

Mucinous tumours and mural nodules: A biological continuum?

Douglas A, Cope N, Mandalia T
Royal Devon & Exeter Hospital, Exeter

Introduction

Mucinous tumours of the ovary can rarely be accompanied by mural nodules (MN). Sarcoma-like nodules (SLMN) are usually associated with haemorrhage and ulceration and were thought to be reactive/non-neoplastic in nature. In contrast, sarcomatous (SN) and anaplastic carcinomatous nodules (ACN) are high grade malignancy and may herald a poor prognosis even in ovary-confined tumours.

The Case

A 61 year old woman presented with a 12 month history of an abdominal mass. Ca-125 was mildly raised (59), and CT scan showed a 38cm mass likely arising from the left ovary. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy.

Macroscopy

The right ovarian mass was 47cm in maximum diameter and weighed 25kg. On opening, the mass was multiloculated and filled with thin to gelatinous fluid. The inner surface was covered with six small friable haemorrhagic yellow nodules, ranging from 4mm to 12mm in size.

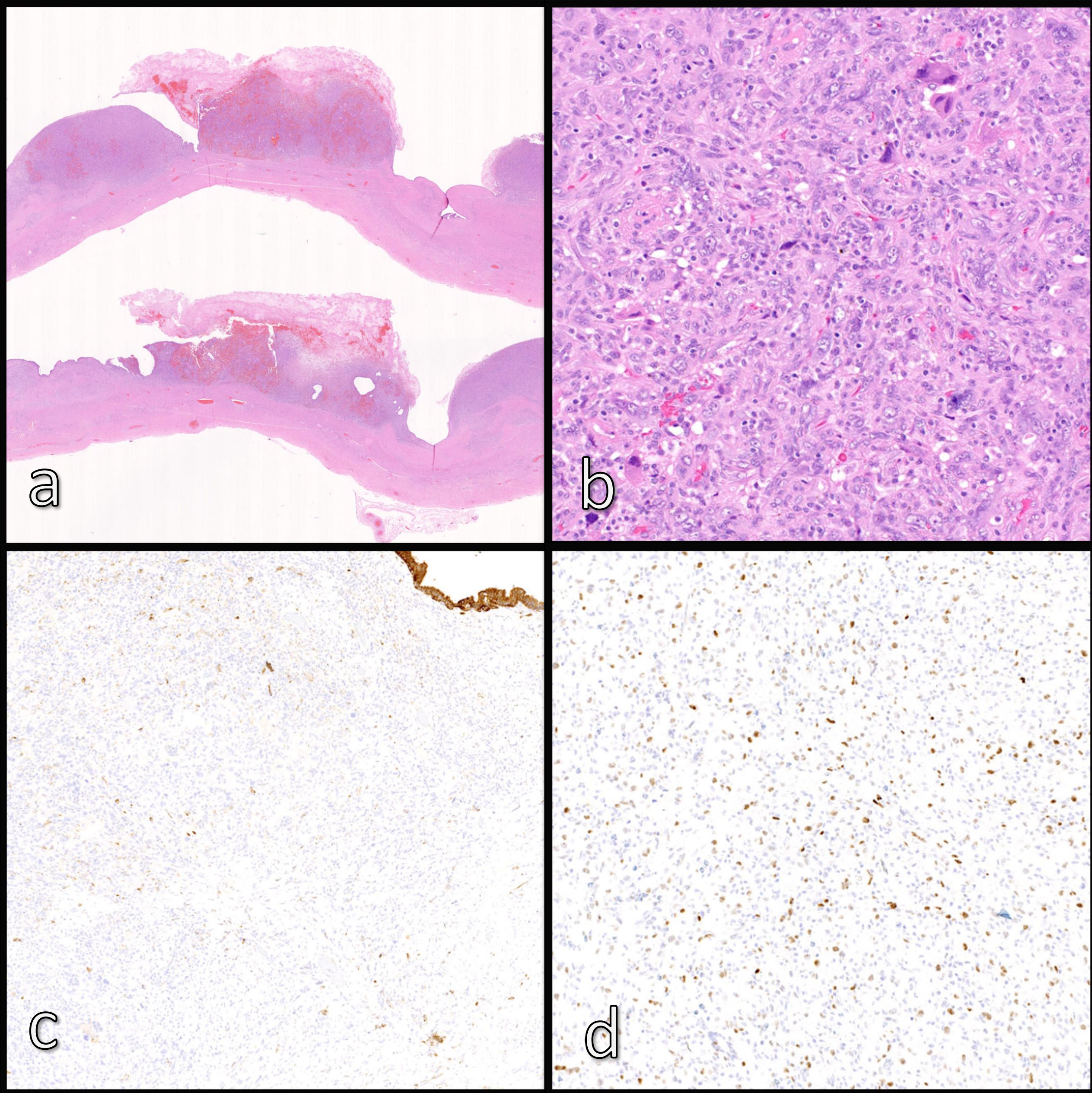


Figure 1: Sarcoma-like mural nodule. a) H&E low power, b) H&E high power, c) AE1/3 negative staining, d) p53 with wild-type staining

