Case Report

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Pathology Section

Unilateral Ovarian Metastasis from an Occult Breast Primary Presenting as a Primary Ovarian Neoplasm: A Case Report

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ABSTRACT

Metastatic ovarian neoplasms may closely mimic primary ones, particularly when unilateral. Metastasis from breast carcinoma is recognised, but presentation as an isolated ovarian mass without an identifiable primary lesion is rare and diagnostically challenging. A 43-year-old female presented with a unilateral right adnexal mass, clinically and radiologically suggestive of primary ovarian malignancy. Histopathological examination revealed a tumour composed of monomorphic cells with focal signet ring morphology, raising differential diagnoses including primary ovarian tumours and metastatic carcinoma. A systematic immunohistochemical panel was applied. Tumour cells were negative for calretinin and inhibin, excluding sex cord-stromal tumours, including signet ring stromal tumours, and negative for Napsin A, ruling out the possibility of clear cell carcinoma. Absence of Cytokeratin 20 (CK20) and CDX2 expression argued against a gastrointestinal origin. Diffuse CK7 and Epithelial Membrane Antigen (EMA) positivity prompted further evaluation, which demonstrated strong Oestrogen Receptor (ER), Progesterone Receptor (PR) and GATA-binding protein 3 (GATA3) expression along with loss of E-cadherin. These findings were consistent with metastatic invasive lobular carcinoma of the breast. Subsequent clinical and radiological evaluation failed to identify a primary breast lesion, confirming occult breast carcinoma. This case demonstrates the importance of immunohistochemistry in resolving diagnostic dilemmas and highlights that metastatic disease should be considered even in unilateral ovarian tumours with ambiguous morphology.

Keywords: E-cadherin loss, GATA3, Krukenberg tumour, Metastatic invasive lobular carcinoma, Signet ring cell tumour

CASE REPORT

A 43-year-old female presented with complaints of progressive lower abdominal fullness and a sensation of pelvic heaviness for six months. There was no significant past medical or family history and the patient denied any breast-related symptoms, including lump, pain, or nipple discharge. General physical examination was unremarkable.

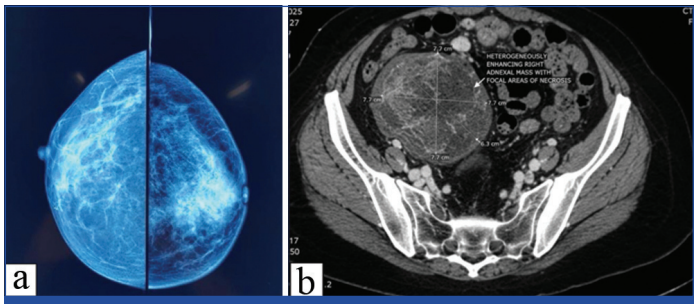
On gynaecological examination, per speculum evaluation revealed a healthy cervix and vagina. A per vaginal examination identified a firm, non-tender mass measuring approximately 6×4 cm in the right fornix, while the uterus, left adnexa, and contralateral fornix were unremarkable. Radiological evaluation was undertaken for further characterisation. Ultrasonography demonstrated a hypoechoic space-occupying lesion in the right adnexal region with irregular margins and internal vascularity. Contrast-enhanced computed tomography revealed a heterogeneously enhancing right adnexal mass measuring approximately 7.7×7.7×6.3 cm with focal areas of necrosis, favouring a neoplastic aetiology. No abnormalities were detected in the uterus, left ovary, or other pelvic structures [Table/Fig-1].

Serum tumour marker analysis showed elevated Cancer Antigen (CA)-125 levels at 560 IU/mL (reference range <35 IU/mL), further supporting the clinical impression of a primary ovarian malignancy.

In view of these findings, the patient underwent total hysterectomy with bilateral salpingo-oophorectomy along with pelvic lymph node sampling for definitive diagnosis and management.

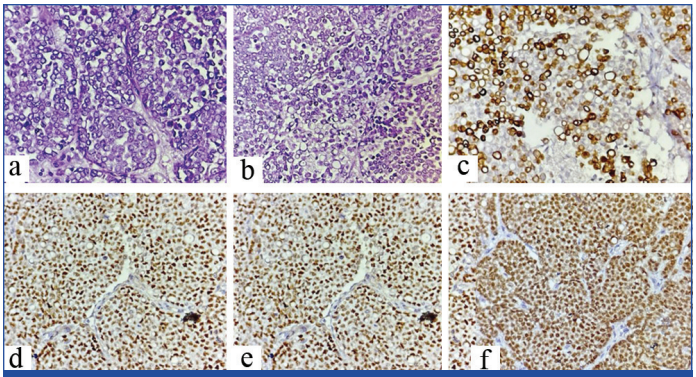
Gross examination revealed a well-encapsulated solid mass involving the right ovary, measuring 7.0×7.0×5.0 cm, with a grey-white cut surface and focal areas of haemorrhage and necrosis. The uterus, cervix, bilateral fallopian tubes, left ovary, omentum, and lymph nodes appeared grossly unremarkable.

