

Primary malignant peripheral nerve sheath tumor of the thyroid--an extremely rare case report of thyroid carcinoma

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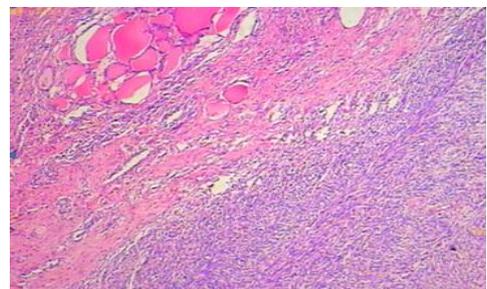
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Abstract: Primary peripheral nerve sheath tumors (PNSTs) of the thyroid are uncommon, and malignant peripheral nerve sheath tumors (MPNSTs) are extremely rare in the literatures. To the best of our knowledge, only three cases of MPNSTs have been previously reported in this location. This paper presents one case in a 30-year-old male, who had no history of neurofibromatosis or schwannoma, presented with a mass in the left lobe and underwent total thyroidectomy. The histological examination and immunohistochemical staining confirmed the mass a malignant PNST. After surgical excision, postoperative adjuvant radiotherapy with 6600cGy was administered. Twenty three months later, the patient was diagnosed lung and pleura metastasis by thoracic cavity biopsy, and then received three cycles of salvage chemotherapy with NVB and DDP. The patient finally died of respiratory failure secondary to severe pulmonary infection 29 months after the initial diagnosis of MPNSTs. Since primary thyroid MPNSTs share similar biological behavior with anaplastic thyroid carcinomas, we suggest that positive surgical excision of the aggressive tumor is essential, and the radiotherapy and chemotherapy are also needed.



Keywords: Thyroid; Schwannoma; Peripheral nerve sheath tumor; Malignant

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1. Introduction

Primary peripheral nerve sheath tumors (PNSTs) of the thyroid gland are quite rare and most are benign. They show features similar to benign and malignant peripheral nerve sheath tumors of other locations. Schwannomas are the most common type of PNSTs and less than 1% becomes malignant [1]. There are two growth modes of Schwannomas: Antoni A and Antoni B. These are extraordinary rare in the head and neck region, especially in thyroid. Schwannomas are very uncommon neoplasms that may be confused with anaplastic carcinoma and other tumors occur in the thyroid region [2]. According to our knowledge, only 3 cases of MPNSTs have been previously reported in thyroid [2,3]. We experienced a case of primary MPNSTs who underwent total thyroidectomy. Unfortunately the patient was diagnosed lung and pleura metastasis, and died of respiratory failure secondary to severe pulmonary infection 2.5 years later.

2. Case Report

A 30-year-old man was admitted to our department after discovered a solid tumor in the left lobe of thyroid by ultrasonography. It showed that a hypoechoic solid nodule (42mm×31mm) occupied almost the entire left lobe. Physical examination revealed an oval, absence of tenderness, approximately 4cm nodule in the left side of the thyroid, which was moving with deglutition. There was no cervical lymphadenopathy. The man had no history of neurofibromatosis.

The laboratory hormonal studies showed normal serum levels of TSH, FT4 and FT3. The concentration of thyroglobulin and antithyroid peroxidase antibody were also within normal range. Because intraoperative frozen section showed thyroid malignancy, complete thyroidectomy was rendered.

Pathologically, the tumor was diagnosed as malignant PNST. On microscopic examination, the tumor was found to be composed of fusiform cells

with fascicular distribution (Figure 1). It was easy to see nuclear division, and the pathologic mitosis phenomenon was visible (Figure 2). Immunohistochemical staining for Vimentin protein was diffusely positive, and S-100 protein was partly positive (Figure 3-4). While smooth muscle actin (SMA) protein assessment was negative.

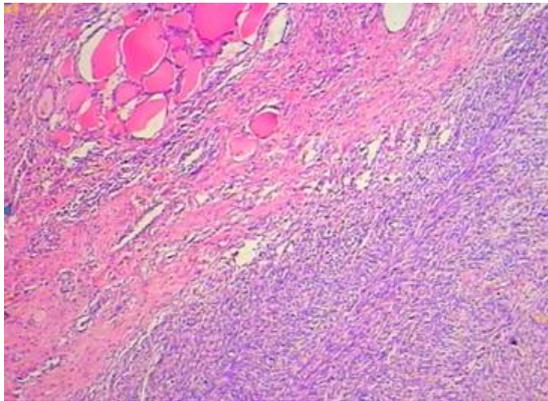


Figure1. Tumor cells were fascicled and adjacent to normal thyroid tissue.

