size of the tumor and possibly to the type of operation, namely, total thyroidectomy and coexision of the infiltrated part of the anterior cervical muscles.
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