



# Thyroid Carcinosarcoma

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## Abstract

Background. A rare case of diagnosis and treatment of thyroid carcinosarcoma has been presented. Methods and Results. A 58-year-old woman was diagnosed with squamous cell carcinoma of the thyroid. Thyroid gland US and MRI examinations showed tumor mass in the right thyroid lobe extending to the tracheal wall and intratracheal component. The patient underwent right-sided neck dissection (level II-VI) and thyroidectomy with resection of the tracheal rings, cricoid cartilage arch and the lower parts of the thyroid cartilage on the right side. Conclusions. The present case of thyroid carcinosarcoma is of interest because the carcinomatous component is a rare squamous cell thyroid carcinoma. Our clinical case confirms the aggressive character of such rare disease as thyroid carcinosarcoma, showing a high potential for regional and distant metastases.

**Keywords:** Thyroid cancer; Thyroid carcinoma

## Introduction

Most thyroid cancers are differentiated cancers. Papillary thyroid carcinoma is the most common type of thyroid cancer accounting for about 80% of all thyroid cancers. Follicular thyroid carcinoma is the second most common type of thyroid cancer (about 10-20%) [1&2]. Medullar thyroid carcinoma comprises 6-8% of all thyroid cancers. Anaplastic thyroid carcinoma, also called undifferentiated thyroid cancer, makes up 2-3% of all thyroid cancers. The incidence of poorly differentiated thyroid carcinoma is 1-6%. Squamous cell thyroid carcinoma accounts for only 0.2-0.7% of all thyroid malignancies. This carcinoma is derived from the embryonic remnants such as thyroglossal duct. The incidence of non-epithelial malignancies (lymphoma, sarcoma, teratoma and others) is 1-2%. Most non-epithelial thyroid carcinomas are different types of thyroid lymphomas [2&3]. Epithelial and non-epithelial thyroid carcinomas are rare and clinically aggressive tumors with poor prognosis. Surgery is the standard treatment for these carcinomas. It is often very difficult to perform such surgery due to extensive extra thyroid spread and regional metastasis. Carcinosarcoma of the thyroid gland is a very rare tumor accounting for only 0.1% of all thyroid malignancies [4]. The exact pathogenesis of thyroid carcinosarcoma is still unknown [5]. Microscopically, carcinosarcomas contain two independent histological malignant

components: carcinoma and sarcoma [5&6]. Carcinosarcoma is extremely aggressive tumor with a poor prognosis [4]. It is known to have early metastasis and progression [4, 5, 7]. To date, 30 cases of thyroid carcinosarcoma have been reported [5]. We report a new case of carcinoma affecting the thyroid gland.

## Methods and Results

A 58-year-old woman was first seen with thyroid nodule in March 2013. Ultrasound examination of the thyroid (March 2013) revealed right thyroid nodule measuring 2 cm. In September 2013, she noticed enlarged lymph nodes in the right side of the neck and shortness of breath. In November 2013, the patient was examined at the Cancer Center in Krasnoyarsk. Histological examination of biopsy specimen from neck lymph node revealed squamous cell carcinoma. Fibro laryngoscopy showed intratracheal tumor growth. Biopsy specimen obtained from the intratracheal tumor component also confirmed squamous cell carcinoma. The patient was referred to the Cancer Research Institute (Tomsk) for further treatment. On admission, local examination of the neck revealed a conglomerate mass of lymph nodes measuring to 4 cm, matted with the sternocleidomastoid muscle and the internal jugular vein, on the right side of the neck in the middle third (level III), that was confirmed by ultrasound and magnetic resonance imaging

findings. Thyroid gland US and MRI examinations showed tumor mass in the right thyroid lobe extending to the tracheal wall and intratracheal component (stenosis of half of the tracheal lumen). Fibro laryngoscopy demonstrated the exophytic component of the tumor with extension to the right tracheal rings and membranous portion of the trachea. Sub compensated stenosis of the trachea, which was manifested by shortness of breath, was revealed. Re-examination of histological specimens confirmed diagnosis of squamous cell carcinoma both in cervical lymph nodes and in the intratracheal component of the tumor.

