

CASE REPORT

Adamantinoma-like Ewing sarcoma of thyroid gland-An unfamiliar mimicker of epithelial and mesenchymal neoplasms of the head and neck

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Abstract

Introduction: Adamantinoma-like Ewing Sarcoma (ALES) is a rare variant of the Ewing family of tumours (EFT) harbouring the EWSR1-FLI1 translocation and with complex epithelial differentiation. Very few cases of ALES involving thyroid have been reported in literature. **Case report:** We report a case of ALES involving the thyroid in a 61-year-old male who presented with an enlarging nodule in the left lobe of the thyroid and underwent hemithyroidectomy. **Discussion:** ALES demonstrates morphologic similarity to a multitude of epithelial and mesenchymal tumours, creating a potential diagnostic pitfall in thyroid and head and neck pathology. Given the rarity of this tumour, there is also a lack of accepted guidelines regarding further surgical management of these cases following hemithyroidectomy.

Keywords: Adamantinoma-like Ewing sarcoma, thyroid, Ewing family of tumours

INTRODUCTION

Adamantinoma-like Ewing Sarcoma (ALES) is a rare variant of Ewing Sarcoma that shows epithelial differentiation and the characteristic EWSR1-FLI1 translocation. It was initially described in tubular long bones as adamantinoma with EWS/FLI1 fusion.¹ More recently, it has predominantly been reported in the head and neck region, including the salivary glands and sinonasal cavity. Until now, only few cases of ALES involving the thyroid have been reported in the literature.¹⁻⁹ The morphological resemblance of ALES to poorly differentiated thyroid carcinoma and small round blue cell tumours can pose a diagnostic challenge in accurate identification of these tumours. Here, we report a patient with ALES involving the thyroid and discuss the morphologic, immunohistochemical and molecular characteristics of the tumour along with the differential diagnosis and a review of the literature.

CASE REPORT

A 61-year-old male with a long-standing thyroid swelling presented with a rapidly enlarging

nodule in the left lobe of the thyroid gland. Ultrasound imaging showed a heterogenous hypoechoic nodule with vascularity in the left lobe of the thyroid. Thyroid function tests were within normal limits. Fine needle aspiration of the nodule showed atypia of undetermined significance. The patient underwent left hemithyroidectomy.

On gross examination, the left lobe of the thyroid gland was replaced by a 14 cm, tan-white to grey predominantly solid mass with cystic areas (Fig 1). Histologic examination showed the entire left lobe of the thyroid was involved by a neoplastic proliferation of round to oval cells with minimal cytoplasm, in sheets and cords, entrapping thyroid follicles (Fig 2 and Fig 3). The neoplastic cells displayed mild pleomorphism, round to oval nuclei, evenly distributed chromatin, variably prominent nucleoli (Fig 4) and increased mitotic activity (7 mitoses/10 high power fields). The tumour cells were seen spreading along the thyroid follicular lining in a pagetoid fashion. Extrathyroidal extension and lymphovascular invasion were not identified. Immunohistochemical analysis of the tumour showed diffuse positivity for CD99

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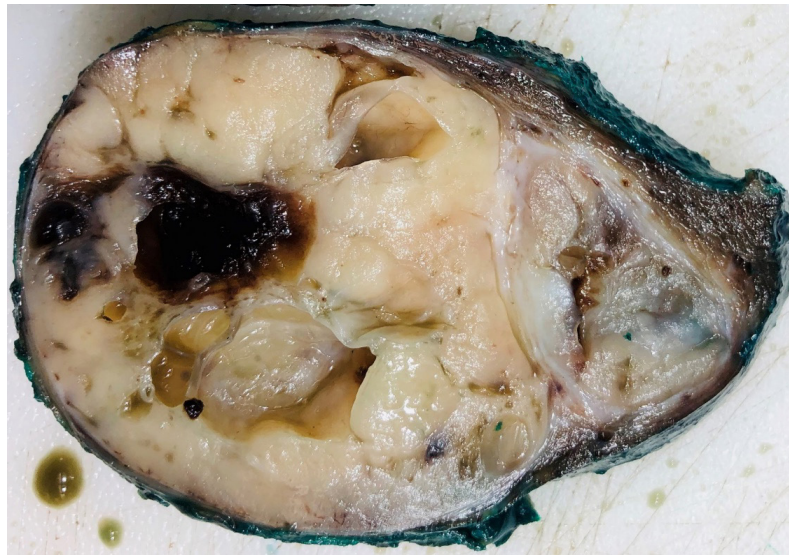


FIG. 1: Lobulated tan-white circumscribed tumor with areas of cystic degeneration almost entirely replacing the thyroid lobe. Normal thyroid parenchyma seen at the periphery.