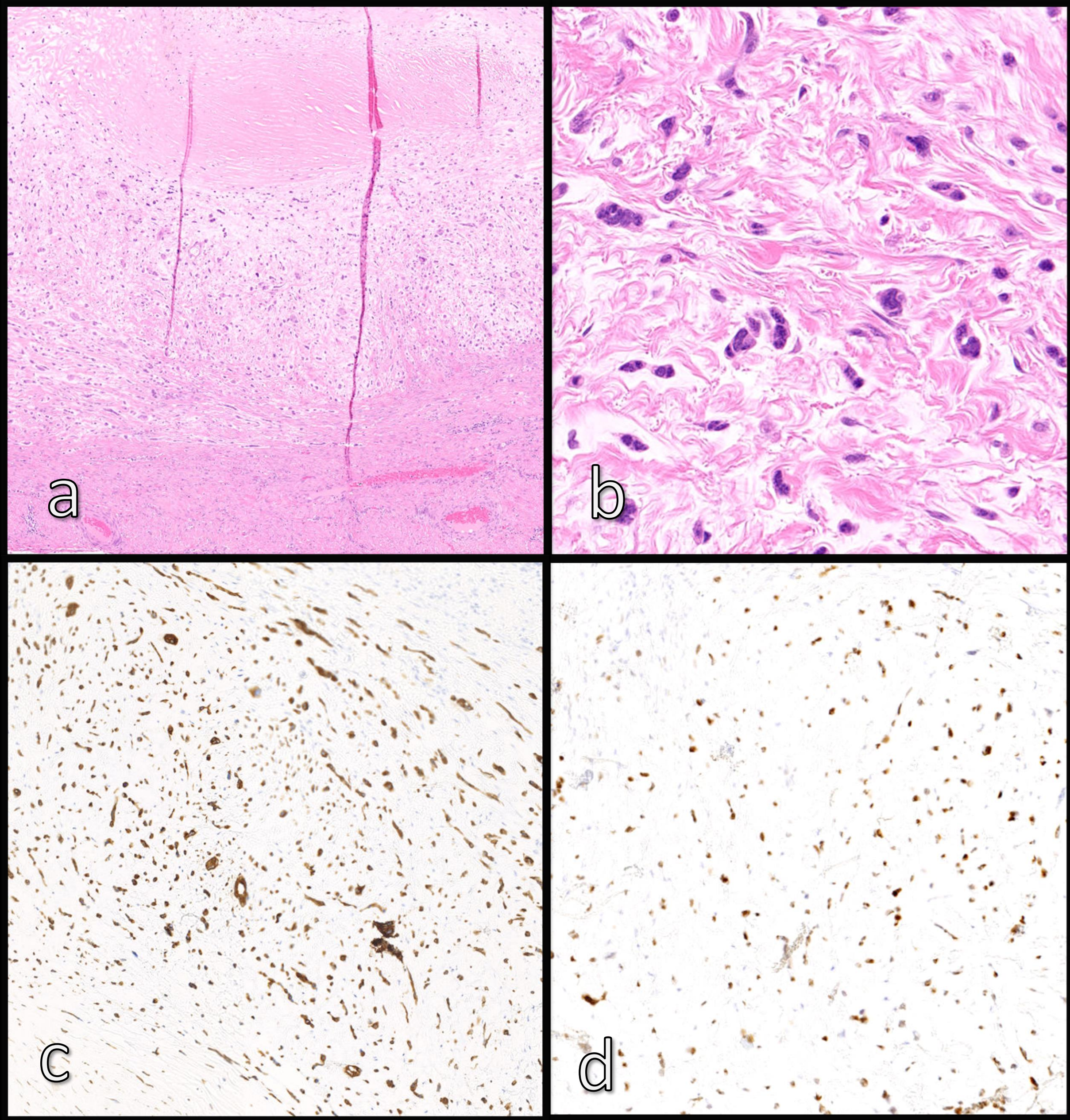


Figure 2: Anaplastic carcinoma nodule. a) H&E low power, b) H&E high power, c) AE1/3 positive staining, d) p53 with mutant positive staining

