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CORRESPONDENCE

Neuroendocrine hyperplasia in mucinous borderline ovarian tumour

To the Editor,

A primary ovarian mucinous borderline tumour shows neuroendocrine hyperplasia with an unusual accentuation at the tips and bases of crypts, enlarging the spectrum of presentation of neuroendocrine differentiation in primary ovarian neoplasms.

A woman in her fifth decade underwent pelvic clearance for a right adnexal mass with complex imaging features following presentation with abdominal pain. Initial tumour markers were CEA 55 μg/L (<3.0 μg/L), CA125 51 units/mL (<35 units/mL) and CA19-9 >140,000 units/mL (<33 units/mL). There were no endocrine-related symptoms.

Intra-operative consultation was performed. Macroscopic findings were of a normal fallopian tube and an intact cyst 150×130×90 mm discharging turbid mucinous fluid on opening. A representative block rendered a provisional diagnosis of a mucinous ovarian tumour of at least borderline malignancy.

Extensively blocked, permanent sections confirmed a borderline tumour comprising cysts of variable size with crypt-like or long filiform papilla surfaced by a mucinous epithelium with frequent goblet cells. Nuclear atypia varied from mild to moderate. No intraepithelial carcinoma was seen and there was no invasion.

Neuroendocrine differentiation was confined to three blocks of the 33 sections sampled. Cells with mildly hyperchromatic nuclei, no nucleoli and inconspicuous cytoplasm formed small nodular proliferations or showed orientation about a lumen in continuity with the epithelium at the tips and base of crypts (Fig. 1). No mitotic activity was seen. The largest proliferation was 0.35 mm, seen at the tips of villi. The proliferation was confined to the epithelial layer and did not form an expansile or infiltrative lesion.

With immunohistochemistry the mucinous component was positive for CK7 (diffuse) and PAX8 with focal staining for CK20 (5%). The tumour was negative for SATB2, oestrogen and progesterone receptors (no nuclear staining). Neuroendocrine differentiation in the small nodules and acini was confirmed with positive staining for synaptophysin and chromogranin (Fig. 2) which also highlighted numerous neuroendocrine cells within the mucinous epithelium that had not been identified on scanning the haematoxylin and eosin stained slide. These were seen singly and in short runs of 3−4 cells including in tumour distant from the florid proliferation, indicating a more widespread mild background neuroendocrine hyperplasia. Neuroendocrine cells were also positive for CK7 and negative for CK20, with no proliferative activity seen on Ki-67 staining.

A focally thinned oedematous tumour capsule and positive washings suggested historic capsular breach. The uterus, cervix, left fallopian tube and ovary, appendix and omental biopsy showed benign changes only.

The patient had an uneventful post-operative course. Planned follow-up is for 6 monthly clinical reviews with tumour marker evaluation and the first two such reviews revealed no evidence of recurrence.

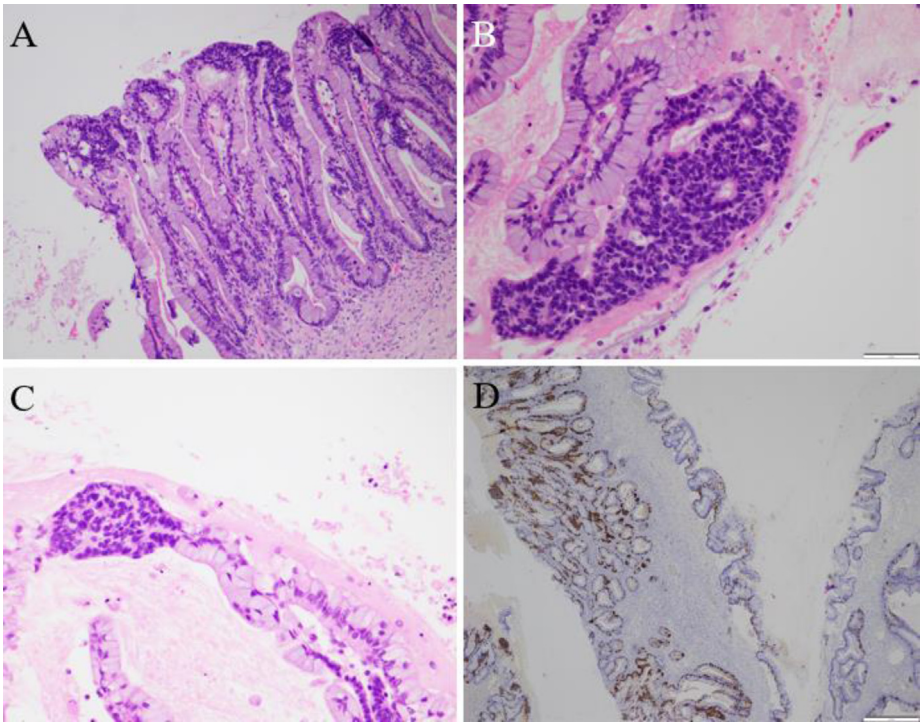

Fig. 1 Mucinous borderline tumour of intestinal type with neuroendocrine differentiation. (A) Neuroendocrine differentiation seen at the tips, (B) as a large cluster and (C) as a single nodule. (D) Neuroendocrine cell population highlighted by chromogranin immunostaining.

