

## Primary Malignant Teratoma with a Primitive Neuroectodermal Tumor Component in Thyroid Gland : A Case Report

Teratomas comprise the most common extragonadal germ cell tumors in childhood. Most teratomas involving the thyroid are benign and occur in children. However, the adult cases reported are mostly malignant and commonly arise in the thyroid. We report a case of a 31-yr-old female with a huge neck mass. Pathologic examination revealed it to be malignant teratoma composed of primitive neuroepithelial tissue with primitive neural tubes and loose myxoid to fibrous immature mesenchymal stroma. The patient underwent extensive evaluation of the thyroid gland with computed tomography (CT) scan and positron emission tomography (PET) scan, which revealed no evidence of metastatic disease. She underwent total thyroidectomy with bilateral modified radical neck dissection, intensive chemotherapy and radiotherapy. At 22-months of follow-up, the patient has remained euthyroid and showed no evidence of recurrence. This is the first case, to our knowledge, of malignant thyroid teratoma with a exuberant primitive neuroectodermal tumor component in Korea.

**Key Words :** Malignant Teratoma; Thyroid Neoplasm; Thyroid Disease

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## INTRODUCTION

Teratomas comprise the most common extragonadal germ cell tumors in childhood (1). Teratomas of the neck in adults are extremely rare. The tumors of the head and neck account for 5% of all benign and malignant germ cell tumors and for 6% of all teratomas, where the most common sites of involvement are the soft tissue of the neck, thyroid, superficial facial structures, oral cavity, nasopharynx, and orbit (1, 2). Most teratomas involving the thyroid are benign and occur in children. We report a case of primary malignant thyroid teratoma in a 31-yr-old female. To our knowledge, this is the first case of malignant teratoma with a primitive neuroectodermal tumor component in the thyroid in Korea.

## CASE REPORT

A 31-yr-old woman presented to our clinic with a two-month history of a fast growing non-tender mass in the neck. No pertinent past medical illness or family history was present. On physical examination, a large hard and fixed mass was palpated in the central neck, mostly occupying the thyroid gland. The laboratory findings were unremarkable, and her thyroid function was normal. The computed tomography scanning of the neck showed a  $7.0 \times 5.5$  cm solid het-

erogeneous enhancing mass arising in the right lobe of thyroid gland (Fig. 1). It was invading beyond the thyroid gland and extended down to the anterior mediastinum. The trachea and right sternocleidomastoid muscle were deviated to the left. The supraclavicular, highest mediastinal, and bilateral prevascular lymph nodes were all enlarged. The largest lymph node was over 2.5 cm at the levels II and III.

The F-18-FDG positron emission tomography (PET) scan showed a huge hypermetabolic mass in the right thyroid gland with multiple hypermetabolic lesions in the neck and in the prevascular area of mediastinum. Fine needle aspiration slides revealed diffusely scattered oval to spindle shaped atypical cells with rare eosinophilic amorphous material suggesting poorly differentiated carcinoma possibly consistent with medullary carcinoma. She underwent total thyroidectomy with bilateral modified radical neck dissection. The tumor was penetrating the thyroid capsule and was invading the adjacent tissue involving the right recurrent laryngeal nerve. The upper portion of the sternum was cut to dissect the inferior portion of right thyroid. The lymph nodes along the chain were removed after the sheaths of the common carotid, and internal jugular vein were opened. The postoperative period was uneventful except transient hypocalcemia. On the third day of operation, the total serum calcium level was 6.7 mg/dL with a ionized calcium level of 0.88 mM/L. Calcium was replaced by oral medication.

