Shedding Light On A Rare Ovarian Malignancy:

Encapsulated Angio-invasive Follicular Thyroid Carcinoma. A Morphologic Pattern of Malignant Struma Ovarii.

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INTRODUCTION

Struma ovarii is a terminology for a monodermal teratoma of the ovary composed of ≥ 50% thyroid tissue. Approximately 5%–10% of struma ovarii harbour malignantfeatures similar to differentiated thyroid carcinomas and are defined by the World Health Organization (WHO) as malignant struma ovarii (MSO). The most common carcinoma arising in struma ovarii is papillary thyroid carcinoma (classic and follicular-variant PTC); less frequently, the malignant component can be other thyroid carcinoma subtypes such as follicular thyroid carcinoma (FTC). In the 2017 WHO classification, FTC was subdivided into three different subtypes to reflect the overall prognosis based on tumor capsule invasion and foci of vascular invasion: minimally invasive FTC, encapsulated angioinvasive FTC and widely invasive FTC.

CASE PRESENTATION

36 year old lady presented to her GP with abdominal distension, pain and reporting that she could feel a pelvic mass. No change in menstrual cycle, normal bowel function and no urinary symptoms. On examination: mass was noted on the right side of abdomen. Referred to local district general hospital where imaging and blood tests performed.

Transabdominal USS:19X19X18 cm pelvic mass, thick wall, multi-loculated. Computed Tomography: Large solid pelvic mass with central necrosis, likely ovarian.

Tumour marker CA 125 was raised. All other markers were normal .

MANAGEMENT

The case was discussed in gynaecology oncology MDT. First recommendation was to perform pelvic MRI which showed mixed solid and cystic contents, no disease elsewhere ,mild ureteric dilation from compression. Subsequent recommendation was to carry out midline laparotomy with frozen section along with hysterectomy, bilateral salpingoophrectomy, lymph node dissection and omentectomy.

Surgery (midline laparotomy):

The patient had right salpingo-oophorectomy which was sent for intra-operative consultation.

