# Primary Cavernous hemangioma of the Thyroid Gland.

## A series of 4 cases and review of literature

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**Primary Cavernous hemangioma of the Thyroid Gland. A series of 4 cases and review of literature**

*Cavernous hemangiomas can arise nearly anywhere in the body where there are blood vessels. The primary hemangioma of the thyroid gland is extremely rare, and only a few cases have been previously reported. The true incidence of cavernous hemangiomas is difficult to estimate because they are frequently misdiagnosed as other venous malformations. We will present 4 cases from the age of 38 to 72 years old, diagnosed with cavernous hemangiomas. All 4 cases are women and the diagnosis was established after total thyroidectomy by histopathological examination. They clinically present as asymptomatic cervical tumors, are occasionally fast-growing, especially if intratumoral bleeding is present.*

KEY WORDS: Cavernous Hemangioma, Thyroid, Pathology, Histology

### Introduction

Cavernous hemangioma, also called cavernous angioma, venous malformation, cavernoma or cavernous cerebral malformation (when seen in cerebral tissue) [1,2], is a type of venous malformation due to endothelial dysmorphogenesis from a lesion which is present at birth. The abnormal tissue causes a slowing of blood flow through the cavities, or "caverns". The blood vessels do not form the necessary junctions with surrounding cells, and the structural support from the smooth muscle is hindered, causing leakage into the surrounding tissue. It is the leakage of blood, that causes a variety of symptoms known to be associated with the condition. Cavernous hemangiomas can arise nearly anywhere in the body where there are blood vessels. The primary hemangioma of the thyroid gland is extremely rare, and only a few cases have been previously reported [3-5]. Primary thyroid hemangiomas are considered as a developmental anomaly that is associated with an inability of angioblasticmesenchyma [6].

Unlike capillary hemangiomas, cavernous ones can be life-threatening and do not regress. The true incidence of cavernous hemangiomas is difficult to estimate because they are frequently misdiagnosed as other venous malformations.

Histologically cavernous hemangioma is a circumscribed proliferation of variably sized, dilated and thin walled vessels lined by a single layer of flat endothelial cells. In cavernous hemangioma no cytologic atypia or mitosis are observed. Vascular spaces separated by fibrous septa containing small vessels, focal thrombi, calcification, hyalinization, extramedullary hematopoiesis and stromal edema may be present.

Generally, no prominent clinical manifestations but a cervical mass can be found in the patient with thyroid hemangioma. In addition, the preoperative diagnosis is difficult to be made because no distinctive signs are observed by ultrasonography or computed tomography (CT) scans.

We will present 4 cases from the age of 38 to 72 years old, diagnosed with cavernous hemangiomas. All 4 cases are women and the diagnosis was established after total thyroidectomy by histopathological examination.

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## Case Report

### Case n. 1

The first case is a 73-year-old female patient who presented with a formation at the left thyroid lobe measuring 6 cm, with a sinking tendency. In the ultrasound examination, the entire left lobe was transformed into a nodule with a diameter of 6 cm, heterogeneous with calcifications and cystic degeneration inside, with increased vascularization (TIR3), which gives deviation of the trachea to the right.
A thoraco-abdominal tomography was performed where a 6 cm hypodense nodule with calcifications was observed at the left lobe. FNA of the nodule was performed and the cytopathological description was smears with poor cellularization and few cell groups with mild atypia. In the scintigraphy, a hot nodule was observed at the left lobe.
Blood calcium was measured, which results in normal values ™of 8.73 mg/dl. Total thyroidectomy was performed. In the macroscopic description, the right lobe measures 4 x 2 x 1.5 cm, parallel sections were without visible lesions, only colloidal view. The left lobe measures 8 x 7 x 6 cm, with a multinodular appearance, in section with colloidal nodules, hemorrhage and numerous calcifications.
The histopathological findings show proliferation of variably sized, dilated and thin walled vessels lined by a single layer of flat endothelial cells consistent with cavernous hemangioma with a diameter of 6 cm.
The other part of the thyroid presents multinodular goiters with cystic-hemorrhagic and sclerohyaline degenerations (Fig. 1).