On gross examination, the mass was occupying most of the right lobe of thyroid gland with a ill-defined border, measuring  $7.5 \times 5.0 \times 4.7$  cm. The cut surface was grayish white, hemorrhagic, and necrotic with focal cystic changes. Many lymph nodes were grossly involved by the tumor (Fig. 2). The microscopic examination showed that the tumor was

mainly composed of primitive neuroepithelial tissue with primitive neural tubes and loose myxoid to fibrous immature mesenchymal stroma (Fig. 3). The normal thyroid follicles were intermingled or adjacent to the tumor. The tumor cells were pleomorphic and partly necrotic with hyperchromatism and frequent mitotic figures (4-6/10 high power fields). A

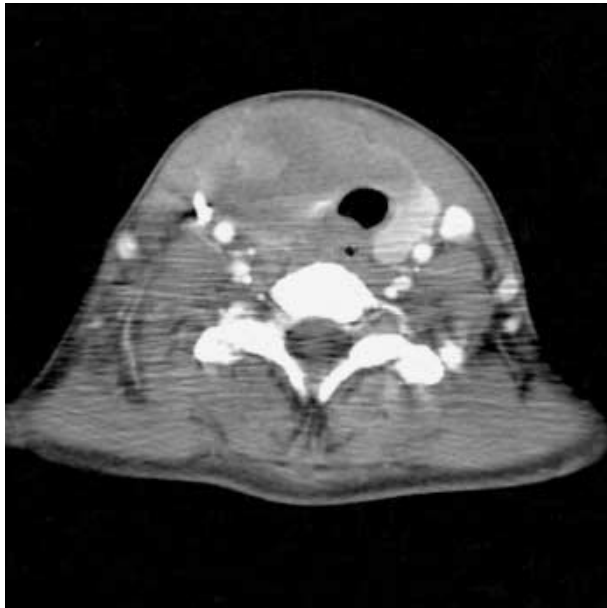


Fig. 1. Computed tomography (CT) scan of malignant teratoma. A  $7.0 \times 5.5$  cm mass is observed within the right anterior neck. The trachea and right sternocleidomastoid muscle are deviated to the left.

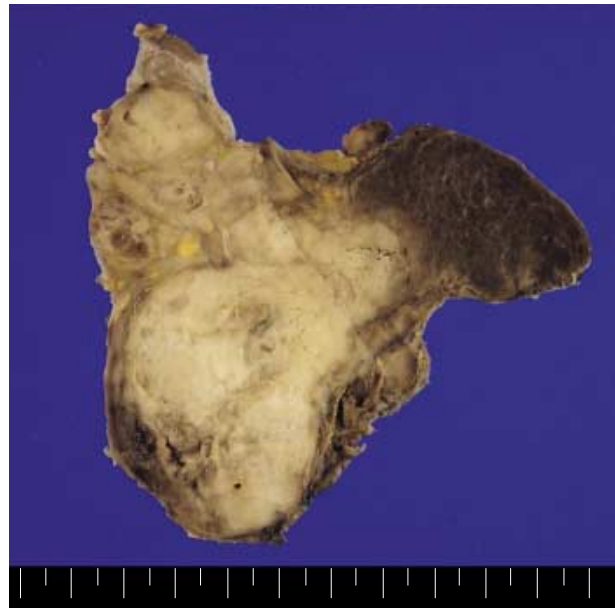


Fig. 2. Gross finding of malignant teratoma. The mass is mainly located in the right lobe of thyroid with extrathyroidal extension and multiple lymph node involvement.

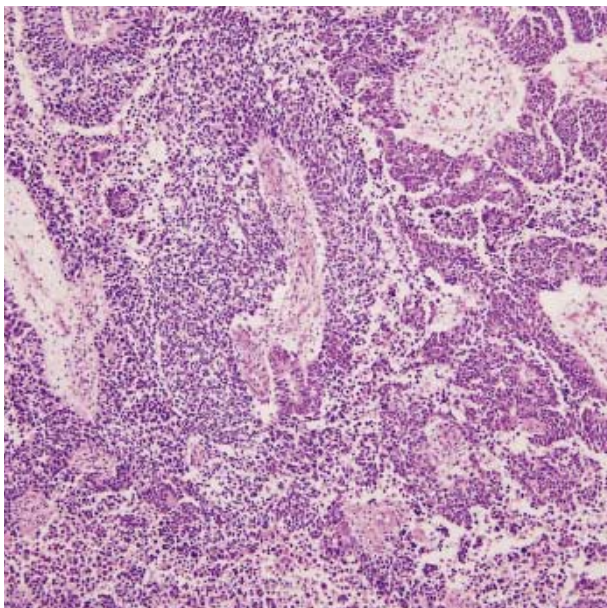


Fig. 3. Microscopic findings of malignant teratoma. The tumor is mainly composed of primitive neuroepithelial cells and neural tubules (H&E stain,  $\times 100$ ).

