

## Case report

### Rhabdoid tumor of the thyroid gland: a variant of anaplastic carcinoma, case report with review of the literature



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#### Abstract

Anaplastic thyroid carcinoma (ATC) with rhabdoid features is extremely rare and only few cases have been reported in literature. We report a case of ATC with rhabdoid features in a 66-year-old female, who presented with a rapidly enlarging neck mass. Computed tomography (CT) revealed a multiheteronodular goiter with presence of a suspected nodule in the left lobe. The patient underwent total thyroidectomy with lymph node dissection. Pathology report showed rhabdoid phenotype of thyroid anaplastic carcinoma. This entity is highly aggressive and associated with a poor prognosis. The patient died one month after the operation before receiving adjuvant therapy.

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## Introduction

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Rhabdoid tumor was first described in 1978 as a variant of Wilms' tumor in children [1] with unfavorable outcome, but designated as a distinct entity in 1981 [2]. Later, this tumor was also reported in the central nervous system [3] and in many other extrarenal sites. Anaplastic thyroid carcinoma (ATC) with rhabdoid features is extremely rare [4] and only few cases have been reported in literature. The rhabdoid phenotype is a pathological presentation associated with aggressive nature not only in thyroid gland but also in other organs [5]. Morphologic findings in this tumor include the presence of large pleomorphic cells with abundant cytoplasm, typical eosinophilic inclusions and eccentric nuclei with distinct nucleoli. We report a case of a rhabdoid variant of a thyroid anaplastic carcinoma and we describe morphologic and immunohistochemical features of this very rare variant, diagnosis difficulties, prognosis and treatment.

## Patient and observation

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A 66-year-old female presented with painful anterior cervical mass, associated with dyspnea and dysphagia. There was no family history of thyroid disease or radiation exposure to head and neck region. Physical examination revealed an anterior, hard, mobile cervical mass measuring 10cm, without pain or inflammatory signs. Serum thyroid hormones and calcitonin hormone were normal. Cervical ultrasonography showed the presence of multiheterodular goitre with presence of nodules classified TIRADS 4b with adenopathies. Computed tomography (CT) revealed a multiheteronodular goiter with presence of a suspected nodule in the left lobe associated with cervical lymphadenopathies and lung metastatic lesions. Total thyroidectomy, with lymph node dissection were performed. Macroscopic examination revealed in the left lobe a heterogenous nodule measuring 6cm with whitish and

blackish areas (Figure 1). Histologically, the tumor was composed of poorly differentiated large cells having an abundant cytoplasm with vitreous eosinophilic inclusion, and eccentric nuclei containing distinct nucleoli (rhabdoid cells) (Figure 2, Figure 3). Vascular emboli was present. This proliferation infiltrated the perithyroid fat tissue (Figure 4). On immunohistochemistry, tumor cells were positive for CKAE1/AE3, EMA and vimentin (Figure 5, Figure 6, Figure 7) and negative for TTF-1, thyroglobulin, chromogranin and synaptophysin. Based on those characteristics, the diagnosis of anaplastic carcinoma in its rhabdoid variant of the thyroid was retained. The patient died one month after the operation before receiving adjuvant therapy.

## Discussion

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The initial concept of the rhabdoid cell has been used for the first time in 1978 to describe a variant of Wilms' tumor in children with a rhabdomyosarcomatous pattern [1]. Eight years later, rhabdoid tumors have been described in different organs in adults [6-10]. These cells have been observed in extra-renal location and they were not considered as a separate entity but as a final pathway of dedifferentiation of tumors derived from multiple cell types including tumors of neuroectodermal, myogenic, histiocytic, melanocytic and epithelial origin [7,8]. Wick *et al.* [7] propose to separate these extra-renal tumors into two categories: the first contains only rhabdoids cells and the second contains rhabdoid cells that are combined with another morphological entity, called composite extrarenal rhabdoid tumor. It is interesting to identify the percentage of rhabdoid cells in a tumor, because these cells confer a more aggressive behavior to the tumor. A cutoff of at least 10% of the tumor cell population expressing the rhabdoid phenotype has been proposed as having an adverse prognosis [6].