(Fig. 5), patchy positivity for pancytokeratin AE1/AE3, CD56 and focal p63 expression. Thyroglobulin, TTF-1, PAX 8, p40, calcitonin, S100, synaptophysin, chromogranin, CD45 were negative. Molecular analysis using a next-generation sequencing panel showed presence

of the EWSR1-FLI1 fusion transcript without variants in other relevant genes including BRAF, KRAS, HRAS, NRAS, TP53, PTEN, NTRK, PPARG and RET.

Following the diagnosis, the patient underwent completion thyroidectomy. No residual tumour

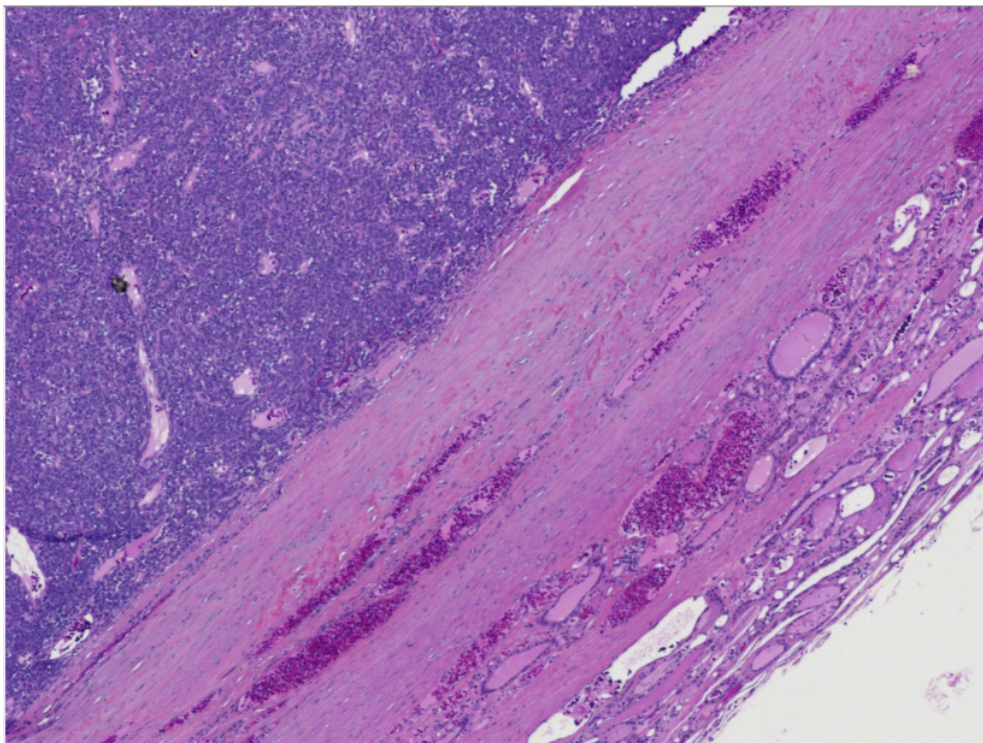


FIG. 2: Low power view showing circumscribed tumour and thyroid parenchyma at the periphery (H&E stain 40X)

