

# An unusual tumour metastasis in the left supraclavicular neck

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## Abstract

Metastases of adult granulosa cell tumours are uncommon. We report a case of a late metastasis of adult granulosa tumour that presented as supraclavicular mass. We review the literature on metastatic adult granulosa cell tumour to this site. We discuss the molecular features that help differentiate adult granulosa cell tumour from other lesions.

**Keywords** FOXL2; granulosa; Virchow's node

## Case report

A 65 year old female presented to the haematology team with a persistent painless left supraclavicular mass, with a preceding administration of the AstraZeneca (ChAdOx1) COVID-19 vaccine and no B symptoms. Ultrasound showed a 3.9 cm left neck level 4 well-defined, predominantly solid mass containing irregular cystic components.

The biopsy showed a diffuse uniform population of small cells with angulated nuclei, single nucleoli, minimal cytoplasm, occasional nuclear grooves, some vacuolation and occasional mitoses (Figure 1). In places these were arranged around blood vessels, creating pseudo-rosettes but no Call-Exner bodies were identified. There was no identifiable lymphoid tissue.

Immunohistochemical staining demonstrated the atypical cells were positive for inhibin-alpha, calretinin, WT1, CD56, and ER (Figure 2). Otherwise, there was patchy weak staining for CD99, S100 and p16 with occasional positive staining for pan-cytokeratin and CAM5.2. Negative stains included synaptophysin, chromogranin, TTF1, p63, CD34, cyclin D1 and neurofilaments. The Ki-67 positive proliferation index was approximately 10%. No mucin was appreciated with PAS-diastrase. Genomic testing detected a FOXL2 mutation on exon 1 (Cys134Trp, coding DNA 402C > G) using the RMH200solid panel, in keeping with adult granulosa cell tumour.

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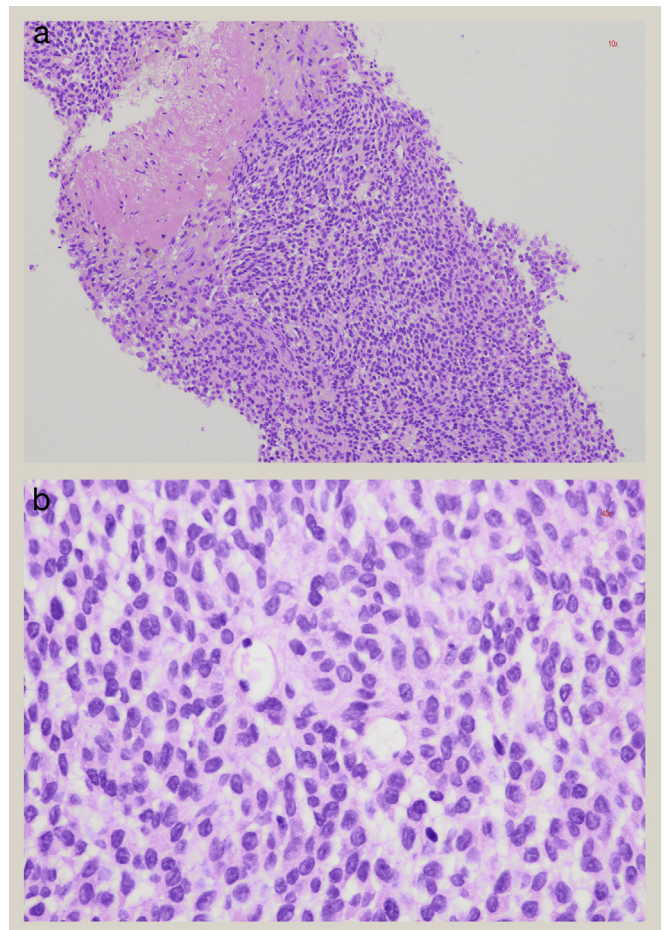
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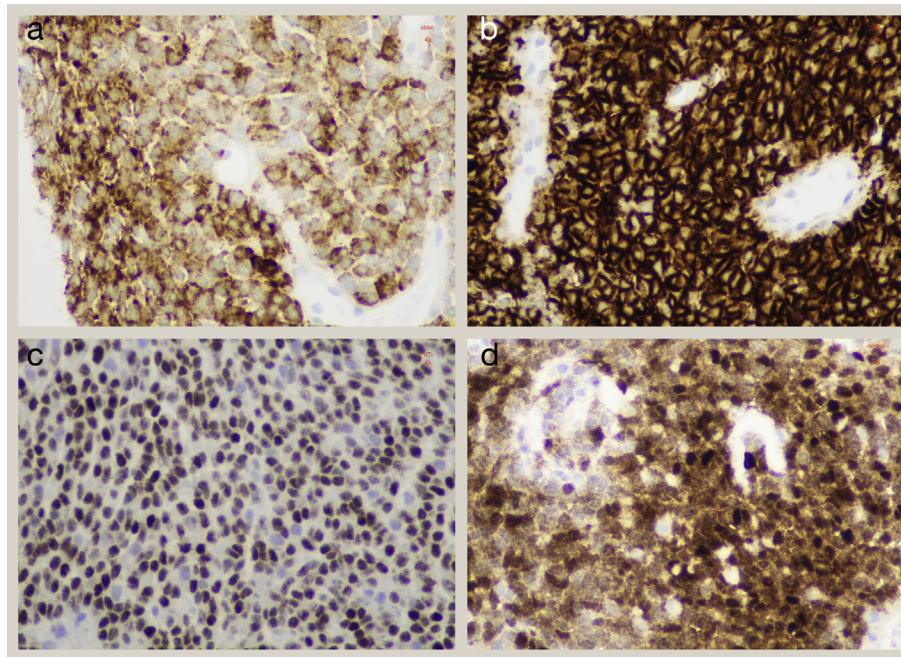
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On review, there was a previous history of stage 1a adult granulosa cell tumour in 2004 which was treated with a total abdominal hysterectomy and bilateral salpingo-oophorectomy, with no evidence of metastasis for 18 years. Serum inhibin A was raised at 11.4 pg/ml (<5 pg/ml postmenopausal) and inhibin B was within normal range at 292 ng/L (0–341 ng/L).