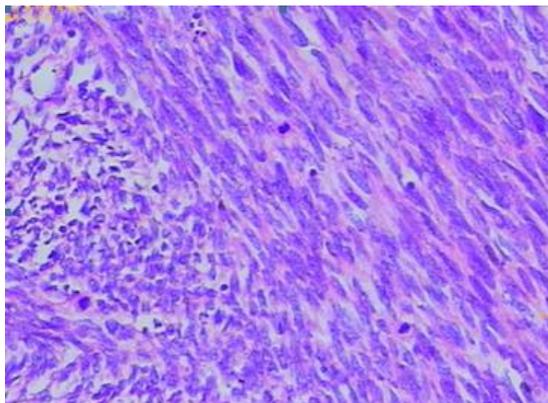


Figure 2. The pathologic mitosis in the tumor cells.

After surgical excision, postoperative adjuvant radiotherapy with 6600cGy was administered. Twenty three months later, the patient was found a mass in left lung with CT after emerged symptoms of cough and chest pain. Lung and pleura metastasis were diagnosed by thoracic cavity biopsy. The patient refused to take any surgical operation. Then, the patient received three cycles of salvage chemotherapy with Navelbine (NVB) and Diammine dichloro platinum (DDP, Cisplatin). Twenty-nine months after the initial diagnosis of malignant PNST, the patient died of respiratory failure secondary to severe pulmonary infection.

3. Discussion

MPNSTs represent approximately 10% of soft-tissue sarcomas, and are unusual in the head and neck region. The existence of primary thyroid PNST is indomitability. They have been postulated to originate from the intra-thyroidal sensory nerves or

sympathetic and parasympathetic innervation [3,4]. The tumors may arise within the thyroid parenchyma or the adjacent thyroid capsule. They show features similar to benign PNSTs in other locations. In immunohistochemical, benign PNSTs show diffuse positive of S-100 protein, but MPNSTs are usually focal. And with the degree of malignancy height, the positive rate decreased [4].

MPNSTs can be differentiated from other malignant thyroid neoplasms through hematoxylin and eosin staining as well as immunohistochemical staining with specific markers of peripheral nerves. Histologically, they show spindle cells with fascicular pattern, area of necrosis, tumor calcification, and significant cytological atypia or mitotic activity. The immunohistochemical staining usually show positive for S-100 protein and neuron-specific enolase, as well as actin, vimentin, cytokeratin, and smooth muscle actin in PNSTs. These markers differentiate this type of tumor from other spindle cell sarcomas.

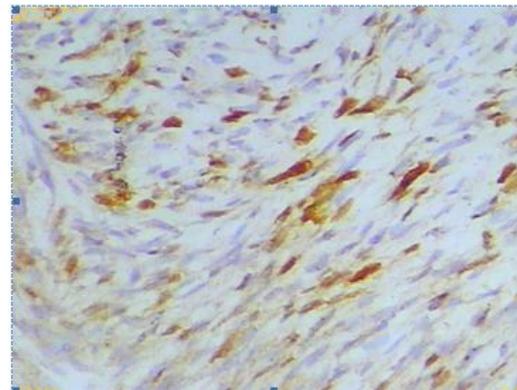


Figure3. S-100 protein part reactivity in the tumor cells.

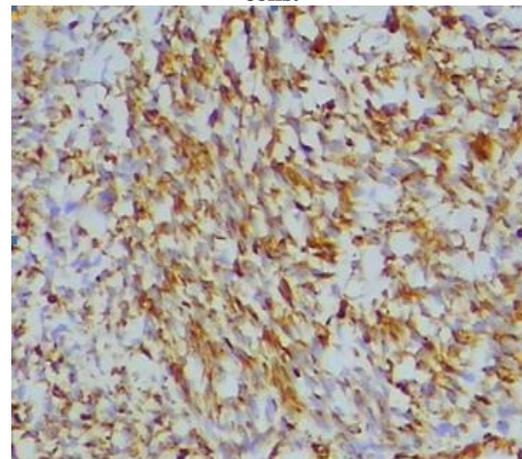


Figure 4. Vimentin protein diffuse positivity in the tumor cells.