ATC with rhabdoid features is extremely rare [4] and only few cases have been reported in literature (Table 1). Among these cases, some showed follicular differentiation in the more differentiated areas, while others showed papillary areas, indicating that the rhabdoid differentiation was a part of either follicular or papillary carcinoma of thyroid. In 1991, Chetty and Govender identified this entity in a poorly differentiated follicular thyroid carcinoma [11]. A recent literature review including 12 cases of rhabdoid tumors of the thyroid has shown that the rhabdoid phenotype is reported in 5 cases of follicular carcinoma, 3 cases of papillary carcinoma and 4 cases of anaplastic carcinoma [12]. The case under discussion showed only areas of undifferentiated carcinoma similar to the cases reported by Carmen Carda [13]. ATC can occur at any age [7]. More than half of cases of ATC with rhabdoid features reported in the literature were women with an age ranged from 22 to 77 years with a mean of 57.4 years (Table 1). Clinically, most of patients present with a rapidly enlarging neck mass with local compressive symptoms, like our patient [6]. This variant appears macroscopically as a solid, irregular mass, with a whitish or greyish color [12]. Microscopically, features include the presence of large pleomorphic cells with abundant cytoplasm and characteristic cytoplasmic eosinophilic inclusions and eccentric nuclei [4]. These rhabdoid inclusions should be distinguished from thyroglobulin inclusions observed in follicular neoplasms and containing thyroglobulin [14]. Unlike rhabdoid inclusions, they are periodic acid-Schiff, alcian blue positive and immunoreactive for thyroglobulin. Immunohistochemically, rhabdoid cells tumor of the thyroid gland shows positivity for vimentine and cytokeratins with variable expression of other markers like as TTF-1, EMA, AML, myoglobine, desmin, NSE and PS100 [15]. The rhabdoid tumor cells of the present case are immune-reactive to vimentin, EMA and CK and negative for TTF1, thyroglobulin, chromogranin and synaptophysin. Immunoreexpression of SMARCB1 (INI1) in primary childhood malignant rhabdoid tumors is characteristically lost, due to biallelic deletions or mutations in INI1 on chromosome 22 [16].

In adults, the immunoreexpression of INI1 helps in distinguishing composite rhabdoid tumors where a rhabdoid cell component, pathogenetically related to primary childhood malignant rhabdoid tumor, coexists with a more differentiated malignancy and shows loss of INI1 expression, from a poorly differentiated carcinoma with rhabdoid phenotype, in which the protein is expressed [5]. The differential diagnosis of such tumor is broad and includes medullary carcinoma of the thyroid, metastatic medullary carcinoma of the kidney, melanomas and variety of sarcomas. These diagnosis are eliminated by the morphological aspect and the immunohistochemical study. The treatment of rhabdoid variant of ATC is not standardized because of the rarity of this entity. Feasible options include surgery, radiotherapy, radio-iodine therapy and chemotherapy [5,11,15,17]. This entity is highly aggressive and associated with a poor prognosis due to lack of response to radio- and chemotherapy. It is associated with local recurrences and metastases with a median survival of 6 months [4]. Some reported thyroid carcinoma with rhabdoid phenotype in the literature are grouped in Table 1 [4,5,11-15,17-20].

## Conclusion

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Thyroid tumor with rhabdoid phenotype is a rare tumor with difficult diagnosis. This entity is highly aggressive with a poor prognosis. Clinical findings, histological analyses and the immunohistochemistry profile are required to achieve the correct diagnosis. Surgery was performed in most cases and the benefit of adjuvant therapy was not clear.

## Competing interests

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The authors declare no competing interests.

## Authors' contributions

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Amal Douida drafted the manuscript. All the authors have read and agreed to the final manuscript.

