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Case report

SYNCHRONOUS OCCULT METASTASISING DUODENAL CARCINOID AND OVARIAN MUCINOUS CYSTADENOCARCINOMA – MULTIPLE PRIMARY MALIGNANCIES IN THE SAME PATIENT

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ABSTRACT

Gastrointestinal carcinoid tumors are uncommon neuroendocrine tumours that may be associated with synchronous or metachronous primary tumours of other histological type, most frequently colorectal adenocarcinomas. Primary ovarian mucinous adenocarcinomas have been reported to coincide with few other ovarian tumours and minority of these tumours may occur in association with Lynch syndrome. However association of duodenal carcinoid with ovarian mucinous adenocarcinoma is distinctly unusual and, to our knowledge, has not been previously described. We report a case of occult metastasising duodenal atypical carcinoid that was incidentally detected during surgical intervention performed for left ovarian mucinous cystadenocarcinoma in a middle aged female. The carcinoid tumour was Stage IIIB with regional nodal metastasis and the ovarian tumour was Stage IA with low grade histology.

Key words: Duodenal carcinoid, multiple primary malignancies, synchronous tumours.

INTRODUCTION

Synchronous and metachronous "Multiple primary malignancies" (MPM) are relatively rare with an overall occurrence rate between 0.73% to 11.7%.[1-3] About 20-29% of small intestinal carcinoid tumours (CT's) are associated with synchronous or metachronous primary non-carcinoid tumours, with colorectal adenocarcinomas being the commonest.[4, 5] Primary ovarian mucinous carcinoma have been reported in conjunction with other ovarian tumors like teratoma, Brenner tumour, and Sertoli-Leydig cell tumour and some occur in the setting of Lynch syndrome.[6] However the simultaneous occurrence of duodenal CT, which is rare, and ovarian mucinous cystadenocarcinoma, which according to recent studies constitutes only 3% all ovarian cancers, in the same patient is unusual. We present a case of metastasising duodenal CT that was incidentally detected during treatment of ovarian mucinous cystadenocarcinoma in middle aged female.

CASE REPORT

A 40 year old female presented with pain and mass per abdomen of one year duration. She also complained of progressively increasing intermittent episodes of respiratory distress, diarrhoea, palpitations and weight loss. She denied history of prolonged therapy with H2 blockers and family history of malignancies. Abdominal examination revealed firm lobulated central pelvic mass. Abdomino-pelvic computed tomography revealed a large complex cystic ovarian mass [Figure 1]. A complete digestive tract endoscopy, chest X-ray and gastric and colonic biopsies were normal. Laparotomy showed a left ovarian tumour, the frozen sections of which revealed mucinous

adenocarcinoma. In addition an area of intramural thickening was present in D1 duodenal segment with associated serosal puckering, omental adhesions and enlarged adherent sub-pyloric nodes suggestive of metastasis/implants. The paraaortic lymphnodes were also enlarged. A clinical FIGO Stage IIIC was assigned and total abdominal hysterectomy, bilateral salpingoophorectomy and pelvic lymphadenectomy, omentectomy, appendicectomy and sampling of duodenal serosal nodularity, sub-pyloric and paraaortic nodes was performed.

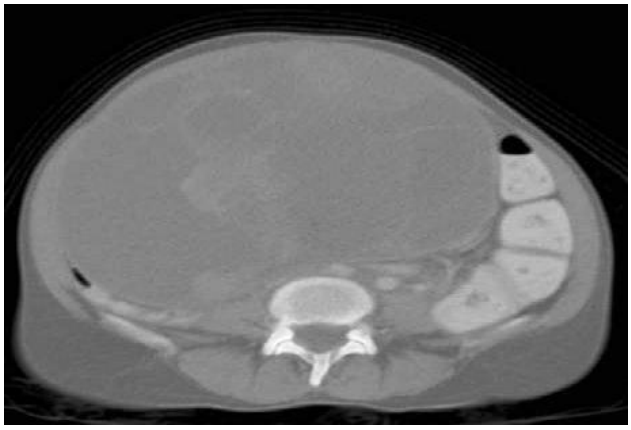

Fig 1: Abdomino-pelvic computed tomography showing a large complex cystic ovarian mass.

Pathological findings: Gross examination revealed a tensely cystic, bosselated left ovarian mass, measuring 23x18x10 cm with intact capsule and multilocular mucoid cut surface with mural ragged solid and nodulocystic areas exhibiting foci of necrosis and haemorrhage [Figure 2]. Microscopy revealed a well differentiated mucinous cystadenocarcinoma with expansile pattern of invasion, grade 1 (Universal grading system) [Figure 3].