Histopathological examination of the right ovarian mass demonstrated an infiltrative tumour composed of monomorphic cells arranged in diffuse sheets and vague lobules. The tumour



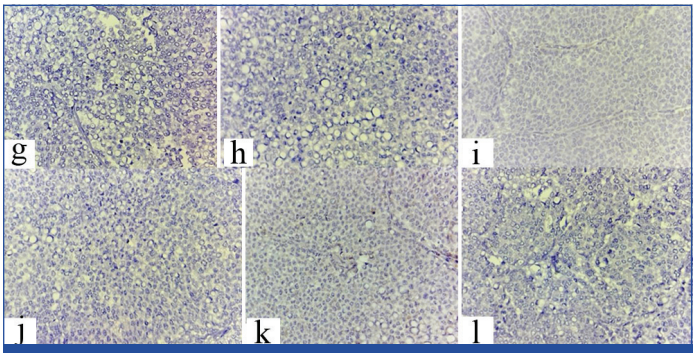
[Table/Fig-1]: a) Bilateral digital mammography in the Craniocaudal (CC) view. The image demonstrates comparison of the right and left breasts. No obvious focal mass, suspicious clustered microcalcifications, or architectural distortion is appreciable on this view; b) Contrast-enhanced axial CT scan of the pelvis showing a large heterogeneously enhancing right adnexal mass (7.7×7.7×6.3 cm) with focal areas of necrosis, radiologically suspicious for an ovarian neoplasm.

cells exhibited vesicular nuclei, inconspicuous nucleoli, occasional nuclear grooves, and areas of cytoplasmic vacuolation, including focal signet ring morphology. No glandular differentiation or extracellular mucin was identified. No lymphovascular or perineural invasion was seen [Table/Fig-2a,b]. Sections from the uterus, cervix, left ovary, fallopian tubes, omentum, and lymph nodes were free of tumours. Based on the above morphology, the main differential diagnoses suggested were primary ovarian signet ring stromal tumour, metastatic gastric diffuse carcinoma, mucinous carcinoma, neuroendocrine carcinoma, and clear cell carcinoma. The differential diagnosis also included metastatic invasive lobular carcinoma of the breast; however, this possibility was considered less likely at the initial evaluation. A stepwise immunohistochemical approach was undertaken. Tumour cells were negative for calretinin and inhibin, excluding sex cord-stromal tumours, including signet ring stromal tumours. Absence of Napsin A expression argued against clear cell carcinoma, while negativity for synaptophysin and chromogranin excluded a neuroendocrine neoplasm. The tumour was also negative for CK20 and CDX2.



[Table/Fig-2]: a,b) Tumour composed of monomorphic cells arranged in diffuse sheets and vague lobules exhibiting vesicular nuclei, inconspicuous nucleoli, occasional nuclear grooves with focal signet ring–like morphology (200X); c-f) Positive immunostaining for CK7, ER, PR and GATA3 (200X).

Diffuse CK7 and EMA positivity supported an epithelial neoplasm. In conjunction with CK20/CDX2 negativity and subsequent mammary markers (ER, PR, GATA3), the immunophenotype favoured metastatic breast carcinoma. The tumour cells demonstrated strong nuclear positivity for Oestrogen Receptor (ER), Progesterone Receptor (PR), and GATA3, along with loss of E-cadherin expression [Table/Fig-2,3]. This immunophenotype strongly favoured metastasis from invasive lobular carcinoma of the breast, prompting further focused clinical reevaluation and radiological correlation (mammography), which failed to identify any primary breast lesion [Table/Fig-1]. In conjunction with the characteristic clinicopathological and immunohistochemical findings, these features were considered most consistent with occult invasive lobular carcinoma of the breast presenting as a unilateral ovarian metastasis. HER2 immunohistochemistry was performed for molecular classification and management, which came out to be negative (score 0).



[Table/Fig-3]: g-k) Negative immunostaining for Calretinin, CK20, CDX2, Synaptophysin and Chromogranin (200X); l) Loss of E-cadherin expression (200X).