A clinical diagnosis of stage T4aN1bM0 thyroid cancer was set and on December 6, 2013, the patient underwent right-sided neck dissection (level II-VI) with ligation and resection of the internal jugular vein and removal of the sternocleidomastoid muscle. Thyroidectomy with resection of the tracheal rings (from 1-th to 5-th tracheal rings), cricoid cartilage arch and the lower parts of the thyroid cartilage on the right side was performed. Laryngotracheostomy was created. During neck dissection in the right side of the neck, there were found enlarged metastatic lymph nodes up to 4cm in the middle third of the neck (level III) and up to 2cm in supraclavicular region (region IV). In the middle third of the neck (region III), the neck lymph node was adherent to the front edge of the sternocleidomastoid muscle and the wall of the internal jugular vein. Wedge resection of the sternocleidomastoid muscle and internal jugular vein ligation were performed. Branches of the cervical and brachial plexus and the accessory nerve were preserved. During mobilization of the right lobe of the thyroid gland, tumor was found to spread to the tracheal wall (up to the 4-th tracheal ring) and the right anterolateral surface of the cricoid cartilage. Tumor adherence to the muscle wall of the esophagus to the level of the right piriform sinus was also observed. Mobilization of the right lobe of the thyroid gland with the wall of the trachea and cricoid arch and the lower parts of the thyroid cartilage was performed. Membranous portion of the trachea at this level was also removed. Wedge resection of the muscular wall of the esophagus on the right side was performed. The right recurrent nerve was not visualized. The left lobe of the thyroid gland was removed without any difficulties. Laryngotracheostomy was formed by suturing the skin edges of the neck to the remnant of the tracheal wall on the left side (1.5 cm wide strip). Macroscopic examination of the specimen showed the presence of thyroid tumor with extension to the anterior-lateral and posterior walls of the trachea and the right arch of the cricoid cartilage. Lymph nodes up to 4 cm in diameter were found. The patient received antibiotic therapy in postoperative period.

Histological (hematoxylin and eosin staining) and immunohistochemical (IHC) studies were carried out using antibodies AE1/AE3 (clone AE1/AE3, Dako), p63 (7JUL, Leika), Ki67(clone MIB-1, Dako), Vimentine (clone V9, Novocastra), CEA (clone 12-140-10, Novocastra), TTF (clone 8G7G3/1, Dako), CD56

(clone 123C3, Dako), SMA (clone 1A4, Dako), Desmin (clone DE-R-11, Novocastra), MyoD1 (clone 5.8A, Dako), GFAP (clone GA5, Novocastra), S-100 (поликлональное, Dako), Thyroglobulin (Novocastra clone), Calcitonin (clone не ук, Novocastra), CD 57 (clone TB-01, Dako). Thyroid tumor was histologically shown to have two components. Tumor from the upper pole of the thyroid and sites of its growth to the trachea was presented as a solid moderately-differentiated squamous cell carcinoma. Foci of keratinization were observed. The pronounced expression of Cytokeratine AE1/AE3, p63 was observed in tumor cells. Proliferative activity was high, the Ki67 antigen was expressed in about of 56% of tumor cells. There was no expression of Vimentine. In tumor tissue specimens from the lower pole of the thyroid gland and sites of tumor growth into the surrounding soft tissues, sharply polymorphic cells with nuclei of irregular elongated shape were found.

Tumor cells expressed Vimentine and CD56. A weak expression of Cytokeratine AE1/AE3 was observed, and SMA was expressed in a small proportion of the cells. Proliferative activity in the sarcomatous component was high and the Ki 67 antigen was expressed in about of 52% of tumor cells. No expression of Desmin, MyoD1 was observed. There were found tumor sites with the structures of squamous cell carcinoma and sarcoma. No expressions of GFAP, S-100, Thyroglobulin, Calcitonin and CD 57 were found in both components of the tumor. The left thyroid lobe was 4.0x2.0x1.0 cm in size. Histological examination revealed parenchyma nodes as large colloid-filled follicles. Tumor metastases were detected in 5 of 10 lymph nodes. Squamous cell cancer metastasis was found in 1 lymph node, sarcoma metastasis in 1 lymph node and metastases from squamous cell and sarcomatous cell components in 3 lymph nodes. Hence, the histopathological diagnosis was carcinosarcoma of the right thyroid lobed extending beyond the thyroid capsule and invading the trachea and soft tissues, with extended necroses.