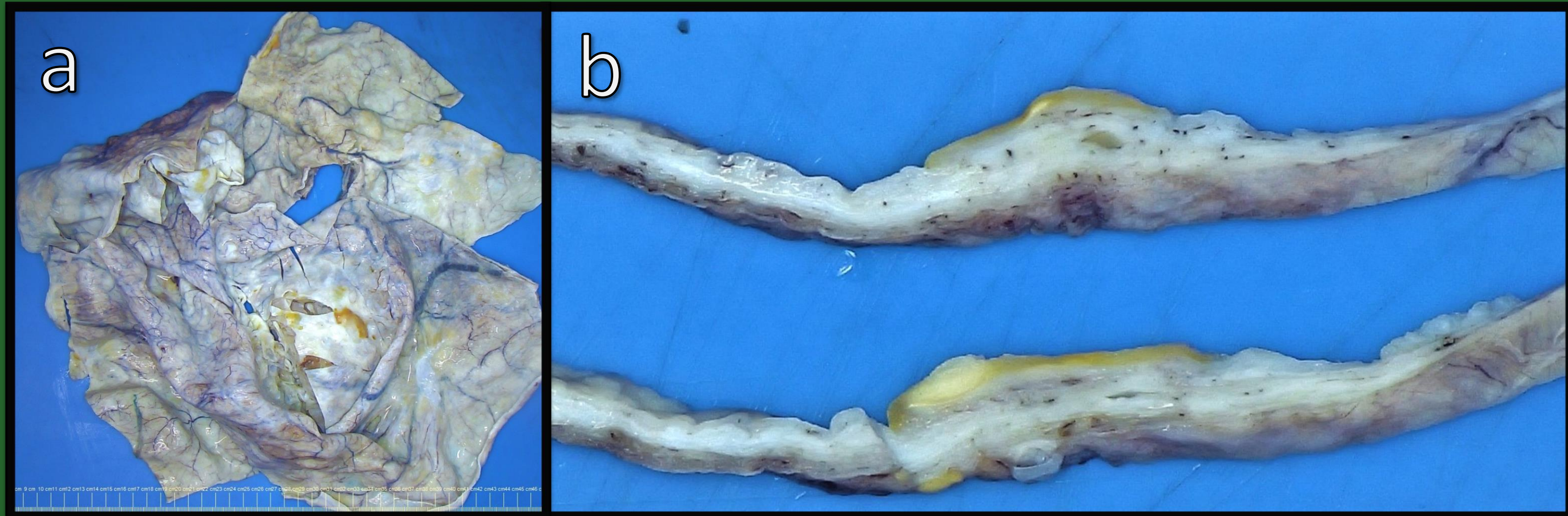


Figure 3: Macroscopy. a) Opened ovarian cyst with mural nodules, b) Section of cyst wall including mural nodules