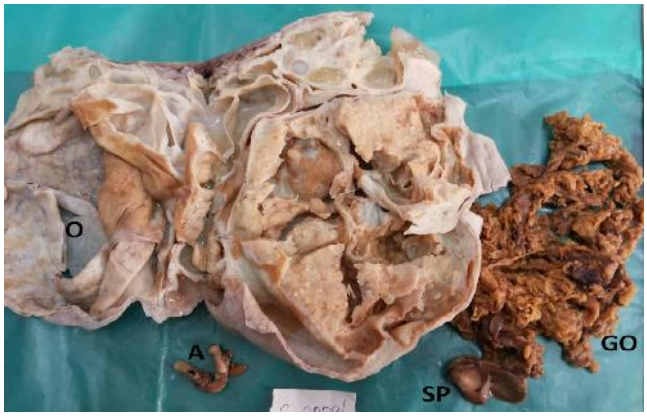

Fig 2: Multiloculated left ovarian mass with mural ragged solid and nodulocystic areas (O), enlarged subpyloric nodes (SP) with greater omental adhesions (GO) and unremarkable appendix (A).

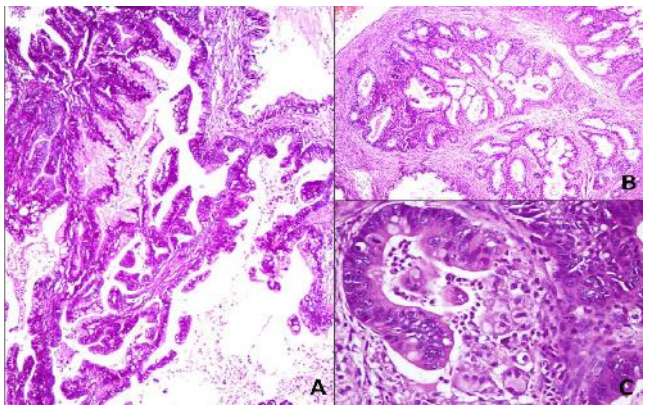

Fig 3: A- Ovarian mucinous adenocarcinoma with architecturally complex papillary cystic areas, B- Expansile pattern of invasion; C- Glandular formations lined by disorderly epithelium exhibiting moderate nuclear atypia (x400 H&E).

The pathological examination of the uterus, right ovary, bilateral fallopian tubes, bilateral pelvic and paraortic lymphnodes, appendix and peritoneal washings revealed no significant abnormality.

The microscopy of the duodenal serosal nodularity revealed a histologically different tumour composed of organoid formations of relatively monotonous cuboidal cells exhibiting stippled chromatin and mitotically active nuclei (4-5/10HPF) consistent with Neuroendocrine tumour, grade II (Atypical carcinoid) [Figure 4]. This was further confirmed by immunohistochemistry which revealed positive staining of pan-cytokeratin and chromogranin in the tumour cells with a 40% Ki67 index [Figure 5]. The 3 subpyloric lymphnodes isolated revealed metastasis of the neuroendocrine tumour (pN_1)

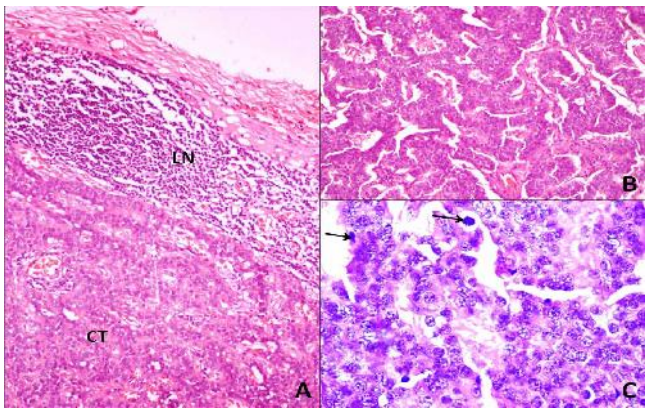

Fig 4: A- Subpyloric lymph node (LN) with metastatic carcinoid tumour (CT); B- Duodenal serosal nodule showing Atypical carcinoid; C- Atypical carcinoid showing monotonous cells exhibiting stippled chromatin and mitotically active nuclei (arrows) (x400 H&E).