### Case n. 2

In the second case, we are dealing with a 61-year-old woman who presents with a nodule at the right lobe of the thyroid. In the ultrasound examination, a nodule with a diameter of 5.5 cm, homogeneous, was observed. FNA of the thyroid was performed, where in the cytopathological description present a hemorrhagic background and watery colloid, with groups of thyrocytes with eosinophilic cytoplasm with mild cellular atypia. In the laboratory analysis, we have slightly reduced values ™of fT3 and increased values ™of TSH.
Other laboratory findings are normal. A total thyroidectomy was performed and the material was sent for histopathological examination. In macroscopic examination, the right lobe measures 10 x 6 x 5 cm with a nodule of 5.5 cm in diameter with beige and white areas can be seen.
The left lobe measures 7 x 3 x 2 cm, in parallel sections without visible macroscopic lesions, with the presence of colloidal nodules. In the histopathological examination, a cavernous hemangioma with a diameter of 1 cm and micro-normo-macrofollicular multinodular goiter was observed (Fig. 2).

### Case n. 3

The third case is a 52-year-old woman who presented with a nodule with a 4 cm diameter at the left lobe of the thyroid. The nodule was diagnosed in the ultrasound examination as a heterogeneous nodule with calcifications inside. Laboratory analyzes are normal. Total thyroidectomy of the patient was performed.



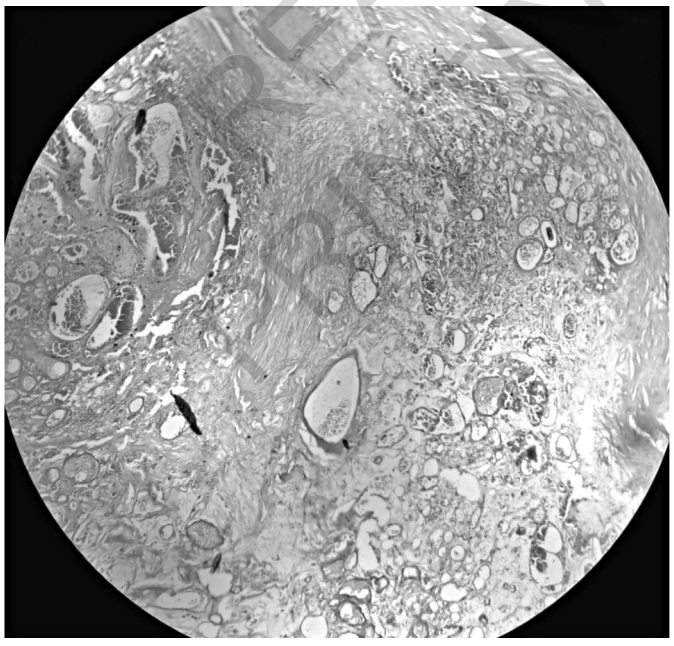


Fig. 1: Case 1 in H-E staining.

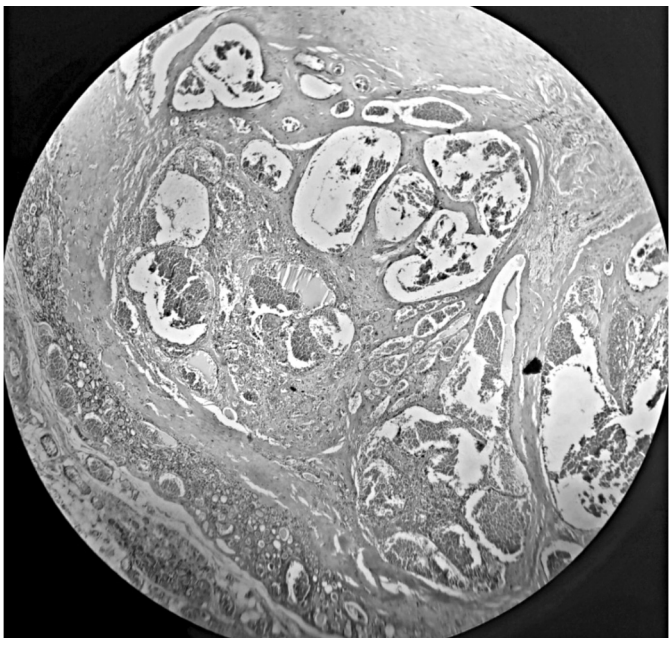


Fig. 2: Case 2 in H-E staining.