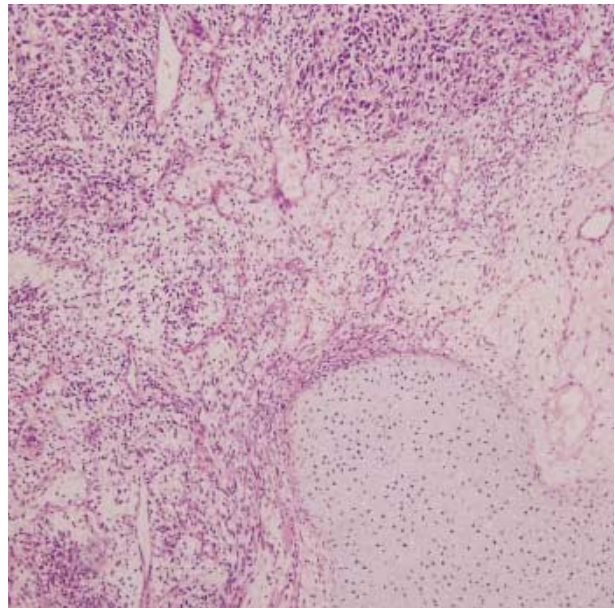


Fig. 4. Microscopic findings. Mature cartilage is also noted within the primitive neuroepithelial tissue (H&E stain,  $\times 100$ ).

multitude of small cystic spaces was lined by mature squamous or glandular epithelium. Islands of mature cartilage were noted within the primitive neuroepithelial tissue (Fig. 4). Metastases were present in 25 of total 58 lymph nodes, where metastatic components were only composed of a primitive neuroepithelial component. The tumor cells were positive for synaptophysin, focally positive for cytokeratin, neurofilament, desmin, and CD99 on immunohistochemical staining. The primitive neuroepithelial component comprised more than 4 in low power magnification fields ( $\times 4$  objective with a  $\times 10$  ocular, using bx.), which thus was categorized as malignant teratoma according to the Thompson *et al.*'s criteria (3).

After she recovered from the surgery, she was placed on an intensive chemotherapy according to the National Cancer Institute protocol reported by Grier *et al.* (4). She received 14 cycles of chemotherapy consisting of VAC (vincristine 2 mg, doxorubicin 75 mg/m<sup>2</sup>, cyclophosphamide 1,200 mg/m<sup>2</sup>, every 3 weeks), alternate with IE (ifosfamide 1,800 mg/m<sup>2</sup> with mesna, and etoposide 100 mg/m<sup>2</sup> for five days by continuous infusion).

After the completion of the 10th cycle of chemotherapy, she received external beam radiation therapy (EBRT) with a total dose of 55.8 Gy, 5 days/week. The treated volume included the thyroid bed, cervical lymph nodes, and upper mediastinum. Upon completion of radiation therapy, she received further chemotherapy. Dactinomycin at 1.25 mg/m<sup>2</sup> replaced doxorubicin. The patient completed total 17 cycles of chemotherapy. Dose reductions along with granulocyte colony-stimulating factor and erythropoietin supports were done.

She has been remains free of disease for 22 months after the diagnosis.

## DISCUSSION

Malignant teratoma of the thyroid in adult was first reported by Lurje in 1908, who described a case of a 53-yr-old woman (5). By 1999, nineteen cases of malignant teratoma of the thyroid had been reported in the medical literature, emphasizing the aggressive clinical course of the disease (1). After then, 3 cases have been reported (2, 6, 7). There were a predominance of primitive neuroepithelial component within mature squamous or glandular epithelial components and mature cartilage in our case.