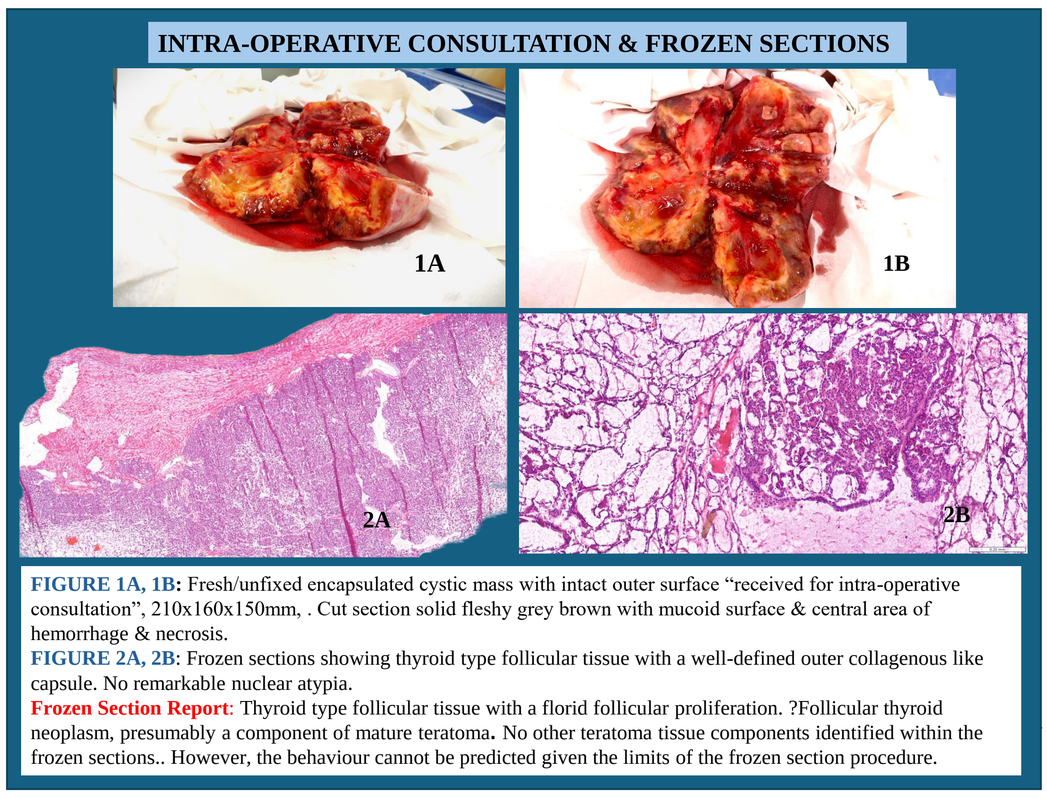


FIGURE 1A, 1B: Fresh/unfixed encapsulated cystic mass with intact outer surface "received for intra-operative consultation", 210x160x150mm, . Cut section solid fleshy grey brown with mucoid surface & central area of hemorrhage & necrosis.

FIGURE 2A, 2B: Frozen sections showing thyroid type follicular tissue with a well-defined outer collagenous like capsule. No remarkable nuclear atypia.

Frozen Section Report: Thyroid type follicular tissue with a florid follicular proliferation. ?Follicular thyroid neoplasm, presumably a component of mature teratoma**.** No other teratoma tissue components identified within the frozen sections.. However, the behaviour cannot be predicted given the limits of the frozen section procedure.

Based on the frozen section report with the normal appearance of left tube and ovary, uterus and upper abdomen. No further surgical resection required, and laparotomy closed.