## Table and figures

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**Table 1:** some reported thyroid carcinoma with rhabdoid phenotype in the literature

**Figure 1:** heterogenous nodule with whitish and blackish areas

**Figure 2:** tumor composed of poorly differentiated large cells

**Figure 3:** rhabdoid cells with an abundant cytoplasm and eccentric nuclei containing distinct nucleoli

**Figure 4:** tumor infiltrated the perithyroid fat tissue

**Figure 5:** rhabdoid cells positive for CKAE1/AE3

**Figure 6:** rhabdoid cell showed immunoactivity for EMA

**Figure 7:** rhabdoid cells immunoreactive for Vimentin

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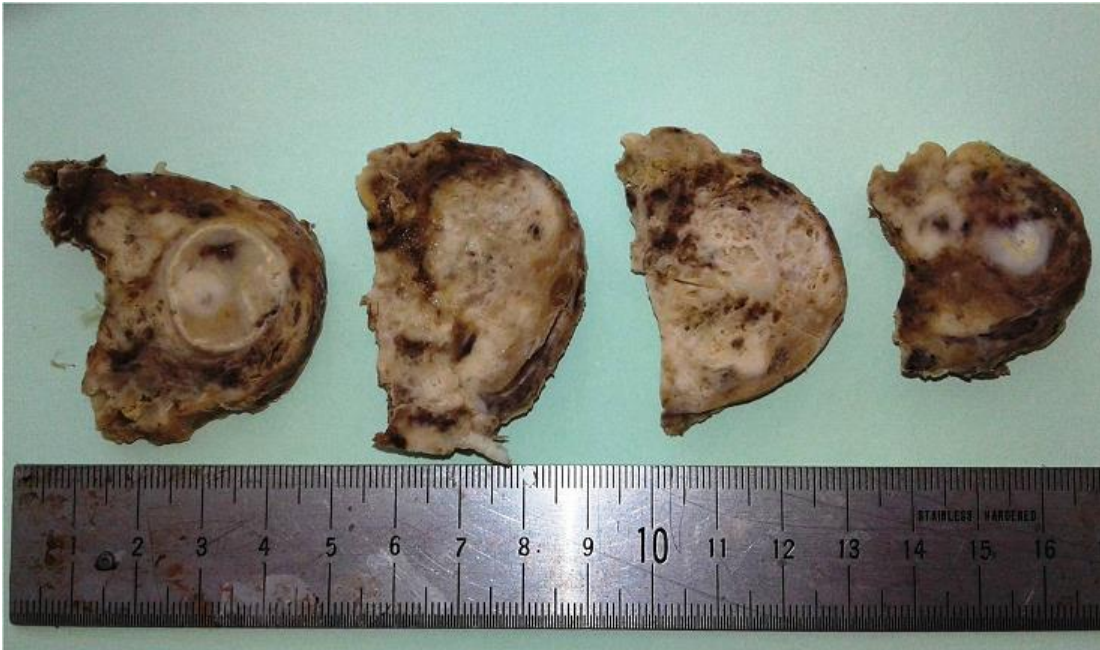
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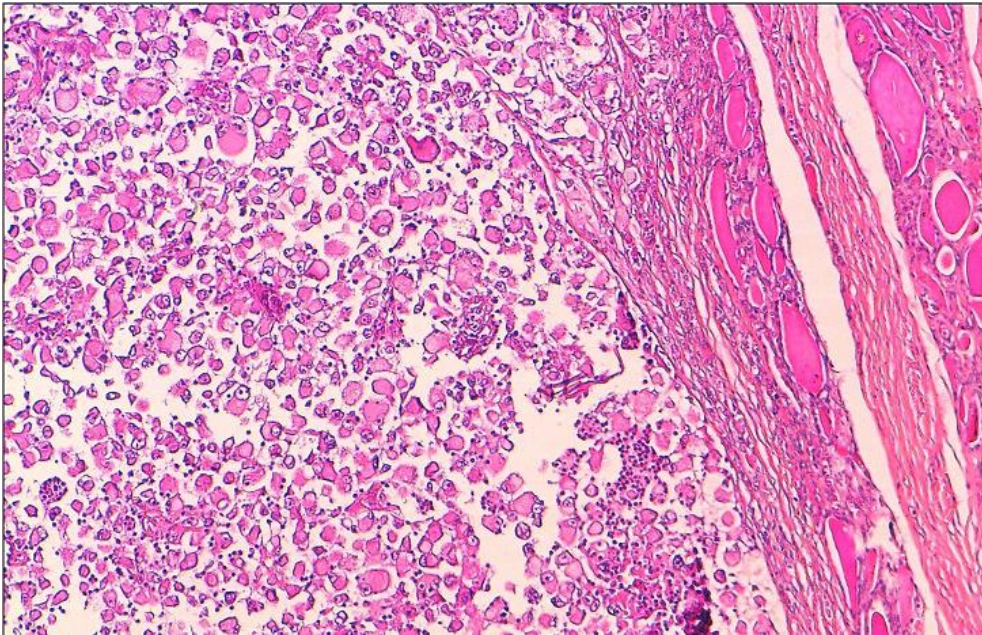
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Table 1: some reported thyroid carcinoma with rhabdoid phenotype in the literature							
Reported cases	Age	Sex	Treatment	Size (cm)	Background	Immunohistochemistry profil	Evolution
1-Runjan and Govender (South Africa)	65	F	right lobectomy	6	Follicular	CK AE1/AE3+ Vimentin +	died 3 months later
2-Runjan and Govender (South Africa)	43	F	right lobectomy	4	Follicular	Vimentine + CK AE1/AE3+	lost to follow- up
3-Runjan and Govender (South Africa)	56	F	right lobectomy	5	Follicular	Vimentine + CK AE1/AE3+	Alive, 1 month later
4-Gong Feng and al (USA)	68	M	FNA and NCB	10,5	-	CK AE1/AE3+ CK19+ PAX-8 + INI-1 +	died 1 month later
5- Sylvia L. Asa (Canada)	66	F	Total thyroidectomy	6	Papillary	CK AE1/AE3+ Vimentine + Myoglobin +	died 1 month later