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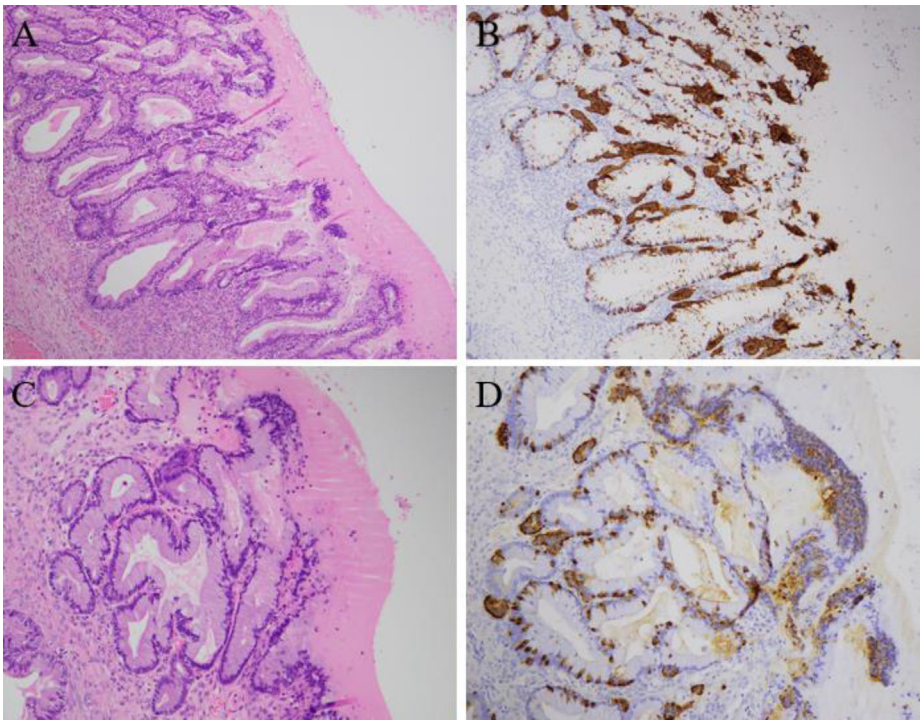

Fig. 2 Mucinous borderline tumour of intestinal type with neuroendocrine differentiation. (A) Pronounced neuroendocrine hyperplasia at the tips. (B) Positive immunostaining for synaptophysin in tumour cells seen at the tips. (C) Pronounced neuroendocrine hyperplasia at the bases of crypts. (D) Positive immunostaining for chromogranin in tumour cells at the base of crypts.

Most primary mucinous tumours of the ovary have an intestinal phenotype and the neuroendocrine differentiation frequently seen is generally considered part of the spectrum of intestinal differentiation.[1–3] Most commonly presentation is as single cells within the mucinous epithelium, sited adjacent to the basement membrane, frequently inconspicuous without immunohistochemistry.[4]

In this case the association is with a primary mucinous borderline tumour and unusually appears to be a genuine endocrine cell hyperplasia. The small tubules at the bases of crypts are a potential mimic for microinvasion although in our case at high power the neuroendocrine phenotype and continuity with the crypt epithelium is more obvious.[4–7]

It is possible such *in situ* proliferations are precursors to the primary ovarian high grade neuroendocrine tumours that have an associated epithelial component.[8] The epithelial component may be serous, endometrioid or transitional as well as mucinous.[9,10]

When not high grade the neuroendocrine component does not usually influence tumour behaviour, although occasionally when functional may cause symptoms (e.g., gastrin producing cells causing Zollinger–Ellison syndrome).[9] High grade neuroendocrine differentiation is associated with a poor outcome.[8,10–12]

The spectrum of ovarian neoplasms with a partial neuroendocrine component also includes the common ovarian carcinoid of germ cell (teratomatous) origin.[9,13] Neuroendocrine differentiation may also be associated with Sertoli–Leydig cell tumours when these have heterologous gastrointestinal epithelium.[9]

In summary we present an example of neuroendocrine cell hyperplasia in a mucinous borderline tumour of the ovary with an unusual accentuation at the tips and bases of crypts.

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