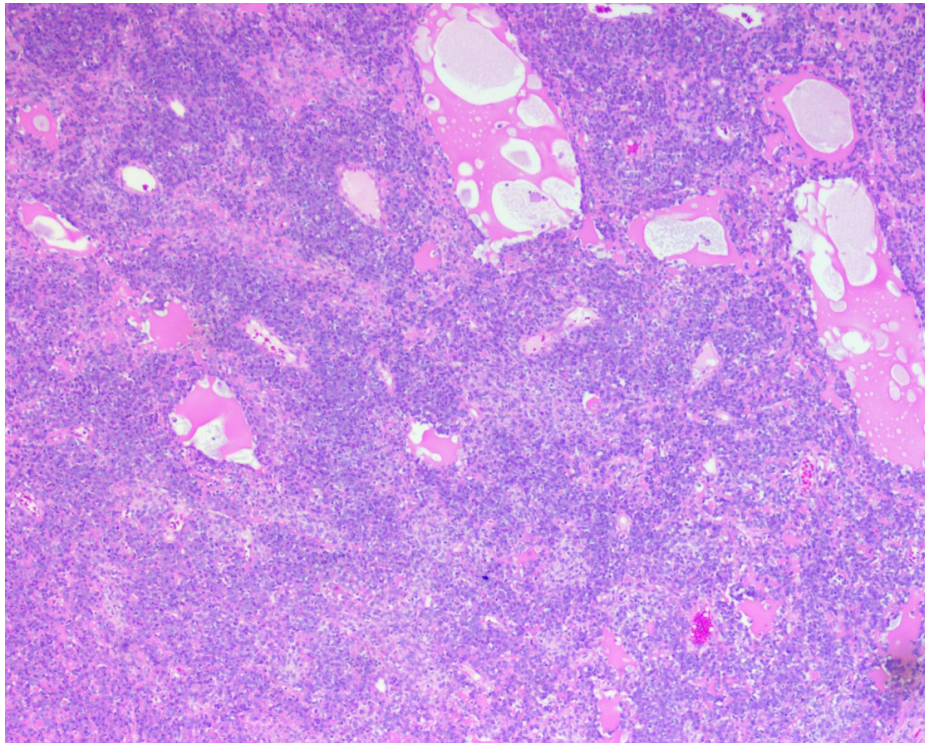


FIG. 3: Low power view showing tumour with entrapped colloid (H&E stain 40X).

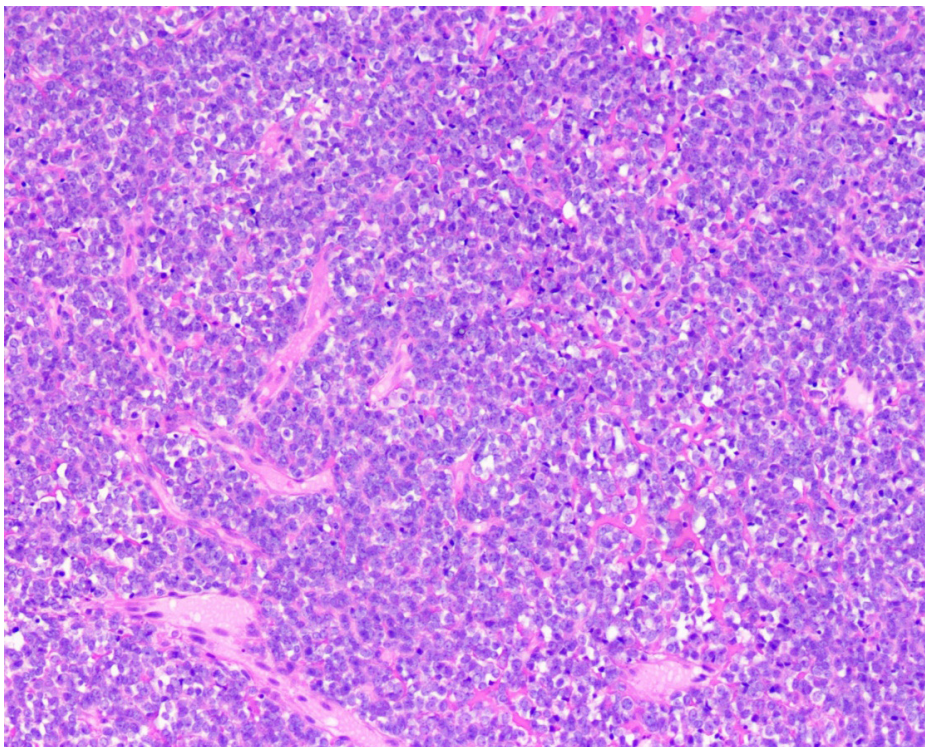


FIG. 4: High power view showing tumour cells arranged in nests and sheets with mild pleomorphism, round to oval nuclei and evenly distributed chromatin (H&E stain 100X).