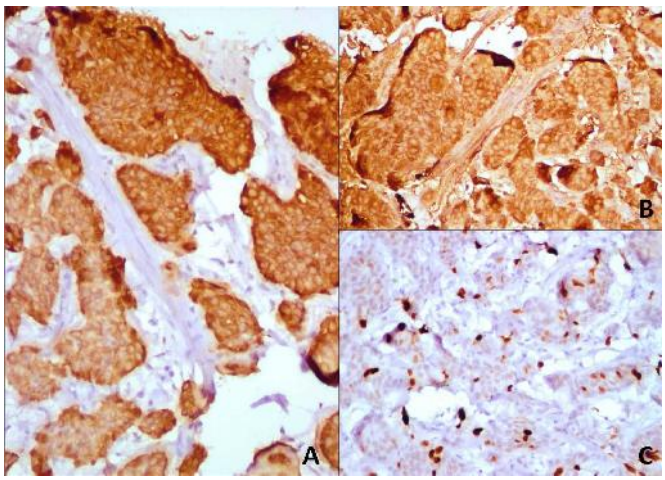

Fig 5: Duodenal tumour showing A- positivity for Pan Cytokeratin; B- positivity for Chromogranin; C- Nuclear positivity for Ki-67 [x400].

Further, extensive sampling of the ovarian tumour failed to reveal any teratomatous/ carcinoid component.

A final diagnosis of Left ovarian mucinous cystadenocarcinoma, $pT1aG_1$ pN_0 pM_0, TNM/FIGO Stage IA with synchronous duodenal Neuroendocrine tumour, grade II, TNM Stage IIIB was made.

DISCUSSION

CT's are relatively uncommon slow growing neuroendocrine tumours, derived from enterochromaffin cells, that are capable of secreting vasoactive substances and 73-85% of these tumours occur in the gastrointestinal tract (GIT).[7] Duodenal carcinoids are rare , accounting for < 2% of all GIT carcinoids, with an annual incidence of 0.07/100,000.[5] About 91% have metastasis at time of detection presumably because they are difficult to diagnose and majority are asymptomatic and behave in an indolent form.[5] Clinical features are varied and depend on the anatomic location, tumour size and metastasis and majority are incidentally detected. [8] They may present as carcinoid syndrome with cutaneous flushing, diarrhoea palpitations, abdominal pain and bronchospasm. G-cell tumours followed by D-cell tumours account for majority of duodenal CT's, the former may occur with multiple endocrine neoplasia type 1 and the latter may occur with neurofibromatosis type 1. Unlike their midgut and hindgut counterparts, proximal duodenal CT are less well characterized and exhibit variable biological course necessitating individualised treatment strategy for each patient.[9]

In the present case the patient had palpitations, diarrhoea and respiratory distress, all of which were attributed to the huge ovarian tumour. The duodenal CT was detected incidentally during the surgical treatment of the associated ovarian malignancy.

CT's may be associated with other synchronous primary malignant tumours. Berner M et al reported that out of 270 GIT CT's analysed 7.8% had synchronous primary malignancy, two thirds of which were colorectal adenocarcinomas and 80% of which were detected during the treatment of the other associated malignancy. [10] Mullen et al reviewed 24 duodenal CT's and found that 38% had synchronous or metachronous non-carcinoid malignancies, 77.8% of which were adenocarcinomas. [9] Associated ovarian malignancies were not detected in these studies. We describe the first case, to our knowledge, of a duodenal CT and a simultaneous ovarian mucinous cystadenocarcinoma.

The mechanisms involved in the occurrence of MPM have not been fully explained. Genetic susceptibility, failure of immunological surveillance and exposure to carcinogens has been implicated.[1, 2, 4] Some authors have hypothesised that CT's produce growth factors which may determine neoplastic transformation or influence tumour growth at other sites.[4]

It has been reported that prognosis of patients with synchronous CT's and non-carcinoid tumours is determined by the stage of the non-carcinoid tumour rather than the CT. [10] This probably is applicable for those cases wherein the CT component is non-metastasising.[4, 5] In the present case the ovarian malignancy was well differentiated and FIGO stage I, with an excellent prognosis and 5 year survival rate of 95%.[6] The CT had regional node metastasis with Stage III B, and logically will determine the survival of this patient. The five year survival rate for CT's with only local spread is 88% in contrast to 25% for those with metastasis.[5]

Combined curative resection is the treatment of choice for synchronous MPM.[1, 2] However, in this case a second malignancy was not suspected pre-operatively. Pancreaticoduodenectomy is the subsequent treatment in the management, which will be done after she recovers from the first surgery.

CONCLUSION

The possibility of MPM should always be considered in the pre-operative evaluation. The association of

CT's with colorectal adenocarcinomas and ovarian mucinous adenocarcinomas with other primary ovarian tumours and Lynch syndrome have been described. As the management may differ in the finding of a second primary, we should not limit ourselves to these known associations. The clinicians should be aware of this rare entity so that pre planned stage specific treatment may be delivered resulting in better outcome.

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