6-Katsuaki Sato (Japan)	77	M	right lobectomy and ND	2	Anaplastic	CK AE1/AE3+ Vimentin + Muscle actin + BAF47/INI1 +	died 6 months later
7- D'Antonio and al. (Italy)	61	F	Total thyroidectomy + ERT + CT	-	Anaplastic	CK+ Vimentine +	died 2 months later
8-Pratima and Kusam (India)	45	F	Total thyroidectomy	7	Papillary	Vimentine + CK-, Pax 8 -	-
9-Jorge Albores- Saavedra et al. (Texas)	42	F	hemithyroidectomy	15	Follicular	Vimentine + CK -, AML - Thyroglobulin-, Desmin -	died 3 years after diagnosis
10- Jorge Albores- Saavedra et al. (Texas)	58	M	total thyroidectomy+ RI 131	6	Follicular	Vimentine + CK -, AML - Thyroglobulin-, Desmin -	died 4 years later
11- Maria Letizia Lai et al. (Italy)	67	F	Total thyroidectomy + ERT	4	Anaplastic	Vimentine +, CK + Sarcomeric actin + Myoglobin + Desmin -, AML - Ps100 -	died 1 month later
12- Yen-Ting Lu et al. (Taiwan)	59	M	Total thyroidectomy+ ND+ RAI + CT	8,5	Papillary	Vimentine +, TTF1+ Thyroglobulin - Chromogranin -, HBME- 1 -	Alive, 1 year later
13- Sumida et al. (Japan)	60	F	Tumor Resection+ RT+CT	6	Papillary	Vimentine +, CK+/- Ps100+/-	died 5 month later
14- Carmen Carda et al. (Spain)	59	M	hemithyroidectomy + ERT + CT	-	Anaplastic	Thyroglobulin -, Calcitonin - Vimentine +, HNF35 + Myoglobin+	died 15 months after diagnosis
15- Carmen Carda et al. (Spain)	62	M	Total thyroidectomy	-	Anaplastic	Thyroglobulin - Calcitonin - Vimentine +, Desmine + HNF35 +/-, Myoglobin +	Lost to follow-up
16- Current case	66	F	Total thyroidectomy+ND	6	Anaplastic	CKAE1/AE3 +, EMA + Vimentin +, TTF-1 - Thyroglobulin - Chromogranin - Synaptophysin -	died one month after surgery