Macroscopically, the thyroid appears multinodular. The right lobe measures 4 x 3 x 2 cm, in parallel sections with colloid appearance and calcifications. The left lobe measures 6 x 5 x 4 cm, in section with a large hemorrhagic nodule measuring 4 cm diameter with solid beige areas. In the histopathological examination, the left lobe presents as multinodular goiter and cavernous hemangioma of the thyroid gland measuring 4 cm. The right lobe presents some suspicious microfollicular areas with a diameter of 0.3 - 0.5 cm, with a thin capsule with changes suspicious for malignancy are also observed. After immunohistochemical examinations with Cytokeratin19, HMBE1 and Galectin 3, it was found that these foci present reactive changes (Fig. 3).

### Case n. 4

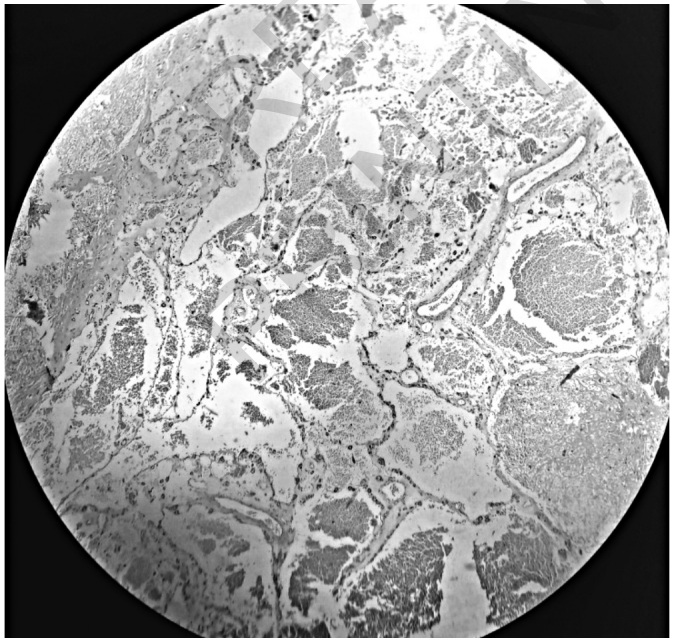
The fourth case is a 38-year-old female patient who presented with a nodule at the left lobe. In the ultrasound examination, the nodule appears heterogeneous with internal calcifications and hemorrhagic areas with a diameter of 3 cm. A thoracic CT examination was performed, which revealed a nodule with a diameter of 3 cm at the left lobe of the thyroid, which appears hypodense and with calcifications inside. Other laboratory analyzes are presented in the normal range. A total thyroidectomy was performed, where macroscopically the thyroid appears multinodular. The right lobe is 4 x 1.5 x 2 cm, in parallel sections with colloidal nodules. The left lobe measures 6.5 x 5 x 3 cm, a hemorrhagic nodule with a diameter of 3 cm is observed in the section. In the microscopic examination, the right lobe presents a multinodular goiter with dystrophic calcifications. The left lobe presents normo-macrofollicular multinodular goiters and cavernous hemangiomas with a diameter of 3 cm (Fig. 4).

## Discussion

Hemangioma is a common benign tumor of the soft tissue, which usually occurs in the skin, liver, and other organs. We could not discern whether it is malformation or hamartoma, real tumor, or reactive lesion in nature, wherever it occurs. In most cases, thyroid hemangioma is associated with FNA biopsy or trauma, which may be regarded as abnormal vascular proliferation following hematoma organization, or as a secondary lesion that resulted from the vascular changes during the development of nodular goiter [7]. Kumar et al [6] suggested that primary thyroid hemangioma originated from the incapability of the canal formation in the angioblastic mesenchyme [6] (Table I).

They clinically present as asymptomatic cervical tumors, are occasionally fast-growing, especially if intratumoral bleeding is present [8].

Hemangiomas, on ultrasonography, show hypoechoic areas with calcifications within the thyroid gland, without specific distinct characteristics [9]. The clinical findings of the hard nature of the mass with associated calcifications, often points to a malignancy. Coarse calcifications, when they are present, are suggested as a reliable sign of the presence of a hemangioma [9]. They may be hard in consistency, due to the presence of phleboliths within the tumor. Though they are unusual, it is often the only reliable sign of a rare hemangioma in the thyroid [8]. Histologically, thyroid hemangiomas are



Fig, 3: Case 3 in H-E staining.

