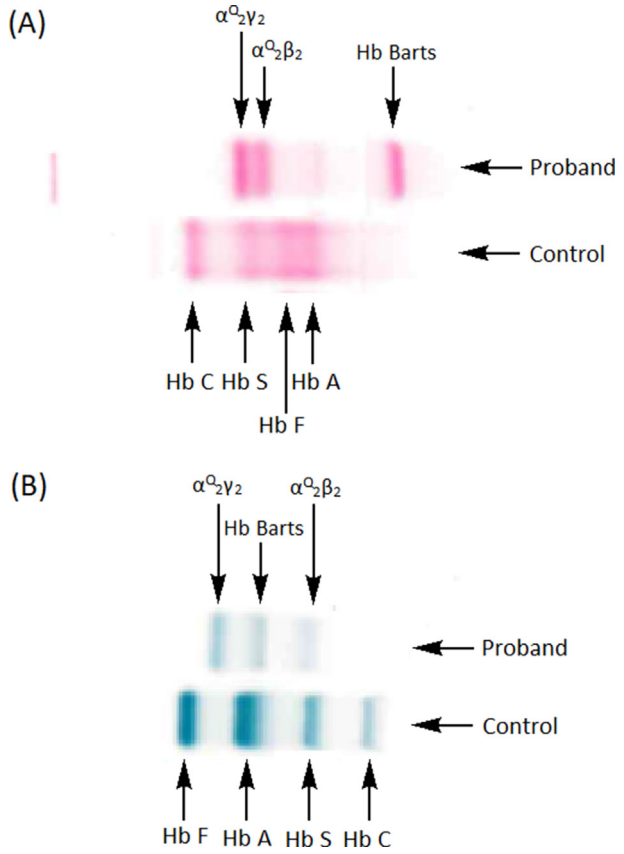


**Fig. 2** (A) Alkaline cellulose acetate gel electrophoresis result of the proband. (B) Acid agarose gel electrophoresis result of the proband.

HBA1 gene on chromosome 16, and it is associated with a leftward single α-globin gene deletion ($-\alpha^{4.2}$).[1,2] This haemoglobin variant is most commonly found in Thai, Chinese and Japanese individuals.[3]

Hb Q-H disease is caused by the co-inheritance of Hb Q-Thailand and $\alpha^{0}$-thalassemia (mainly $--^{SEA}$ deletion). It is a rare disease which is mostly identified in patients of Chinese origins. Hb Q-H disease is associated with the absence of Hb A, presence of Hb Bart's, with Hb Q-Thailand being the predominant fraction of haemoglobin in adults.[4,5] Clinical features of the disease include marked microcytosis, chronic haemolytic anaemia associated with jaundice and hepatosplenomegaly.[6] Although Hb A is absent in patients with Hb Q-H disease, clinical features and blood indices of these patients are similar to that of deletional Hb H disease.[5] This is probably because Hb Q-Thailand has normal oxygen affinity, Bohr effect and cooperativity.[7] This is also supported by the clinical features of the newborn. He did not show hydrops or growth retardation in antenatal follow-up and did not require transfusion up to last follow-up.

To our best knowledge, haemoglobin analyses of newborns with Hb Q-H disease have rarely been reported. The results of cation exchange HPLC and capillary electrophoresis of these patients have not been reported in the literature previously.

Our case demonstrates the haemoglobin analysis results in a newborn with Hb Q-H disease. There was absence of HbF and HbA, and presence of Hb Bart's with two major haemoglobin variants, namely $\alpha^{Q}_2\gamma_2$ and $\alpha^{Q}_2\beta_2$. The percentage of $\alpha^{Q}_2\gamma_2$ variant was slightly higher than that of the $\alpha^{Q}_2\beta_2$ variant. The $\alpha^{Q}_2\gamma_2$ variant had a retention time of about 3.6 min on HPLC by the Variant-II Hemoglobin Testing System. It migrated to Z(S) on capillary electrophoresis by the Capillarys 2 Flex Piercing system. The $\alpha^{Q}_2\gamma_2$ variant migrated to Hb S/D/G position on alkaline cellulose acetate gel electrophoresis and a position between Hb A and Hb F on acid agarose gel electrophoresis. This knowledge is useful for haematologists and laboratory scientists for rapid diagnosis of Hb Q-H disease in newborns, especially if molecular tests are not readily available in the laboratory.

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## A rare case of metastatic endometrial stromal sarcoma mimicking primary breast carcinoma: a diagnostic pitfall

To the Editor,

Non-mammary metastases to the breast are rare and account for approximately 2% of all malignant breast neoplasms,[1] with this number dropping below 1% if haematological malignancies are excluded.[2] Metastatic tumours to the breast

typically present as a rapidly growing, painless firm palpable mass[3] and are associated with a poor prognosis compared to primary breast carcinomas.[2,4] In a series of 169 patients with metastatic tumours to the breast, there was a median survival of 10 months from the time of diagnosis.[2] Hence, differentiation from primary breast cancer is important in order to individualise treatment and avoid unnecessary procedures such as radical breast surgery.[1,4] Herein, we present a rare case of endometrial stromal sarcoma (ESS) metastatic to the breast which mimicked a primary metaplastic carcinoma.