She was subsequently referred to the gynaecology MDT and a further left-para-aortic retroperitoneal nodal mass was detected



**Figure 1** a) Haematoxylin & eosin stain, 10x magnification. b) Haematoxylin & eosin stain, 40x magnification. There is a diffuse uniform population of small cells with angulated nuclei, single nucleoli, minimal cytoplasm, occasional nuclear grooves and some vacuolation.



**Figure 2** Immunohistochemistry, x40 magnification. a) Inhibin A. b) CD56. c) WT1. d) Calretinin.

via FDG PET-CT. The para-aortic lymph nodes were surgically excised and five of nine lymph nodes were positive for metastatic granulosa tumour. Endocrine treatment was considered for the supraclavicular disease.

### Discussion

Adult granulosa cell tumours microscopically consist of small, bland and uniform cells with angulated and often grooved “coffee bean” nuclei. These can be arranged architecturally in various patterns including diffuse, trabecular, insular, microfollicular (Call-Exner bodies with eosinophilic material) and even macrofollicular. Immunohistochemically, they can be positive for FOXL2, SF1, inhibin alpha, calretinin, CD99, low molecular weight cytokeratins, S100, EGFR, vimentin, WT1, CD56 and SMA. Reticulin staining shows a nested pattern.

Granulosa cell tumours of the ovary can occur in a wide range of ages. One study gathered follow-up data on 65 patients with granulosa cell tumours.<sup>1</sup> They found that patients are often postmenopausal (55%) with a median age of 53 years at diagnosis.<sup>1</sup> The most important prognostic factor for 10 year survival is influenced by stage at diagnosis with 87% at FIGO I, 75% at FIGO II, 20% at FIGO III and 0% at FIGO IV.<sup>1</sup> However, the tumours are generally found at early stage (80% FIGO I) with an overall survival rate of 76% at 10 years. Recurrence is a significant possibility with 18 patients with confirmed recurrences in this study; these recurrences are known to be late within adult granulosa cell tumours and in this cohort the average was 69 months with the latest interval in this study between original disease and recurrence being at least 18 years.<sup>1</sup> Recurrence occurs mostly in the pelvis and abdomen while distant metastatic disease is rare with 5.3% of recurrences in this study being above the diaphragm.

There are a few case reports of supraclavicular lymph node metastases from granulosa cell tumours,<sup>2,3</sup> both on the left side

as in our case report; this is the location of Virchow’s node(s) which receive lymphatic drainage from the abdominal cavity. Puri et al. noted a metastases 15 years and Ismi et al. four years after the initial diagnosis.

This case was positive for a FOXL2 mutation. The 402C->G FOXL2 mutation DNA is present in 93–97% of adult granulosa cell tumours.<sup>4,5</sup> It can also be positive 10–25% of the time in juvenile granulosa tumours and other sex cord stromal tumours.<sup>4,5</sup> The FOXL2 immunohistochemical stain is less specific; it is positive >95% of the time in juvenile granulosa cell tumours and 80% of the time in other sex cord-stromal tumours.<sup>5</sup>

### Conclusion

Morphological features can give crucial diagnostic clues to the tumour origin, even if rare or unusual. The previous history should be reviewed in the diagnostic workup of metastases and late metastases are possible. ◆

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### Practice points

- Review of the previous history can provide diagnostic clues that help conserve immunohistochemical tests
- Adult granulosa cell tumour can metastasise and these types of tumours should be considered in tumours of unknown origin
- The majority of adult granulosa cell tumours harbour a FOXL2 mutation and this can be helpful given diagnostic uncertainty

### Self-assessment multiple choice questions

1. What feature is the best diagnostic clue for adult granulosa cell tumour?

- Nuclear grooves
- Hyalinized blood vessels
- Vacuolated cytoplasm
- Pericellular reticulin staining
- Homer-Wright rosettes

Answer: A.

2. What mutation is sensitive for adult granulosa cell tumour?

- FOXL2 202 C > G
- FOXL2 202 A > G
- FOXL2 402 A > G
- FOXL2 202 A > T
- FOXL2 402 C > G

Answer: E.

3. There is overlap in the age ranges between juvenile and adult granulosa cell tumours. What is least helpful in distinguishing between them?

- FOXL2 mutation testing
- FOXL2 immunohistochemistry
- Morphologically small uniform cells
- AKT1 mutation testing
- GNAS, IDH1/2 and DICER1 mutation testing

Answer: B.