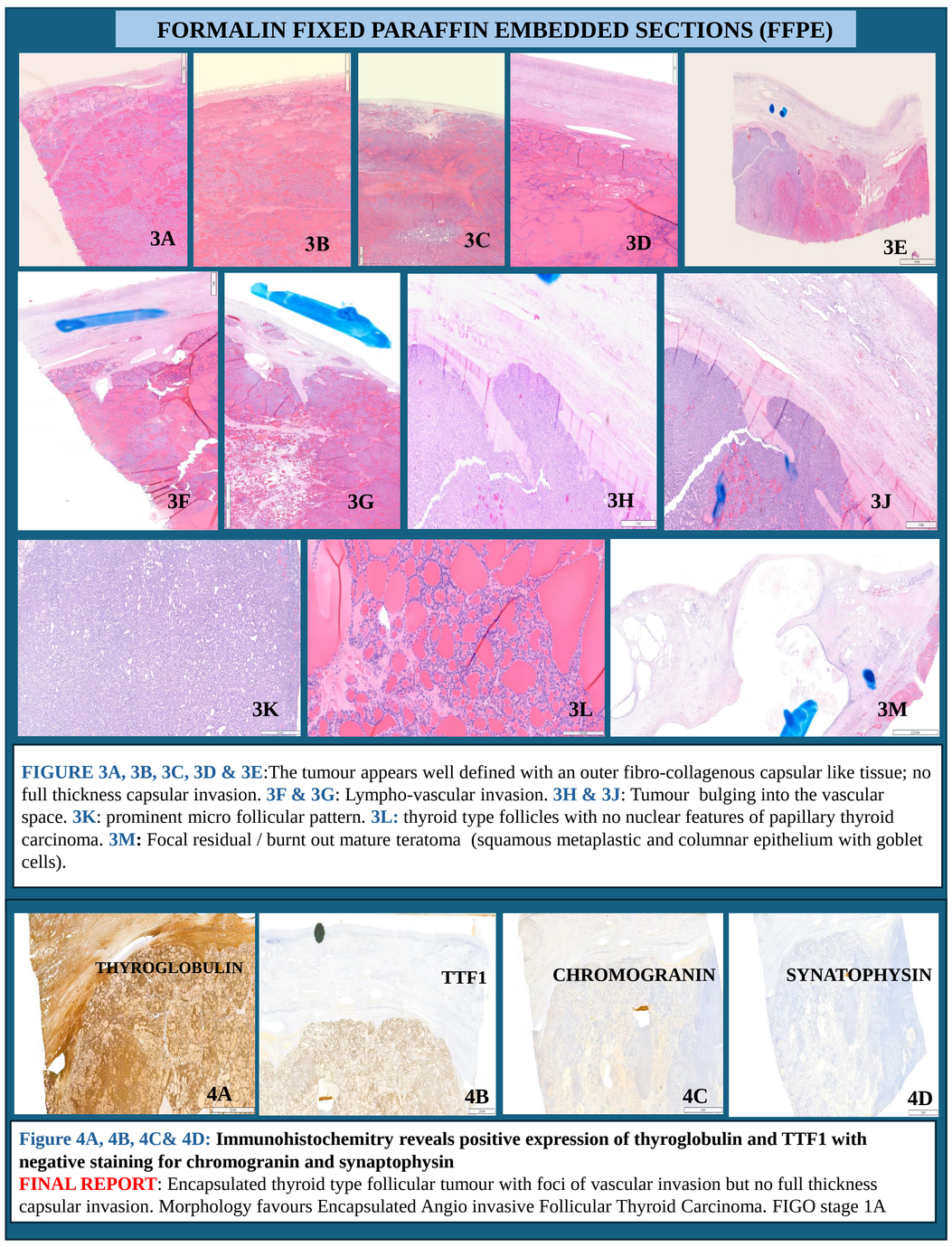


FIGURE 3A, 3B, 3C, 3D & 3E:The tumour appears well defined with an outer fibro-collagenous capsular like tissue; no full thickness capsular invasion. **3F & 3G**: Lympho-vascular invasion. **3H & 3J**: Tumour bulging into the vascular space. **3K**: prominent micro follicular pattern. **3L:** thyroid type follicles with no nuclear features of papillary thyroid carcinoma. **3M:** Focal residual / burnt out mature teratoma (squamous metaplastic and columnar epithelium with goblet cells).

Figure 4A, 4B, 4C& 4D: Immunohistochemitry reveals positive expression of thyroglobulin and TTF1 with negative staining for chromogranin and synaptophysin

FINAL REPORT: Encapsulated thyroid type follicular tumour with foci of vascular invasion but no full thickness capsular invasion. Morphology favours Encapsulated Angio invasive Follicular Thyroid Carcinoma. FIGO stage 1A

MOLECULAR ANALYSIS

Comprehensive pan-cancer gene panel DNA analysis revealed pathogenic alterations within the **NRAS** and **EIF1AX** genes.

GENE	NRAS	EIF1AX
CONSEQUENCE	Missense	Splice_ acceptor _ variant
DNA	c.182A>G	C.338-2A.T
VAF	55%	34%
Pathogenicity	Pathogenic	Pathogenic

