Table 1 Summary of next generation sequencing analysis in the colonic and ovarian carcinomas

Tumour site	Gene	Variant	Allele frequency
Colon	<i>APC</i> <i>PIK3CA</i> <i>KRAS</i>	c.4012C>T, p.(Gln1338Ter) c.3140A>G, p.(His1047Arg) c.35G>A, p.(Gly12Asp)	17.1% 18.6% 29.5%
Right ovary			
- benign/borderline	<i>KRAS</i>	c.34G>C, p.(Gly12Arg)	7.5%
- expansile invasion	<i>TP53</i>	c.746G>T, p.(Arg249Met)	67.8%
- infiltrative invasion	<i>TP53</i>	c.746G>T, p.(Arg249Met)	5.4%

differentiation including expression of markers such as CK20 and CDX2, as in the present case, while the Müllerian marker PAX8 is often negative. Although SATB2 staining is considered more specific for lower gastrointestinal origin, a minority of primary ovarian tumours also express this marker.⁶ Immunohistochemistry for β -catenin may also be helpful in this diagnostic scenario. In one study nuclear β -catenin expression was demonstrated in 19/23 (83%) metastatic CRCs compared to 4/43 (9%) primary ovarian mucinous carcinomas.⁷ However, aberrant activation of the Wnt signalling pathway, in some cases due to *APC* or *CTNNB1* mutations, has been reported in a minority of primary mucinous carcinomas.^{8,9}

Ultimately, the integration of NGS analysis in the present case led to a revised diagnosis of primary ovarian mucinous carcinoma, further illustrating the value of adjunct molecular analysis in determining tumour origin in problematic cases.^{10,11} However, it should be noted that molecular findings also have to be carefully interpreted since tumours may show mutational heterogeneity and there is the possibility of 'clonal evolution' such that metastases may demonstrate a different mutation profile to the corresponding primary tumour.¹² In the current case the complete absence of sequence variant overlap (including different *KRAS* mutations) favoured independent neoplasms.

In summary, the distinction of primary versus metastatic origin for ovarian mucinous carcinoma continues to present a diagnostic dilemma, particularly in patients with a prior history of gastrointestinal malignancy. Accurate diagnosis is important since patients with two independent low-stage tumours generally would be expected to have a more favourable prognosis than those with metastatic carcinoma, and the pathological interpretation could also affect decisions regarding the requirement for and nature of adjuvant therapy. The case presented here demonstrates the value of adjunct molecular analysis in cases with indeterminate or ambiguous clinicopathological findings.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: <https://doi.org/10.1016/j.pathol.2021.03.011>

An unusual case of invasive lobular carcinoma with abundant extracellular mucin

Sir,

Accurate classification of breast cancer subtype is important as subtypes may show clinically distinct behaviours. Invasive lobular carcinoma (ILC) accounts for 5–15% of invasive breast carcinomas. Compared to invasive breast carcinoma of no special type (IBCNST), ILC is more likely to have a multicentric growth pattern, be larger, present at a more advanced stage and show distinctive patterns of distant

spread involving the ovaries, peritoneum and stomach, among other sites, with a worse long-term prognosis. The main subtypes of ILC are classical and pleomorphic, with several growth patterns described including solid and alveolar. Mixed groups are also seen, mostly commonly with IBC NST.

We present the first reported Australian case of ILC showing the exceedingly rare feature of abundant extracellular mucin.^{1–9}

A 62-year-old post-menopausal woman was referred for management of a self-detected right breast lesion. She first noticed right breast pain and associated increase in right breast size over approximately one month, with an 8–10 cm, non-tender mass at 10 o'clock, 6 cm from the nipple. There were no palpable axillary lymph nodes.

A right breast ultrasound and magnetic resonance imaging noted a 49×39×35 mm hypoechoic lesion at 10–11 o'clock, with enhancing tissue extending inferiorly to 8 and 9 o'clock, 7 cm from the nipple, with no axillary pathology. Core biopsy of the lesion demonstrated infiltrating lobular carcinoma with classical morphology and provisional classification of grade 2 (Nottingham modified Bloom and Richardson grading – nuclear pleomorphism 2/3, tubules 3/3, mitoses 1/3). A very minor component of atypical lobular hyperplasia of classical type was noted. The lobular nature of the malignancy was confirmed with loss of expression of E-cadherin and cytoplasmic rather than membranous staining for p120 catenin. The ILC was oestrogen receptor (ER) positive (100%), progesterone receptor (PR) negative, human epidermal growth factor receptor 2 (HER2) *in situ* hybridisation negative and the Ki-67 count was 5%.

A wide local excision of the right breast lesion with a bilateral breast reduction mammoplasty, using the inferior pedicle approach, and sentinel lymph node biopsy, was performed. The nipple was preserved. An intraoperative frozen section of the right retroareolar tissue was indeterminate with some suspected areas of lobular carcinoma *in situ*. She recovered well post-operatively with no complications.

Macroscopic examination demonstrated a firm, ill-defined mass measuring 70 mm superior/inferior × 55 mm anterior/posterior × 65 mm medial/lateral. Microscopy demonstrated a grade 2 (nuclear pleomorphism 3, tubules 3, mitoses 1) ILC with a mixture of classical and pleomorphic patterns. Signet ring cells were seen and the rare feature of extracellular mucin production was noted in approximately 20% of the tumour. The cells within the mucin pools showed typical lobular morphology with a mix of pleomorphic and classical types, as shown in Fig. 1.