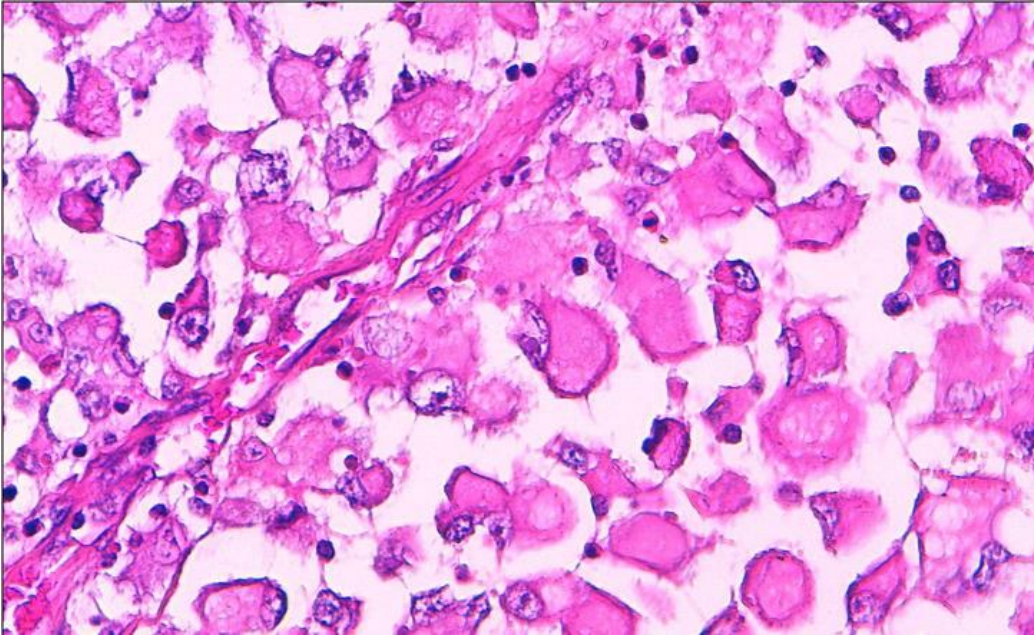
**FNA and NCB:** Fine Needle Aspiration and Needle Core Biopsy. **ND:** neck dissection. **ERT:** external-beam radiotherapy. **CT:** chemotherapy. **RI:** radioactive iodine. **RAI:** radio-iodine ablation therapy.



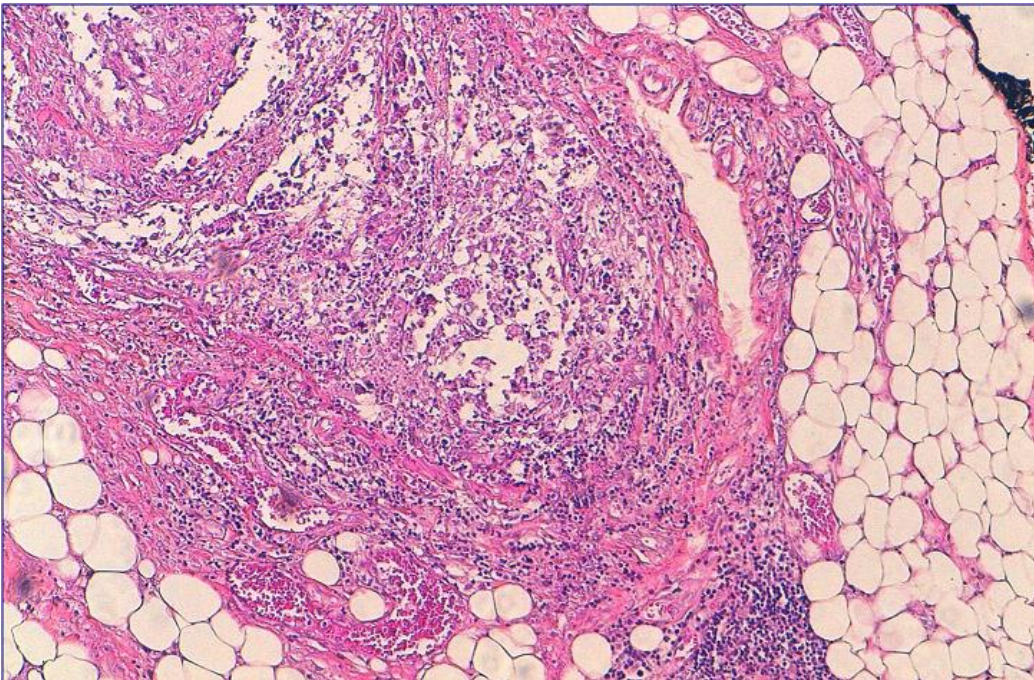
**Figure 1:** heterogenous nodule with whitish and blackish areas