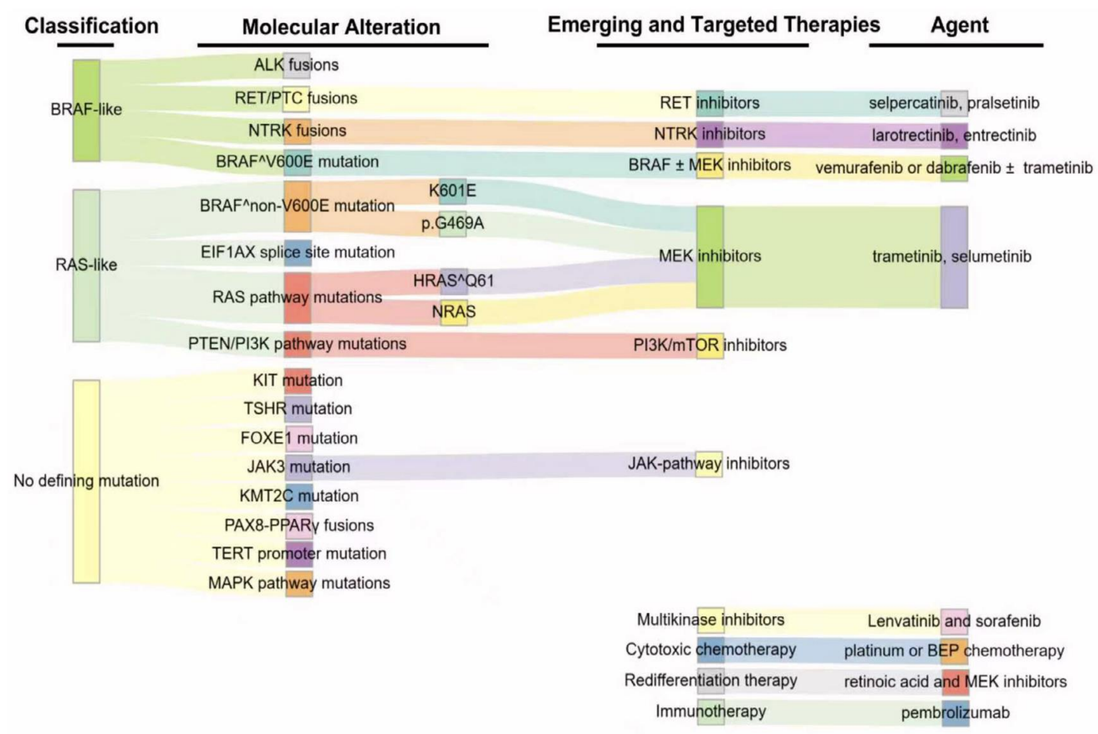
FURTHER MANAGEMENT

The case was discussed at the Endocrine MDT. Following which thyroidectomy performed to lower the risk of recurrence.

DISCUSSION

MSO is a rare ovarian tumour defined by the presence of thyroid carcinoma arising in ovarian teratomatous thyroid tissue. Papillary thyroid carcinoma (classic and follicular-variant PTC) is the most common subtype of thyroid carcinoma identified in MSO (70%–80%), followed by follicular thyroid carcinoma (FTC) (10%–20%). The diagnostic criteria for PTC in struma ovarii parallel those used in the thyroid gland, centred on identifying the characteristic nuclear features of PTC. In contrast, diagnosing follicular carcinoma in struma ovarii can be more problematic because it relies on the demonstration of invasion. In the thyroid gland, FTC is diagnosed by capsular and/or vascular invasion; however, in the ovarian teratoma setting, a true fibrous capsule may be absent. Thus, one must look for tumour invading into mature teratoma elements or ovarian stroma, as well as vascular invasion or metastases to confirm malignancy.

Recent studies have shown that MSO shares many of the genetic alterations found in thyroid carcinoma, reinforcing that these are biologically thyroid cancers in an ectopic site. These shared histo-molecular features of MSO with primary thyroid carcinoma validate WHO 2022 thyroid tumor classifcation for risk stratifcation in malignant struma ovarii. The 5th edition WHO Classifcation of Thyroid Tumors (2022) introduced a molecular classifcation for diferentiated thyroid carcinoma, stratifying tumors into RAS-like and BRAF-like subtypes. RAS-like tumors are typically encapsulated or well-demarcated, predominantly follicular in growth, often harbour RAS or RAS-pathway gene mutations, and display only subtle PTC-type nuclear features. Genetic alterations in RAS like tumors extend beyond RAS mutations to include BRAF K601E, DICER1, EZH1, and EIF1AX mutations. In contrast, BRAF-like tumours often show papillary architecture, infltrative growth, and the characteristic nuclear features of PTC (ground-glass nuclei with grooves and inclusions—"BRAF-like nuclei"). Common alterations in BRAF-like tumours include BRAF V600E and fusions of genes such as ALK, RET, NTRK1/3, and MET.



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CONCLUSION

This case demonstrates the significant role of integrated approach (morphology and molecular analysis) in the diagnosis of MSO.

It highlight the application of thyroid-type classification and risk stratification to these tumours.

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