Abstract. Different types of malignant tumors can occur within the thyroid. Primary cancer is the most common type of thyroid malignancy. Non-epithelial malignancies can also arise within the thyroid. The aim of the present study was to analyze clinical and radiological characteristics of reported primary thyroid sarcomas (PTS), based on a large sample of cases. The PubMed database was screened for articles from between 1990 and 2014. Overall, 86 articles with 142 patients were identified. Ultrasound evaluation was reported for 36 patients. Data regarding computed tomography of the neck were available for 29 cases. Magnetic resonance imaging was performed for eight patients. The following data were retrieved for the identified sarcomas: localization, size, homogeneity, internal texture, and margin characteristics. In most cases, PTS occurred in patients over 40 years of age, with a peak incidence for the group aged 60-79 years. Angiosarcoma was diagnosed in 29 cases (20.4%), followed by malignant hemangioendothelioma (n=23, 16.3%), malignant fibrous histiocytoma (n=20, 14.1%), leiomyosarcoma (n=16, 11.3%), and fibrosarcoma (n=13, 9.2%). In most patients (n=113, 79.6%), PTS manifested clinically as a painless goiter. On ultrasound, PTS were predominantly mixed hypo-to-hyperechoic in comparison to the normal thyroid tissue. On non-contrast computed tomography, most sarcomas were inhomogeneous hypo-to-hyperdense. On post-contrast magnetic resonance images, most sarcomas showed marked non-homogenous enhancement. In 26.8%, infiltration of the adjacent organs was seen. The trachea or esophagus was affected more frequently in patients with malignant histiocytoma and liposarcoma. Different strategies were used in the treatment of PTS. Our analysis provides clinical and radiological characteristics of PTS. The described features should be taken into consideration in the differential diagnosis of thyroid tumors.

Different malignant tumors can occur within the thyroid (1-3). Primary cancer is the most common type of thyroid malignancy (1). There are four sub-types of cancer affecting the thyroid: follicular, papillary, medullary and anaplastic (1, 2). However, non-epithelial malignancies can also arise within the thyroid (1, 3). In particular, primary lymphomas and sarcomas (3, 4). Their frequency is very low. For example, according to the literature, the prevalence of thyroid lymphoma ranges from 1.5% to 5% of all thyroid malignancies (4-7). The reported frequency of primary thyroid sarcoma (PTS) ranges from 0.01% to 1.5% (4, 8, 9). Because of this fact, there are only isolated case reports of different PTS in the literature.

The aim of this study was to analyze clinical and radiological characteristics of reported PTS based on a large sample of cases.

Materials and Methods

Patients. The PubMed database was screened for articles between 1990 and 2014 using “thyroid sarcoma” “primary thyroid sarcoma” and “sarcoma of the thyroid” as key words. Secondary references were also reviewed. Publications in a my language other than English were excluded. Overall, 86 articles with 142 patients were identified (4, 8-92). The following data were retrieved: localization, size, homogeneity, internal texture, and margin characteristics of the identified sarcomas.
Imaging. Ultrasound evaluation was reported in 36 patients. Data regarding computed tomography (CT) of the neck were available for 29 cases. Magnetic resonance imaging (MRI) was performed for eight patients.

Statistical analysis. The SPSS statistical software package (SPSS 17.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Collected data were evaluated by means of descriptive statistics (absolute and relative frequencies). Continuous variables are expressed as the mean±standard deviation (SD), and categorical variables as absolute and relative frequencies. Analyses of metastatic patterns of PTS were performed by ANOVA and subsequent post-hoc tests. p-Values were adjusted for multiple testing (Bonferroni correction). The significance level was chosen to be at 0.05.

Results

Patients, primary diagnosis, clinical signs, localization, and size of PTS. A total of 142 patients were included in the analysis. There were 88 women (62.0%) and 53 men (37.3%). The male/female ratio was 0.6:1. In one case (0.7%), the gender was not provided.

The mean age of the patients was 60.0±16.8 years (median=64 years, range=7 months-90 years). In most cases, patients were over 40 years of age, with a peak in the group of those aged 60-79 years (Table I).

Most frequently, angiosarcoma was diagnosed (n=29, 20.4%), followed by malignant hemangiendothelioma (n=23, 16.3%), malignant fibrous histiocytoma (n=20, 14.1%), leiomyosarcoma (n=16, 11.3%), and fibrosarcoma (n=13, 9.2%).

Other types of PTS were rare (Table II). In most patients (n=113, 79.6%), PTS manifested clinically as a painless goiter. Dyspnea occurred in 33 (23.2%) and dysphagia in 22 (15.5%) of the patients. A total of 15 patients (10.6%) complained of cervical pain and four patients (2.8%) had a cough. In 22 cases (15.5%), clinical signs were not reported.

PTS affected the right lobe in 55 patients (38.7%), and the left in 48 (33.8%). Bilateral involvement of the thyroid was present in 13 cases (9.2%). PTS was located in the thyroid isthmus in three patients (2.1%). In 23 cases (16.2%), no information regarding sarcoma localization was given.

The mean size of identified sarcomas was 63.0±33.6 mm in the left to right direction (median size=60 mm, range=15-210 mm) and 56.6±33.7 mm in the anterior to posterior direction (median size=50 mm, range=5-180 mm). There was no significant difference in size between different PTS.

Imaging findings and stage of disease. On ultrasound, the 36 described PTS were predominantly mixed hypo-to-hyperechoic in comparison to the normal thyroid tissue (n=21, 58%) (Figure 1). In 13 cases (36%), the identified sarcomas were hypoechoic and in two cases (6%) hyperechoic.