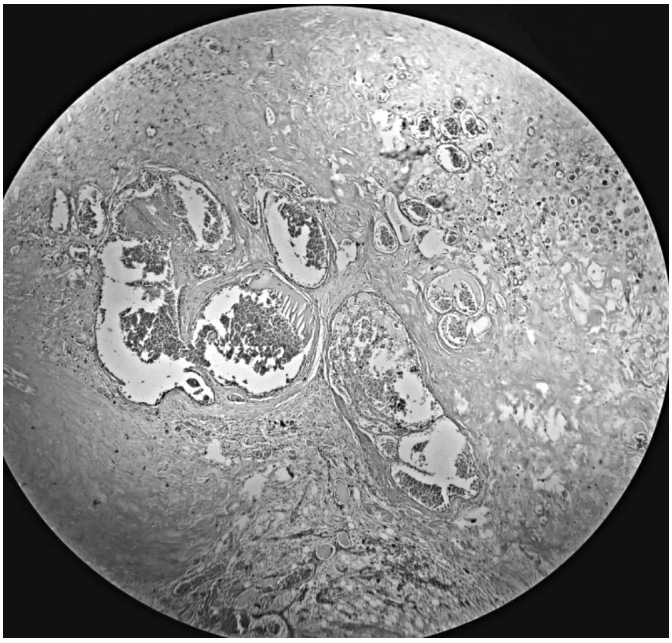


Fig. 4: Case 4 in H-E staining.

TABLE I - *Reported cases of thyroid hemangioma together with our cases.*

| Patient | Sex | Age | Location | Size, cm | First author, year | Histology |
|---|---|---|---|---|---|---|
| 1 | F | 57 | Right | 3.5 × 2 × 1.5 | Okiyama 1966 | Cavernous |
| 2 | M | 56 | Left | 7.5 × 3 × 2 | Pickleman et al [14] | Cavernous |
| 3 | F | 48 | Left | 9 × 6 × 5 | Komatsubara 1976 | Cavernous |
| 4 | M | 30 | Right | | Shamin 1978 | Cavernous |
| 5 | F | 29 | Right | 6.5 × 4 × 2.5 | Queiroz 1978 | Cavernous |
| 6 | M | 33 | Right | 9 × 7 × 5.5 | Queiroz 1978 | Cavernous |
| 7 | M | 54 | Right | 9 | Queiroz 1978 | Cavernous |
| 8 | F | 55 | Right | 2 | Hernandez 1979 | Capillary |
| 9 | M | 55 | Right | 10 × 6 × 5 | Ismailov 1981 | Cavernous |
| 10 | M | 7 | Difuse | | Okuno 1981 | Capillary |
| 11 | M | 59 | Left | 11 × 8 × 5 | Kamimura 1982 | |
| 12 | M | 46 | Right | 14 × 10 × 9.5 | Ishida 1982 | Cavernous |
| 13 | M | 4 | Istmus | 1.8 × 0.9 × 0.3 | Ishida 1982 | Cavernous |
| 14 | F | 57 | Right | 8 × 6.5 × 3 | Ishida 1982 | Cavernous |
| 15 | F | 64 | Right | 7.2 × 6 × 4 | Yokota 1991 | Cavernous |
| 16 | M | 67 | Right | 4.5 × 3.5 | Kato 1993 | Venous |
| 17 | M | 21 | Right | 5.5 × 3 × 2 | Kitamura 1993 | Cavernous |
| 18 | M | 17 | Right | 4 × 3 | Karamatsu 1995 | Venous |
| 19 | M | 53 | Right | 4 × 3 | Pendse 1998 | Cavernous |
| 20 | F | 63 | Left | 5 × 3 | Rios 2000 | Cavernous |
| 21 | F | 48 | Left | 5 × 4 | Rios 2000 | Cavernous |
| 22 | M | 53 | Right | 4 × 4 | Kumar et al [6] | Cavernous |
| 23 | F | 50 | Left | | Niimi 2000 | Cavernous |
| 24 | M | 24 | Right | 6 × 5 | Senthilvel,2005 [20] | Cavernous |
| 25 | F | 56 | Right | 7 × 6 | Kumamoto 2005 | Cavernous |
| 26 | M | 21 | Right | 5.5 × 3 × 2 | Kano et al [17] | Cavernous |
| 27 | M | 66 | Left | 17 × 16.5 | Lee, 2007 | Cavernous |
| 28 | M | 25 | Left | 4.9 × 4 × .4 | Datta, 2008 | Cavernous |
| 29 | M | 78 | Right | 4 × 4 | Michalopoulos et al [3] | Cavernous |
| 30 | F | 80 | Left | 22 × 21 × 17 | Maciel et al [9] | Cavernous |
| 31 | M | 48 | Right | 4 × 3.5 | Miao J. et.al [19] | Cavernous |
| 32 | F | 3M | Right | 3.1 × 3.7 × 2.2 | Jacobson D, et al. [22], 2014 | Cavernous |
| 33 | F | 12 | Right | 2.0 × 1.0 | Li Quanjiang, et al. [23], 2019 | Cavernous |
| 34 | F | 2M | Left | 3 × 1 × 1 | Liang, Y et.al 2020 [21] | Cavernous |
| 35 | F | 56 | Right | 4.0 × 4.0 × 2.4 | Robert T et. al 2021 [24] | Cavernous |
| 36 | F | 73 | Left | 8 × 7 × 6 cm | Our case | Cavernous |
| 37 | F | 61 | Right | 10 × 6 × 5 | Our case | Cavernous |
| 38 | F | 52 | Left | 6 × 5 × 4 | Our case | Cavernous |
| 39 | F | 38 | Left | 6.5 × 5 × 3 | Our case | Cavernous |