**Figure 2:** tumor composed of poorly differentiated large cells

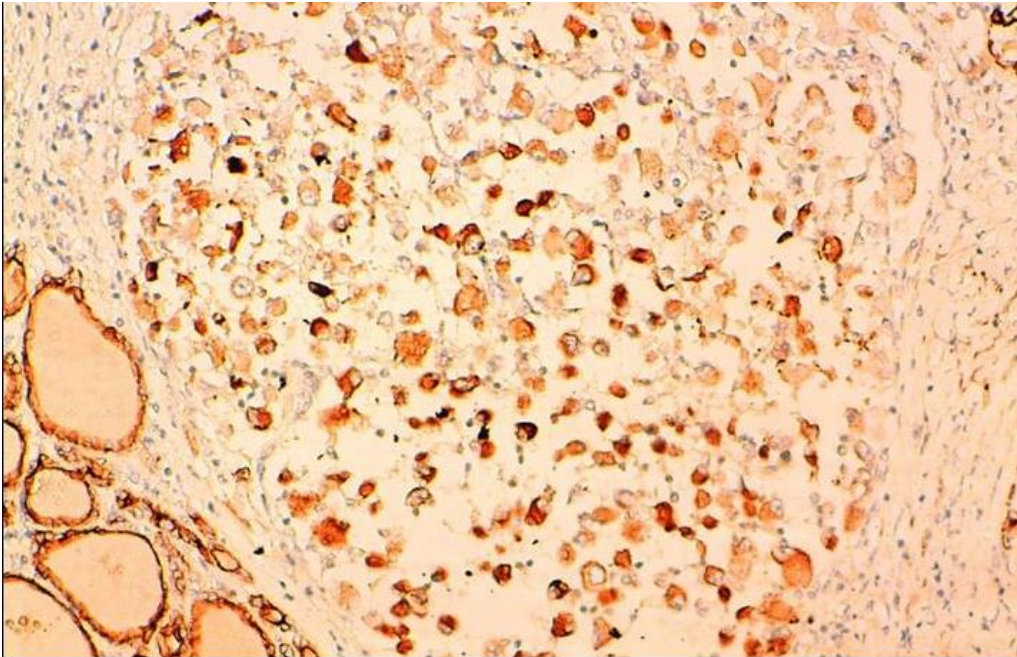


**Figure 3:** rhabdoid cells with an abundant cytoplasm and eccentric nuclei containing distinct nucleoli

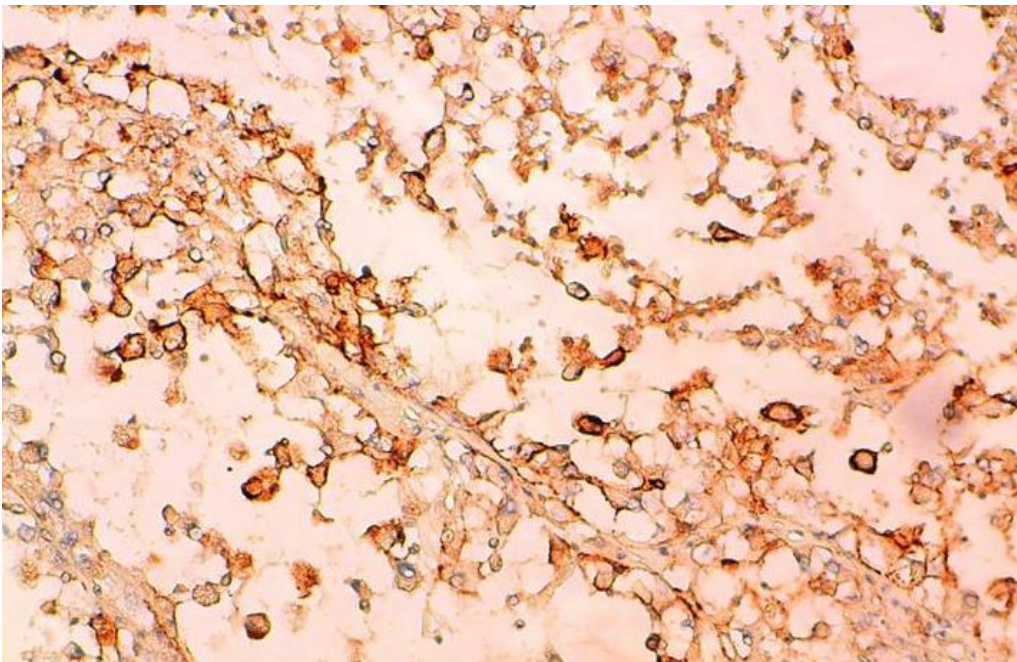