A 47-year-old woman presented with a palpable solid, irregular left breast mass. Previous medical history included a high-grade ESS with vaginal metastasis. Ultrasound showed a 24 mm solid irregular breast mass in the left breast, 9 o'clock position (Fig. 1), corresponding to a Tabar 4/5. Due to the concern for malignancy, a core biopsy was performed under ultrasound guidance.

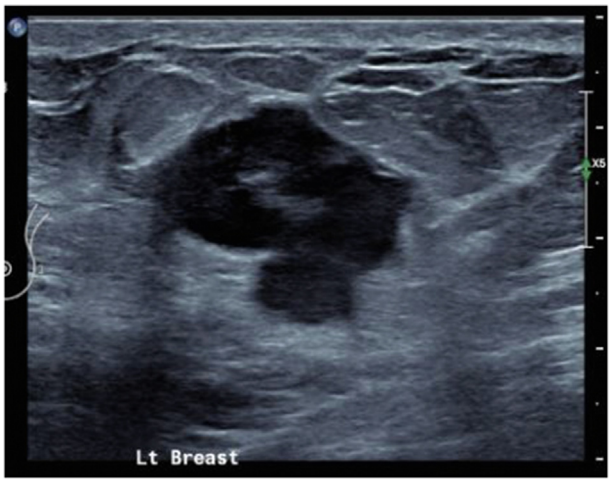


**Fig. 1** 24 mm lesion in the left breast as seen on ultrasound.

The biopsy revealed a cellular population of plump spindled cells occurring in short fascicles, set in a mildly fibrous stroma (Fig. 2A). The cells demonstrated moderate to marked atypia in the form of enlarged, pleomorphic and hyperchromatic nuclei and easily identifiable mitoses. There was no necrosis. There was also no associated malignant epithelial/glandular component or ductal carcinoma *in situ* (DCIS).

An extensive immunopanel was performed and showed positive staining with CKAE1/AE3 (diffuse), CKCAM 5.2 (focal) and p63 (focal) (Fig. 2B). CD10 and CyclinD1 were also added, due to the prior history of ESS, showing diffuse staining. There was no staining for ER, PR, S100, CD34, desmin and ERG. The favoured diagnosis following this immunopanel was that of a primary breast metaplastic spindle cell carcinoma, due to the extensive expression of cytokeratins.

Given the history of malignancy, the previous hysterectomy and vaginal biopsy were reviewed, confirming the prior diagnosis of ESS, metastatic to the vagina, expressing CD10 and CyclinD1 (Fig. 2C). The morphological appearances were similar to the breast tumour, prompting CKAE1/AE3 to be carried out retrospectively on the vaginal metastasis, which also showed diffuse reactivity (Fig. 2D).

Fluorescence *in situ* hybridisation (FISH) studies had been previously performed on the uterine tumour, revealing a disruption of *BCOR* at Xp11.4 with a loss of one copy of the allele in 25% of nuclei. To assist with the diagnosis of the breast lesion, FISH analysis was performed on the breast core biopsy, showing a similar signal pattern with *BCOR* disruption and loss of one allele in 74.5% of nuclei.

The findings overall were consistent with metastatic high-grade ESS to the breast from the uterus, associated with a *BCOR* gene rearrangement.

The difficulty of the pathologist in recognising metastatic lesions to the breast is often due to the lack of a prior cancer history provided by the clinician.[1] In patients with a history of cancer, it is useful for the pathologist to compare the primary