classified as cavernous, synovial, arteriovenous, venous, capillary, and racemose [17]. Histologically cavernous hemangioma is a circumscribed proliferation of variably sized, dilated and thin walled vessels lined by a single layer of flat endothelial cells. In cavernous hemangioma no cytologic atypia or mitosis are observed. Vascular spaces separated by fibrous septa containing small vessels. The tumor should be mainly differentiated from benign diseases such as endothelial reactive hyperplasia in goiter and malignancies, including undifferentiated sarcomatoid carcinoma, hemangiosarcoma, or angiosarcoma. Benign reactive endothelial hyperplasia, which looks like malignancy, may develop within the nodular goiter, due to spontaneous bleeding, granulation tissue formation, and fibrous organization. It may be secondary to the FNA biopsy [16].

So far, as described in (Table I). Our research shows that there are 34 cases published in the English literature with cavernous thyroid hemangiomas [10] without considering our cases. Together with cases described in this study the total number of reported cavernous thyroid hemangioma is 38. The youngest age reported is a 2-month-old infant, published by Liang et al in 2020 [11]. The oldest age reported as 80 years by Maciel et al [12]. From the published cases together with our 4 cases, there are 19 women and 19 men, an almost 1:1 ratio. Also, in 24 cases the hemangioma is located at the right lobe, 12 cases at the left lobe, 1 case at both lobes and 1 case at the isthmus [10,13].

The first reported case of cavernous thyroid hemangioma was reported in 1975 by Pickleman et al [14]. The largest cavernous hemangioma of the thyroid reported is by Maciel et al measuring 22 x 21 x 17 cm [12]. From our search there is only one case with cavernous hemangioma concomitant with papillary thyroid carcinoma reported by Robert T et al [24].

FNAC is essential for the diagnosis of thyroid tumors in most cases. However, the specimens of hemangioma will contain only blood components as a feature. Therefore, they will be inconclusive [25]. Anyway, in cases with thyroid cytology where there is abundant hemorrhage and only few thyroid cells a cavernous thyroid hemangioma should be considered.
The treatment of choice for thyroid hemangioma is surgical removal by hemithyroidectomy or total thyroidectomy [13]. Making a diagnosis before surgery is difficult. Hemangiomas should be considered in the diagnosis of any pulsatile mass which involves the thyroid gland [26].

## Conclusion

Although the primary hemangioma of the thyroid gland is extremely rare, primary thyroid hemangioma should be considered when there is a well-circumscribed capsule mass. Pre-operative diagnosis is difficult, as there are no specific pathognomic findings on radiological investigations or FNAC. A definitive diagnosis can only be achieved in postoperative preparation by histopathological examination.


### Riassunto

Gli emangiomi cavernosi possono svilupparsi ovunque nel corpo umano ovunque vi siano vasi sanguigni. L'emangioma primario della ghiandola tiroidea è estremamente raro e solo pochi casi sono stati precedentemente riportati. La vera incidenza dell'emangioma cavernoso e difficile da stimare in quanto sono spesso non diagnosticate così come altre malformazioni venose. Noi presentiamo 4 casi che variano di età tra i 38 ed i 72 anni, diagnosticati con emangioma cavernoso. Tutt'e 4 i casi erano donne e la diagnosi fu fatta tramite esame istopatologico dopo tiroidectomia totale. Trattasi di tumori cervicali clinicamente asintomatici ed occasionalmente di rapida crescita specialmente quando vi e presente un sanguinamento intratumorale.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