This patient had no history of neurofibromatosis in other locations. The tumor progressed aggressively and emerged distant metastasis. Microscopic examination revealed an encapsulated nodule composed of spindle

cells with no pleomorphism. And Immunohistochemical staining Vimentin and S-100 (partly) protein was positive, while SMA protein assessment was negative. So these findings bolstered the diagnosis of specifically thyroid malignant PNST by its clinical presentation and pathologic features.

The main differential diagnosis includes benign PNSTs, anaplastic carcinoma and other malignant spindle cell tumors occurring in the thyroid.

Benign PNSTs include neurofibromas and schwannomas. Neurofibromas arise from cutaneous or peripheral nerve. It may show a wide variety of microscopic patterns, including storiform, wavy, desmoidlike, palisading, and hemangiopericytic. Meanwhile, tumor cells usually show positive immunostaining for CD-34, CD-99, and Bcl-2 [5]. Schwannomas originate from neuronal sheath cells. The typical cytological features of schwannoma include the presence of cells with slender wavy nuclei, fibrillary stroma, nuclear palisading and the presence of Verocay bodies. S-100 and CD-34 positive immunostaining, especially S-100 showing diffusely may aid in the diagnosis of neural sheath tumors and may be mandatory for distinguishing schwannomas from other tumors such as leiomyomas and solitary fibrous tumors [6].

Anaplastic thyroid carcinoma (ATC) is the most aggressive solid tumor known to man. Histologically, ATC is a mixture of pleomorphic cells, spindle cells, and squamoid cells, and shows considerable variation in both the proportion and distribution of these cell types. And immunohistochemical staining is positive for cytokeratin (low molecular weight keratin CAM5.2 most diagnostic value) and epithelial membrane antigen (EMA) in squamous cell ATC, but negative or weakly positive in spindle cells and giant cells ATC. Vimentin in the three types are positive and thyroglobulin is focal weak positive or negative in most ATC [7].

Malignant fibrous histiocytoma (MFH) is a subtype of sarcoma. Primary MFH of the thyroid(MFH-T) is extremely rare. The diagnosis of primary MFH-T is usually made on clinical and histopathologic examination. MFH-T presents a rapidly enlarging thyroid mass that is firm and fixed to surrounding structures in an elderly patient. A detailed clinical evaluation is mandatory to rule out metastasis from a previously treated soft tissue sarcoma (MFH), because metastases to the thyroid may occur after a prolonged period of latency. The morphologic features of MFH-T performant spindle cells, pleomorphism, and storiform pattern. Immunohistochemically, MFH-T is positive for CD68, a1-antichymotrypsin, a1-antitrypsin, and vimentin, but negative for thyroglobulin and calcitonin [8].

Synovial sarcoma (SVS) represents 5~10% of all soft-tissue sarcomas. They may occur in the head and neck region, and only 5 cases of primary thyroid SVS

have been reported in the literature [9]. The spindle cells of monophasic synovial sarcoma are usually arranged in dense cellular sheets and a prominent hemangiopericytic pattern. However, synovial sarcomas may exhibit dense fibrosis, myxoid change, as well as alternation of hypocellular and hypercellular areas. On immunohistochemistry tumor cells stained strongly for epithelial membrane antigen (EMA) [9].

Thompson LD et al. had reported two schwannomas and two MPNSTs in 1996 [3,4]. The two primary thyroid MPNSTs were demonstrated malignant histological features characterized by increased cellularity, fascicular "herringbone" arrangement, nuclear and cellular pleomorphism, coarse nuclear chromatin, prominent mitotic activity, necrosis, hemorrhage, and invasive growth.

Primary thyroid MPNSTs share a similar biology with anaplastic thyroid carcinomas. These are high-grade and aggressive tumors that are lethal within a short of time following diagnosis and appear unresponsive to all modes of therapy. It is similar to MPNSTs in other anatomic locations, which have a poor 5-year survival rate [3]. Treatment modalities for MPNSTs consist of surgical excision, systemic chemotherapy, or radiotherapy. Complete surgical excision with a safety margin is the mainstay treatment in patients with localized diseases. The role of radiotherapy and chemotherapy remains controversial.

So the treatment modalities of thyroid MPNSTs may learn from other locations. Pallares J reported a MPNST patient who was treated with radiotherapy in 2004, and the patient was alive without evidence of disease 10 months after surgery 2. In this case, the patient died of respiratory failure 29 months after the first diagnosis. We suggest that positive surgical excision of the highly aggressive tumor is essential, and the radiotherapy and chemotherapy are also necessary.

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