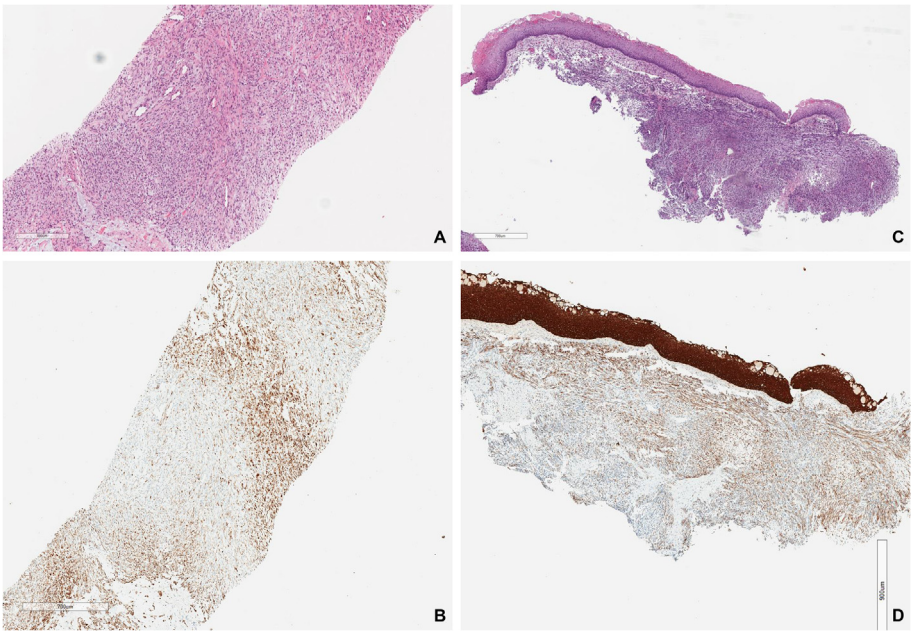


**Fig. 2** (A) H&E stained sections of the breast biopsy with the presence of a spindle cell neoplasm. (B) Positive diffuse staining with CKAE1/3 in the breast core lesional cells. (C) H&E stained sections of the vaginal biopsy with the presence of a spindle cell neoplasm. (D) Positive diffuse staining with CKAE1/3 in vaginal biopsy lesional cells.

histology with that of the breast lesion.[2] In our case, the valuable history of a previous metastatic ESS was communicated by the referring clinician, prompting pathological review of the histology, immunoprofile and FISH analysis of the primary uterine tumour.

The case also illustrates that diffuse cytokeratin staining in malignant spindle cell lesions of the breast should be interpreted with caution. ESS can be confused with several neoplasms due to their diverse morphological appearance and expression of a variety of immunohistochemical stains including cytokeratins.[5] Results from one study showed 47% of ESS staining positive with CKAE1/AE3.[5] The diffuse positive staining in our case illustrates a significant diagnostic pitfall that not all malignant breast lesions with cytokeratin positivity are primary carcinomas, with misdiagnosis likely leading to inappropriate clinical management such as wide excision/mastectomy and axillary nodal clearance.

ESS metastasising to the breast is rare. To our knowledge, there is only one other report of a breast metastasis from a low-grade ESS which occurred after a prolonged period of 17 years.[6] ESS account for less than 1% of uterine cancers,[7] with the most commonly reported sites of distant metastases being pelvic and abdominal cavities, lungs and bones.[7] The World Health Organization (WHO) classification subdivides ESS into low- and high-grade types.[8] High-grade ESS are often associated with *YWHAE-NUTM2A/B* fusions, *BCOR* internal tandem repeats and *BCOR* fusions, the latter present in this case.[9]

In conclusion, we present a rare case of high-grade ESS metastatic to the breast, mimicking a primary metaplastic breast carcinoma due to extensive expression of cytokeratins. It reinforces the utility of molecular techniques and the importance of pathologists working in a multi-speciality team to guide the appropriate work-up and diagnosis of unusual and challenging cases.

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## *ASPSCR1-TFE3* fusion in a case of Xp11 translocation PEComa of the liver: are *ASPSCR1-TFE3* fusion-bearing tumours Xp11 translocation PEComa or alveolar soft part sarcoma?

To the Editor,
Perivascular epithelioid cell tumour (PEComa) expresses melanocytic and smooth muscle markers, and often harbours tuberous sclerosis complex (*TSC)* abnormalities. Different from conventional PEComa, Xp11 translocation PEComa is considered a more aggressive subtype of PEComa with the feature of *TFE3* rearrangement but lack of *TSC* alterations.[1,2] Some cases have rich melanin production. Recently, it was proposed to rename them as 'melanotic Xp11 neoplasm' instead of 'Xp11 translocation PEComa', in order to genetically distinguish them from conventional PEComas harbouring *TSC* rearrangement.[3,4] However, the term 'melanotic Xp11 neoplasm' still remains controversial. In 2020, Wang *et al.*[5] reported the largest series of 27 cases of melanotic Xp11 neoplasm, strengthened the malignant behaviour of the tumour, and suggested that melanotic Xp11 neoplasm and alveolar soft part sarcomas (ASPS) might belong to a spectrum of the same entity. To date, the reported *TFE3* fusion genes in Xp11 translocation PEComa have included *SFPQ (PSF)*,[3,6] *NONO*,[6,7] *RBM10*,[8] *RBMX*,[9] etc. In this study, the unique case occurred in the liver with melanocytic immunophenotype (cathepsin K and HMB45 positive), and *TFE3* rearrangement. Thus, it was diagnosed as Xp11 translocation PEComa. Interestingly, following RNA sequencing, it was found this case harboured an *ASPSCR1-TFE3* fusion, which is considered the common fusion in ASPS. Thus, are *ASPSCR1-TFE3* fusion-bearing tumours Xp11 translocation PEComa or ASPS? The answers might be debatable, but these results could provide evidence for the opinion that the two tumours represent different subtypes of the same entity.

The patient was a 33-year-old Chinese female who presented with abdominal pain. A computed tomography (CT) scan and B-mode ultrasound (Fig. 1A) showed a mass approximately 15 cm in size in the right posterior lobe of the liver. It was mainly solid, well-defined, and rich in blood flow signals. The patient had a history of posterior peritoneal mass but the pathological specimens were unavailable. Partial hepatectomy was undertaken. Follow-up study showed no recurrence and metastasis.

Grossly, the mass was relatively well-defined and measured 15 cm at the greatest diameter, with haemorrhage