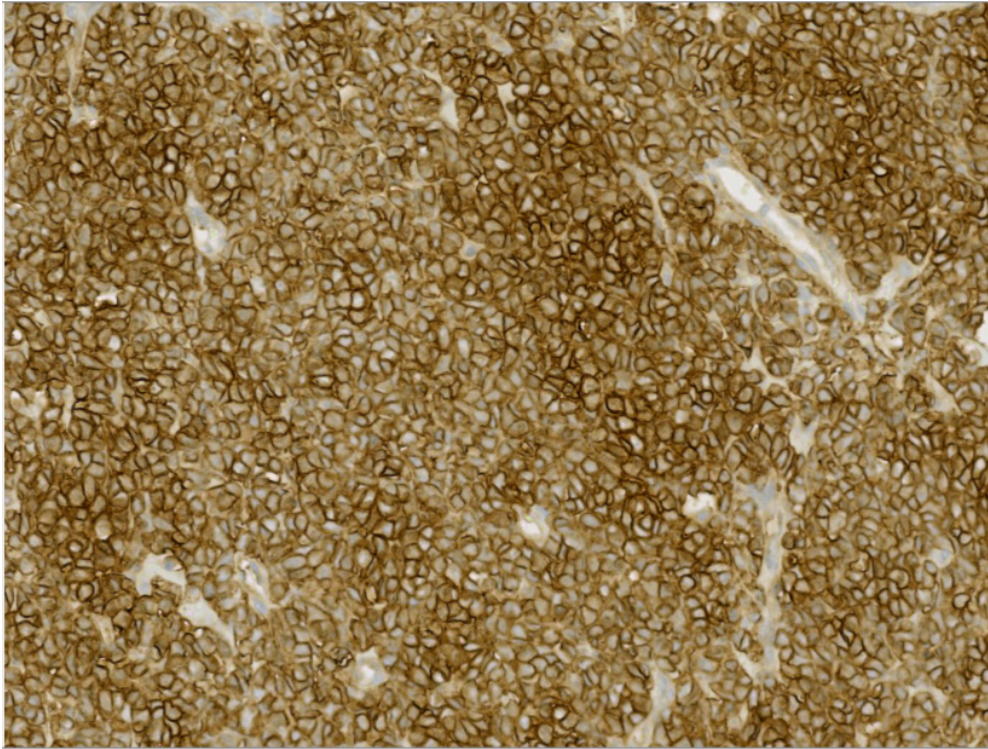


FIG. 5: Diffuse membranous expression of CD99 (CD99 immunostaining 200X).

was present. As the patient was late for follow up (more than 6 months following surgery) adjuvant chemotherapy was not recommended. Six month and one year follow up CT and PET CT showed no evidence of recurrent disease or metastasis. The patient is now 19 months post-surgery without any evidence of recurrence.

DISCUSSION

ALES were initially reported in long tubular bones in 1999, where the tumours were originally described as adamantinoma with EWS/FLI1 fusion.¹ To this date, twenty-three cases of ALES involving the head and neck have been reported in the literature, which include six cases of ALES involving thyroid (Table 1).²⁻⁹ All cases demonstrated the EWSR1- FLI1 translocation either by break-apart FISH or by reverse transcriptase-polymerase chain reaction.

ALES of the thyroid presents as a large thyroid/neck mass with a lobulated tan-white cut surface and variable amounts of cystic degeneration. It is predominantly seen in adults (19-61 years). Clinical features of the reported cases of ALES are summarised in Table 1. This patient had long-standing thyroid swelling for a few years with rapid enlargement of the

left lobe in the past few months. The patient's clinical presentation, the presence of entrapped colloid-filled thyroid follicles with macrophages in the tumour, and the nodular hyperplasia of the remaining thyroid tissue all point to the development of this neoplasm in a pre-existing nodular colloid goiter.