On non-contrast CT, most sarcomas were inhomogeneous hypo-to-hyperdense (n=17, 59%), five (17%) were isodense and seven (24%) hypodense (Figure 2). Post-contrast CT was reported in 14 cases. In 13 (93%) of them, non-homogenous enhancement was seen and in one patient (7%), enhancement was homogenous.

MRI was performed in eight patients. On T1-weighted images, four PTS were iso-intense, one hyper-intense and three mixed iso-to-hyperintense. After administration of contrast medium, seven PTS showed non-homogenous enhancement and one sarcoma had homogenous contrast accumulation (Figure 3).

In 38 cases (26.8%) infiltration of the adjacent organs was seen. The trachea or esophagus were more frequently affected in patients with malignant histiocytoma and liposarcoma (Table III). At the time of diagnosis, local lymph node metastases were diagnosed in nine patients (6.3%). Distant metastatic lesions occurred in 20 patients (14.1%). In these 20
**Figure 1.** Ultrasound of primary thyroid angiosarcoma. The images showing a large non-homogeneous predominantly hypoechoic mass with partial indistinct margin within the left thyroid lobe.

**Figure 2.** Primary angiosarcoma of the thyroid gland. Non-contrast CT showing a large non-homogenous mass (arrows): a: transversal and b: sagittal reconstruction.

**Figure 3.** Imaging findings of primary rhabdomyosarcoma of the thyroid. Magnetic resonance imaging showing a large mass in the left lobe of the thyroid with massive compression of the trachea. The mass was non-homogeneous hyperintense on T2-weighted imaging (a) with non-homogenous enhancement on post-contrast T1-weighted imaging (b).
patients, the lung was the most frequent side where distant metastatic lesions were detected (14 cases, 70%). Other organs were rarely affected. Local lymph nodes were affected more often in patients with fibrosarcoma (Table III). Distant metastases were identified frequently in patients with leiomyosarcoma, osteosarcoma, and angiosarcoma. Patients with malignant hemangioendothelioma, liposarcoma, and malignant fibrous histiocytoma had no detectable distant metastases at the time of diagnosis (Table III).

In 100 patients (70.4%), no local or distant metastases were identified. In the remaining 13 patients, no information regarding metastatic lesions was provided.

**Therapy and follow-up.** In 75 patients (52.8%), only surgical resection of PTS was performed. Resection was combined with chemotherapy with/without local radiation in 53 cases (37.3%). Isolated local radiation was administered in one case (0.7%), isolated chemotherapy in two (1.4%), and combination chemotherapy and radiation in four patients (2.8%). Five patients (3.5%) received palliative care only. Information about the therapy was missing for two patients (1.4%).

The reported observation time of the identified cases with PTS ranged from 0.5 to 120 months, with a mean of 14.6±18.9 months, and median of 7 months. During the observation time, 45 patients (31.7%) were alive and 73 patients (51.7%) died. In 24 cases, the outcome was not reported.

**Discussion**

Our report provides first data about PTS based on a large sample of studied cases. As seen, there were five frequent types of sarcoma arising in the thyroid, namely angiosarcoma, malignant hemangioendothelioma, malignant fibrous histiocytoma, leiomyosarcoma, and fibrosarcoma. We also identified a slight female predominance in the analyzed cases with PTS. Furthermore, most PTS occurred in older patients. Clinically, PTS had no specific signs and presented with painless large goiter. It can be accompanied by cough, dyspnea and dysphagia because of compression or infiltration of the trachea or esophagus.

The identified sarcomas presented with several imaging features. It is impossible to compare imaging findings of different sarcomas due to the fact that not every report of PTS contained a sufficient description of the radiological findings. Furthermore, a very small group of PTS was investigated by CT or MRI.

The present analysis showed that on ultrasound, most PTS were mixed hypo-to-hyperechoic in comparison to the normal thyroid tissue. Non-contrast CT in most cases documented non-homogeneous hypo-to-hyperdense lesions, which demonstrated an non-homogenous enhancement on post-contrast CT. On post-contrast MRI, non-homogenous enhancement was also seen in most patients.

The identified radiological features are non-specific and PTS can be misdiagnosed as other malignant thyroid tumors, such as primary carcinoma or lymphoma.

According to the literature, on ultrasound, differentiated thyroid carcinomas inhibited solid internal content with hypoechoic echogeneity and ill-defined or speculated margins (93-99). Anaplastic thyroid carcinomas had predominantly irregular margins (100).

As previously reported, thyroid lymphoma manifested most frequently on ultrasound as a hypoechoic mass with well-defined margins (5, 101). In contrast to other thyroid malignancies, it typically had no calcifications (5). In addition, in contrast to primary thyroid cancer, infiltration of the adjacent organs was reported to be rare (5, 6, 101).

Our analysis showed that several PTS had different behavior in regard to infiltration of adjacent organs, metastatic invasion of local lymph nodes and occurrence of distal metastases. Most patients (70.4%) had no local or distant metastases at the time of diagnosis. Infiltration of the trachea or esophagus were detected more often in patients with malignant histiocytoma and liposarcoma, whereas local

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lymph node metastases were more frequent in fibrosarcoma. Distant metastases occurred more frequently in leiomyosarcoma, osteosarcoma, and angiosarcoma.

In contrast to thyroid cancer, there exist no general recommendations regarding therapy and follow-up of PTS. We found there to be a broad spectrum of treatment strategies for PTS ranging from surgery, with or without additional chemotherapy and local radiation to palliative care. Therefore, it is impossible to compare different treatment approaches in PTS.

In conclusion, the present analysis provides the clinical and radiological characteristics of PTS. The described features should be taken into consideration in the differential diagnosis of thyroid tumors.

Conflicts of Interest

The Authors have no conflicts of interest with regard to this study.

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