The carcinomatous component was present as a moderately differentiated squamous cell carcinoma with foci of keratinization. The sarcomatous component was undifferentiated sarcoma (G2). Five of 10 lymph nodes were found to be histologically positive. Macrofollicular nodular goiter was found in the left lobe of the thyroid gland. Considering findings of immunohistochemical analysis, the final diagnosis was stage T4aN1bM0 thyroid carcinosarcoma. Postoperative radiation therapy was administered after the completion of treatment to eliminate inflammation around tracheolaryngostomy. Disease progression occurred in January 2014. On admission, soft tissue infiltration was seen to the left of tracheolaryngostomy. Subcutaneous nodular lesions measuring up to 1.5 cm were found in the area of postoperative scar on the left side of the neck Chest x-ray (January 16, 2014) revealed mediastinal lymph node metastasis. Ultrasound examination (January 24, 2014) revealed cervical and paratracheal lymph node and diffuse damage to the liver.

Spiral computed tomography (January 22, 2014) revealed lung metastases and showed suspicion of intrathoracic lymph node metastases. Magnetic resonance imaging of neck soft tissues (January 28, 2014) confirmed the presence of large lesion in the bed of the removed thyroid gland and metastases in neck lymph nodes. The final diagnosis was stage T4aN1bM0 thyroid carcinosarcoma, disease progression, continuous tumor growth and the evidence of neck, mediastinal and lung metastases. Considering histopathological results, spread of recurrent tumor, presence of regional and distant metastases, a special treatment was not given. Symptomatic therapy was recommended.

## Discussion

The term "carcinosarcoma" was first used by Rudolf Virchow in 1865 [8]. Carcinosarcomas have been observed in various organs throughout the body including the ovary, uterus, larynx, lungs, prostate, salivary glands, breast, esophagus, liver and other organs [5]. Indeed, this tumor type usually affects visceral organs and is characterized as unusual and uncommon neoplasm that is comprised by an admixture of two components: carcinomatous and sarcomatous [5&9]. Carcinosarcoma components have different histological patterns. Carcinomatous component is more often associated with follicular and papillary cancers [5, 6, 7, 10]. Sarcomatous component usually has the following histotypes: osteosarcoma, fibrosarcoma, undifferentiated sarcoma and chondrosarcoma [4, 5, 6, 7]. In most cases, structural components of carcinosarcoma are in a tumor by isolated areas with the formation of transition zones with interpenetration of the components [9, 10].

## Conclusion

The present case of thyroid carcinosarcoma is of interest because the carcinomatous component is a rare squamous cell thyroid carcinoma. Biopsy material showed only squamous cell carcinoma. The aggressive tumor growth can be explained by the nature of squamous cell carcinoma. Accurate diagnosis was possible only after studying surgical specimens. Both tumor components have ability to invasive growth. Lymphogenous metastasis is typical for squamous cell carcinoma. In contrast, lymphogenous metastasis of sarcomas rarely occurs in comparison with carcinomas. In our case, lymph node metastases from undifferentiated sarcoma were detected in equal number with lymph node metastases from

squamous cell carcinoma. In accordance with previously approved hypothesis, mesenchimal to epithelial transition is one of the key conditions for developing sarcoma metastases [10]. Signs of mesenchimal to epithelial transition are present in the sarcomatous component of thyroid carcinosarcoma. This is evidenced by the expression of cytokeratin, which is detected using AE1/AE3 antibodies. The presence of distant metastases (lung metastases) is typical for sarcomatous component of carcinosarcoma. Our clinical case confirms the aggressive character of such rare disease as thyroid carcinosarcoma showing a high potential for regional and distant metastases. At present, a comparative study of chromosomal abnormalities of carcinomatous and sarcomatous components is considered a promising approach to clarify the exact histogenesis of carcinosarcoma and to assess the treatment options.

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