Classical lobular carcinoma *in situ* was scattered throughout the specimen and invasive carcinoma involved the inferior margin, with characteristic loss of E-cadherin expression as seen in Fig. 2. Lymphovascular invasion was also noted. The tumour was ER positive (80%, 1+), PR focally weakly positive (2%, 1+), HER2 immunohistochemistry was equivocal and silver-enhanced *in situ* hybridisation was negative. The Ki-67 count was 10%.

One of the four sentinel lymph nodes had micrometastasis of 0.3 mm and another contained isolated tumour cells. The right retroareolar tissue demonstrated classical lobular carcinoma *in situ*.

Given the above, the patient underwent a re-excision of the right breast inferior margin, re-do right breast reconstruction and right axillary clearance with clear margins achieved and

Fig. 1 H&E high power view of the pleomorphic (black arrow) invasive lobular component with abundant pools of extracellular mucin. Signet ring cells are also seen (red arrow).

no involved lymph nodes on histopathology. At the time of writing she had been commenced on adjuvant chemoradiotherapy and hormone therapy and had not experienced any complications.

While intracellular mucin production is a common characteristic of ILC, especially in signet ring cells, extracellular mucin production is exceedingly rare.

Rosa *et al.* first described a new variant of ILC that displayed extracellular mucin production.¹⁰ Following this, to the best of our knowledge, only 21 cases have been reported in the English literature as summarised by Koufopoulos *et al.*²

Characteristic morphological features of invasive lobular are discohesive single cells infiltrating in a linear fashion, frequently circling pre-existing normal structures such as ducts.² Classical lobular carcinoma is the most common morphology showing only mild nuclear pleomorphism and a low mitotic count. The pleomorphic subtype is composed of cells showing more marked nuclear pleomorphism, >4 times the size of normal duct cells and a higher mitotic rate. ILCs of all subtypes typically have mutations in the genes encoding E-cadherin or less commonly other components of other E-cadherin complex molecules such as β -catenin and p120-catenin.¹

ILC with extracellular mucin production is an exceedingly rare subtype of ILC. Koufopoulos *et al.*² recently conducted a review observing seven articles describing single cases and

Fig. 2 E-cadherin showing loss of expression characteristic of invasive lobular carcinoma.

two case series by Cserni *et al.* and Singh *et al.* describing eight and four cases, respectively.^{1–9} Overall, all patients were female, the median age was 64 years and most patients presented with a palpable mass and/or mammographic abnormality.² All cases contained a mucinous and non-mucinous component with five also including focal areas of classical lobular neoplasia.² The majority were grade 2. These features are consistent with the findings in this case.² There were varying numbers of signet ring cells observed, consistent with intracellular mucin formation. Similarly to our case, E-cadherin was negative and cytoplasmic p120 was positive in nine cases, both of which are recommended as additional immunohistochemistry stains that help classify these unusual tumours,^{1,2} although the diagnosis of lobular carcinoma is primarily based on the morphology.

In all cases with available data, ER was positive, PR was positive in 10 (50%) and negative in four (20%) cases, and HER2 was over-expressed in two (10%), negative in 11 (55%), and was scored 1+ in one (5%) and 2+ in two cases (10%).² None of these cases were HER2 amplified. Ki-67 proliferation index expression ranged from 7 to 40%.²

It is rare for any involved lymph nodes to have mucinous ILC, with only one observed by Cserni *et al.*¹ This is in keeping with the current case, where the positive lymph nodes did not have mucinous morphology.

We present here the first reported case in Australia with these atypical features to further contribute to the limited available evidence on this variation of ILC. While cytology was not undertaken in this case, it is prudent to keep this rare mucinous subtype of ILC as a possible differential diagnosis for mucinous carcinoma. At this stage the clinical significance of this rare variant of ILC is uncertain but may become clear in the fullness of time.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: <https://doi.org/10.1016/j.pathol.2021.04.006>

Giant porta hepatis schwannoma: a rare cause of a cystic hepatic neoplasm

Sir,

Porta in Latin translates to 'city gate' or 'entrance', porta hepatis, therefore the gateway to the liver. The hepatic artery, the portal vein, bile duct, lymphatics and autonomic nerves within the hepatoduodenal ligament potentially give rise to a variety of lesions. Pre-operative tissue diagnosis is difficult due to the high risk of complications including damage to adjacent structures. A 14 cm cystic porta hepatis schwannoma with 'ancient change' is presented. This represents a rare cause of a porta hepatis lesion with only 28 cases identified in the literature to date. To our knowledge it is the largest lesion so far described and first Australian case reported.

A 37-year-old woman of Asian ethnicity presented with intermittent right upper quadrant pain and fullness, and a palpable mass. She was otherwise well with no other relevant medical history. Magnetic resonance imaging showed a 140 mm heterogeneous, multiseptated cystic lesion reported to be consistent with a biliary cystadenoma or cystadenocarcinoma originating from the caudate lobe and pushing into the porta hepatis. No pre-operative tissue diagnosis was attempted. The lesion was removed successfully via an open approach with a left hemihepatectomy and hepatic artery reconstruction.

Grossly the lesion was found to be centred in the porta hepatis and adherent to but not involving the liver. It was 140×130×80 mm, thin-walled (2–5 mm) and multiloculated with thin fibrous septations and degenerate material within. There were no solid or calcified areas. The adjacent hepatic parenchyma appeared normal. A representative radiological image and macroscopic photograph of the cystic structure is shown in Fig. 1.

At microscopy, the cyst wall was predominantly fibrous with a spindle cell proliferation of variable thickness with central cystic degeneration, focal hyaline and myxoid change with mild to moderate nuclear variation favoured as 'ancient change'. No epithelial lining was identified on extensive sampling. There was no necrosis, glandular components or heterologous elements seen. There was moderate inflammation including lymphocytes and plasma cells and occasional