In light of this clinical development, the management plan was revised. While the patient had already undergone surgical management for the ovarian mass, further treatment was tailored toward the occult primary breast malignancy. The patient was started on endocrine therapy with letrozole and palbociclib. The patient remains clinically stable without evidence of disease progression at 6-month follow-up. The multidisciplinary team continues to monitor her response to treatment closely. Additionally, genetic counselling was offered to assess any hereditary factors that may influence her ongoing care and the risk for family members.

DISCUSSION

Ovarian tumours exhibiting signet ring cell morphology represent a well-recognised diagnostic challenge due to the considerable overlap between primary ovarian neoplasms and metastatic lesions. Traditionally, the presence of signet ring cells in the ovary raises a strong suspicion for metastatic disease, particularly Krukenberg tumours of gastrointestinal origin, although primary ovarian tumours may occasionally demonstrate similar morphology [1,2].

A primary ovarian signet ring stromal tumour is an extremely rare benign ovarian neoplasm characterised by scattered signet ring cells within a fibrous or stromal background. Unlike true signet ring cell carcinomas, the vacuolated cytoplasm in these tumours does not contain mucin, and the cells lack significant cytologic atypia and mitotic activity. Immunohistochemically, these tumours are typically negative for epithelial markers such as cytokeratins and EMA and may show positivity for stromal markers, helping to distinguish them from metastatic carcinomas [3].

Primary ovarian mucinous and clear cell carcinomas may exhibit overlapping features; however, metastatic tumours from the gastrointestinal tract, colorectum, and breast are more frequently associated with true or mimicking signet ring morphology [1,2,4]. Neuroendocrine neoplasms may rarely be considered due to cytoplasmic vacuolation but can be excluded based on morphology and immunohistochemistry. In the present case, the overall morphology together with the complete immunophenotypic profile favoured metastatic breast carcinoma over primary ovarian and gastrointestinal tumours [4-7].

Ovarian metastases from breast carcinoma are typically bilateral and occur in patients with a known history of breast malignancy [5,6,8]. However, studies have demonstrated that a subset of cases may present as unilateral ovarian masses, thereby adding to diagnostic confusion [9]. More importantly, occult breast carcinoma presenting initially as an ovarian tumour is exceedingly rare, with only isolated case reports documented in the literature [Table/Fig-4] [10-12].

Previously reported cases of ovarian metastasis from occult breast carcinoma were identified through a literature search of PubMed/MEDLINE and Google Scholar using the keywords occult breast carcinoma, ovarian metastasis, ovarian tumour, Krukenberg tumour, and breast cancer metastasis to ovary. No predefined filters were applied during the search. Only three published cases relevant to the present clinical scenario were identified and are summarised in [Table/Fig-4], highlighting their clinicopathological features relevant to the present case.

Among these limited reported cases, occult primary bilateral ovarian involvement appeared to be the usual phenomenon, making the unilateral presentation seen in this case highly unusual and diagnostically challenging. To the best of our knowledge, reports of unilateral ovarian metastasis from occult invasive lobular carcinoma of the breast remain exceedingly rare.

The present case highlights a critical diagnostic principle: metastatic disease cannot be reliably excluded solely on the basis of unilateral ovarian involvement or the absence of a known primary tumour. Large clinicopathological series have emphasised that metastatic tumours to the ovary frequently mimic primary ovarian neoplasms, particularly when presenting as solid masses [1,2,5,6]. Therefore, in all ovarian tumours with unusual morphology, especially

Author (Ref)	Year	Cases	Presentation	Laterality	IHC markers used	Occult/ Known	Key findings
Egami A et al., [10]	2024	1	Suspected ovarian malignancy	Bilateral	ER, PR, GATA3	Occult	Diagnosed after IHC
Yousefnezhad A et al., [11]	2025	1	Bilateral ovarian masses	Bilateral	GATA3, CKAE1/AE3, GCDFP-15	Occult	MRI negative; IHC confirmed
Li P et al., [12]	2026	1	Ovarian metastasis	Bilateral	ER, PR	Occult	Hormone receptor positive case
Present case	2026	1	Unilateral ovarian mass	Unilateral	ER+, PR+, GATA3+, CK7+, EMA+	Occult	Diagnosis after extended IHC

[Table/Fig-4]: Synopsis of cases of ovarian metastasis from occult breast carcinomas [10-12].

those demonstrating signet ring cell features, a comprehensive immunohistochemical evaluation is essential to avoid misdiagnosis and to guide appropriate patient management.

CONCLUSION(S)

This case highlights the importance of maintaining a high index of suspicion for metastatic disease in ovarian tumours, even in the absence of clinical and radiological evidence of a primary breast lesion. Comprehensive immunohistochemical evaluation is indispensable in resolving such diagnostic dilemmas. Recognition of this rare presentation is crucial to ensure appropriate staging, proper management, and prognosis.

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