Histologically, ALES resembles the typical Ewing sarcoma family. The neoplastic cells appear round/basaloid with focal peripheral palisading and fibrosis between nests often entrapping thyroid follicles. Occasional presence of necrosis, extrathyroidal extension and metastases has been reported.⁸⁻⁹ Multifocal areas of necrosis were seen in another case.⁹ All cases demonstrated high mitotic activity (3 to 10 mitoses per 10 high power fields). ALES of the thyroid and salivary glands are largely organ-confined whereas ALES of the sinonasal cavity and soft tissues demonstrates destruction of surrounding tissues.¹⁰

The differential diagnosis of ALES of the thyroid includes poorly differentiated thyroid carcinoma, small cell variant of medullary thyroid carcinoma and other small round blue cell tumours. Poorly differentiated thyroid carcinoma shares morphologic similarity to ALES. However,

TABLE 1: Summary of clinical and demographic features in cases reported as adamantinoma-like Ewing sarcoma of the thyroid

Case	Reference	Age	Sex	Presenting symptom	Initial diagnosis	Final diagnosis
1	Cruz <i>et al</i>	42 years	F	Anterior cervical mass	Small cell thyroid carcinoma	CEFTE
2	Eloy <i>et al</i>	24	M	Large thyroid nodule	Poorly differentiated carcinoma	CEFTE
3	Bishop <i>et al</i>	19	M	Neck mass	ALES	ALES
4	Bishop <i>et al</i>	36	F	Goiter	ALES	ALES
5	Ongkeko <i>et al</i>	36	M	Enlarging thyroid mass	Poorly differentiated thyroid carcinoma	ALES
6	Morlote <i>et al</i>	20	F	Non painful left neck mass	ALES	ALES
7	Current case	61	M	Large left thyroid nodule	ALES	ALES

ALES, Adamantinoma-like Ewing sarcoma; CEFTE carcinoma with Ewing family tumor elements; M male; F female

most of these tumours are negative for CD99 and express TTF-1, PAX-8 and thyroglobulin. Medullary carcinoma of the thyroid can be excluded by absence of neuroendocrine differentiation, absence of amyloid, and lack of calcitonin and TTF-1 staining. Anaplastic thyroid carcinoma is an extremely aggressive tumour and shows propensity to invade nearby structures along with extensive lymphovascular invasion. There is also marked pleomorphism, necrosis and mitotic activity. These tumours are thyroglobulin and TTF-1 negative. However, around half of the tumours are positive for PAX8. However, the other small round blue cell differential diagnoses including lymphoma, rhabdomyosarcoma and synovial sarcoma also should be ruled out. These tumours generally lack cytokeratin expression but express lineage-specific markers. The tumour cells in ALES showed strong membranous CD99 expression and positivity for cytokeratin. The consistent cytokeratin and p63 expression distinguish ALES from other members of Ewing family of tumours. The immunohistochemical findings of all ALES cases of the thyroid reported in the literature are summarised in Table 2. Detection

of the EWSR1-FLI1 translocation is necessary for confirming the diagnosis of ALES.

CONCLUSION

The major pitfall in the diagnosis of ALES is that the morphology and immunoprofile resemble poorly differentiated/undifferentiated thyroid carcinoma. Although there are no accepted guidelines for treatment, this entity is treated under sarcoma protocol. Thus, accurate identification of ALES by CD99 immunohistochemistry and EWSR1-FLI1 fusion detection is necessary for establishing prognosis and guiding therapy. There is no recommended guideline for surgical management following a hemithyroidectomy with a diagnosis of ALES. In our patient, no residual tumour was present on completion thyroidectomy. Furthermore, as ALES of the thyroid and salivary gland are organ-confined and unifocal, we need to revisit the need for additional surgery in these patients.

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TABLE 2: Summary of clinical and demographic features in cases reported as adamantinoma-like Ewing sarcoma of the thyroid

	Cruz <i>et al</i>	Eloy <i>et al</i>	Bishop <i>et al</i>	Bishop <i>et al</i>	Ongkeko <i>et al</i>	Morlote <i>et al</i>	Current <i>et al</i>
CD99	+	+	+	+	+	+	+
Pan CK	+	+	+	+	+	+	+
P63	+	+	ND	ND	ND	ND	+
P40	ND	ND	Focal +	+	ND	+	–
S100	–	–	Focal +	–	–	ND	–
Thyroglobulin	–	–	ND	ND	–	–	–
TTF-1	–	–	ND	ND	–	–	–
PAX 8	ND	ND	ND	ND	ND	–	–
Calcitonin	–	–	ND	ND	–	–	–
Synaptophysin	–	–	–	Focal +	–	+	–
Chromogranin	–	–	–	+	–	ND	–

+, positive; –, negative; ND, not done

Conflict of interest: The authors declare no conflict of interest.

Author's contribution: Not provided.

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