Malignant thyroid teratoma is an aggressive tumor, with a short median survival (median, 8 months) after surgery without postoperative chemotherapy. The commonly used drugs are the same agents effective in the treatment of germ cell tumors (6, 8, 9). It usually consists of bleomycin, cisplatin, and etoposide (BEP) protocol alone or in combination with other agents aimed to treat the sarcomatous component. The most common agents included are vincristine, cyclophos-

phamide and actinomycin-D (2, 6).

Chen *et al.* reported a 32-yr-old woman with malignant thyroid teratoma who underwent a simple lobectomy of the thyroid (8). She received chemotherapy of BEP and was still alive without evidence of disease after 6.7 yr. No further local radiotherapy or operation was arranged.

Djalilian, *et al.* reported a 33-yr-old woman with malignant thyroid teratoma who underwent 5 cycles of chemotherapy with vinblastin, ifosfamide, and cisplatin (1). After 3 further cycles of carboplatin and etoposide, the patient underwent autologous bone marrow stem cell transplant. She did well with evidence of stable disease in the lungs at 21 months from the diagnosis but died of metastatic teratoma. Recently, high-dose chemotherapy in combination with autologous stem cell transplant has been found to be effective in prolonging the survival in some patients with gonadal germ cell tumors (10, 11).

Jayaram *et al.* treated a malignant teratoma of the thyroid with predominantly neuroepithelial differentiation with surgery alone (7). She died after 15 months with metastases to liver, vertebra, paraaortic and paracaval lymph nodes.

Craver *et al.* reported a 15-yr-old black girl with a malignant thyroid teratoma with exuberant primitive neuroectodermal tumor components. There were bilateral nodal involvement and mediastinal extension (6). She was treated with an aggressive combination chemotherapy of BEP and radiation. Further chemotherapy included vincristin, actinomycin-D, and cyclophosphamide alternating with ifosfamide and etoposide for six cycles. These agents were included to treat the sarcomatous component. Presently there is no residual disease 16 months after the diagnosis.

Kushner *et al.* treated 36 patients with poor-risk primitive neuroectodermal tumor (12). The P6 protocol consists of high-dose cyclophosphamide, doxorubicin, and vincristine. The protocol achieved excellent pathological or clinical responses in 34 patients and partial responses in two patients. All six patients with metastatic disease limited to lungs achieved a complete response and did not relapse for the follow-up period of 7 to 36 months.

Primary thyroid malignant teratoma is rare. For teratomas of other sites with primitive neuroectodermal tumor components, the suggestion is to tailor the chemotherapy regimens known to be effective in the treatment of the transformed histology, after complete surgical resection (13). Most of chemotherapeutic agents chosen for malignant teratomas of the thyroid have been selected and established for teratomas of other origins (10, 11). Therefore, we decided to administer an intensive chemotherapy regimen according to the NCI protocol INT-0091 (4). Grier *et al.* compared the 49 weeks of standard chemotherapy consisting of doxorubicin, vincristine, cyclophosphamide and dactinomycin to chemotherapy alternating with ifosfamide and etoposide in primitive neuroectodermal tumor (Ewing's sarcoma) patients. They concluded that for nonmetastatic patients, the 5-yr disease free

survival (69% vs. 54%) and overall survival (72% vs. 61%) were superior in the later group. We used the combination chemotherapy altering with ifosfamide and etoposide for this specific patient of primary malignant teratoma with a primitive neuroectodermal tumor component.

Some investigators have reported the role of EBRT for residual tumor tissues (5). Although EBRT has frequently been used, its role in front-line therapy is not clear. Locoregional control at the time of recurrence seems to provide short-term palliation. We opted for the radiation treatment in this patient in light of the extensiveness of the disease and the residual microscopic disease after the surgery.

It is suggested that patients with primary malignant teratoma of the thyroid should be managed according to their major malignant component. The complete surgical excision and extensive chemotherapy are recommended for most patients with primary malignant teratoma (1, 6). As for the exuberant primitive neuroectodermal tumor component in this particular case with an extensive involvement of the surrounding soft tissue and lymph nodes, best clinical outcome could be obtained with intensive multidisciplinary therapies consisting of complete excision, chemotherapy and radiation therapy to the lesion.

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