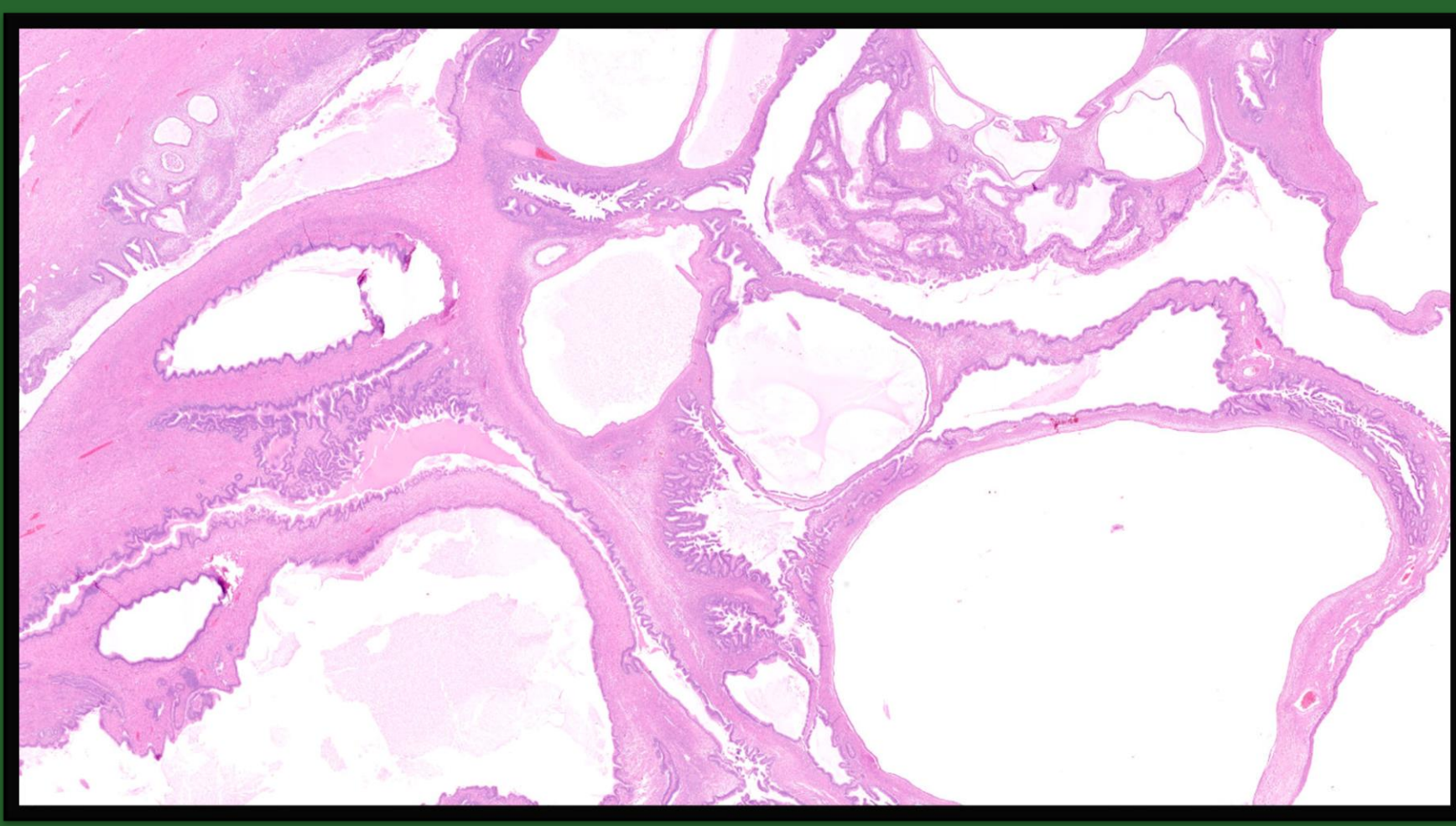
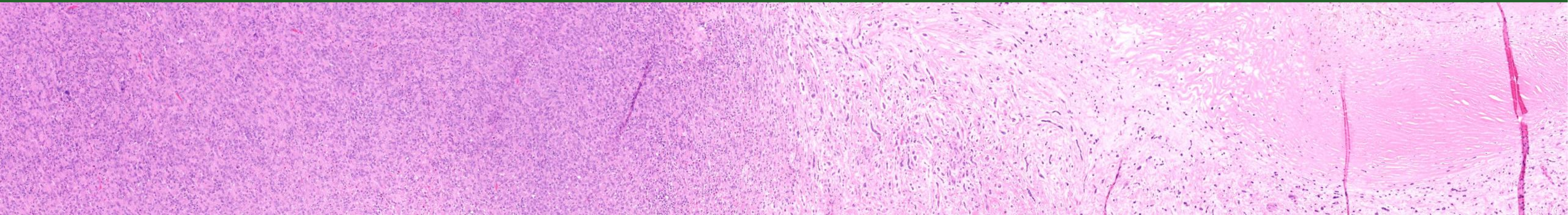


Figure 4: Borderline mucinous tumour, H&E low power

We demonstrate a clonal relationship between a borderline mucinous tumour and mural nodules, with evidence of a biologic continuum between different nodules.

Figure 5: Transition between sarcoma-like morphology (left) and infiltrative anaplastic carcinoma component (right), H&E



Pathology

The histology showed borderline mucinous tumour (BMT) with multiple MNs. Most nodules showed typical SLMN morphology with pleomorphic spindle and epithelioid cells and numerous multinucleated giant cells. Two nodules showed infiltrative ACN morphology and diffuse cytokeratin positivity. Immunohistochemistry demonstrated aberrant p53 expression in the ACNs next to wild-type staining in the adjacent SLMN (shared by the background BMT). Testing with Sanger sequencing revealed a shared KRAS activating variant within the BMT, SLMN and ACN. (Exon 2, 35G>A, p.(Gly12Asp))

The patient was offered systemic therapy to treat the anaplastic component, but declined and opted for remote follow-up with periodic Ca-125 testing.

Discussion

Recent studies have suggested that all morphologic sub-types of mural nodules, including SLMN, are clonally related to the accompanying primary mucinous tumours. To the best of the authors knowledge, this is the first described case of shared clonality between sarcoma-like and anaplastic carcinoma mural nodules.

The combination of sarcoma-like morphology and anaplastic carcinoma within the same mural nodule suggests a morphological spectrum, and the acquisition of a TP53 mutation may be the trigger for progression to a more aggressive tumour.

The literature surrounding mural nodules is sparse and further studies are required for definitive guidance in management of these cases.

References

1) D Chapel et al. Mural nodules in mucinous ovarian tumors represent a morphologic spectrum of clonal neoplasms: a morphologic, immunohistochemical, and molecular analysis of 13 cases. Mod Pathol. 2021 Mar;34(3):613-626.