**Figure 4:** tumor infiltrated the perithyroid fat tissue

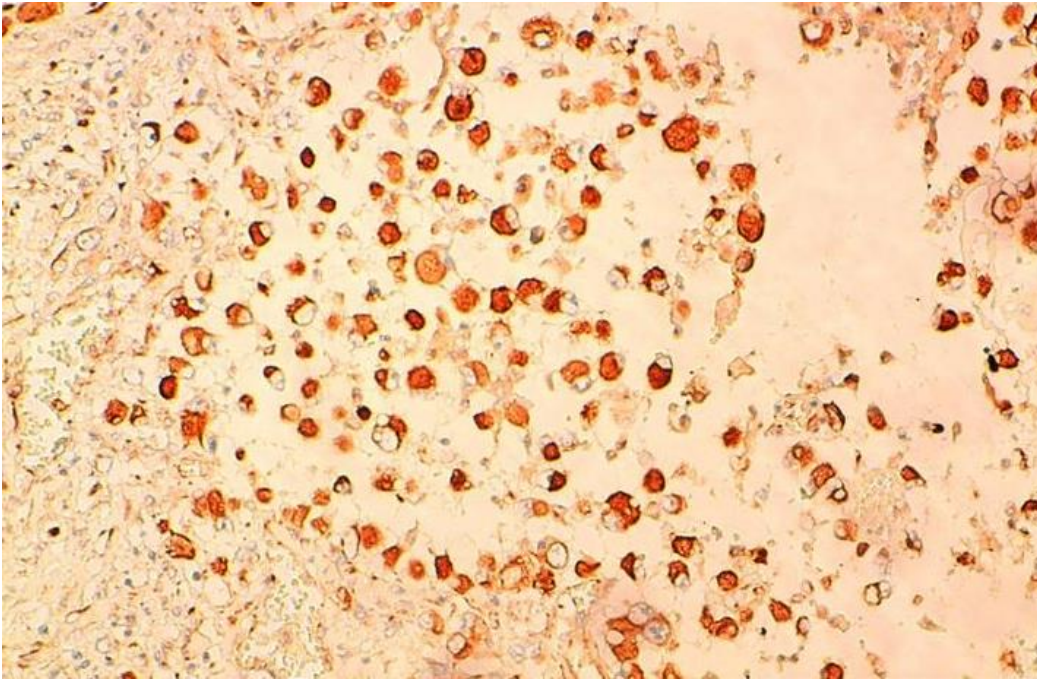




**Figure 5:** rhabdoid cells positive for CKAE1/AE3



**Figure 6:** rhabdoid cell showed immunoreactivity for EMA



**Figure 7:** rhabdoid cells immunoreactive for Vimentin