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Case Report

An Unusual Dual Site Late Recurrence following Surgery for Low-Risk Endometroid Carcinoma: A Report of a Case

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Abstract

Low grade endometroid endometrial carcinoma has a low recurrence rate. We report diagnosis and management of an unusual case of late recurrence at dual site.

ABBREVIATIONS

FIGO: International Federation of Gynaecology and Obstetrics; LVSI: Lymphovascular Invasion; GO MDT: Gynaecological Oncology Multidisciplinary Team; DVT: Deep Vein Thrombosis; ALT: Alanine Transaminase; CT: Computed Tomography; PET: Positron Emission Tomography; ER: Estrogen Receptor; ESMO: European Society of Medical Oncology; ER: Estrogen Receptor; PR: Progesterone Receptor

INTRODUCTION

Cancer of the uterus is the fourth most common female cancer in the United Kingdom, with an increasing trend of incidence of approximately 65% since 1970. Most patients with uterine cancer are diagnosed at an early stage, with up to 83% diagnosed at stage 1 or 2 and have a five-year survival of up to 90% [1-3]. Literature review suggests that approximately 10-15 % of patients with early-stage endometrial cancer will recur [4,5]. Most recurrences are loco regional and up to 80% are within three years of the initial diagnosis [6]. We report an unusual case of late dual site recurrence from an initial early stage endometroid carcinoma and discuss the dilemma of diagnosis and management.

CASE PRESENTATION

A 55-year old postmenopausal woman was referred to our one-stop gynaecology clinic with history of persistent vaginal discharge and was found to have an endometrial thickness of 12 mm on transvaginal ultrasound. She underwent an endometrial biopsy which identified a grade 1 endometroid endometrial carcinoma. On immunohistochemistry, there was normal expression of the DNA mismatch repair gene proteins MLH-1, MSH-2, MSH-6 and focal loss of PMS-2. Her body mass index was 44 with a weight of 123 kg. She had a total laparoscopic hysterectomy and bilateral salpingoopherectomy. There was no evidence of endometriosis. Pathology confirmed International Federation of Gynaecology and Obstetrics (FIGO) stage 1A grade 1 endometroid endometrial carcinoma (Figure 1A). There was no

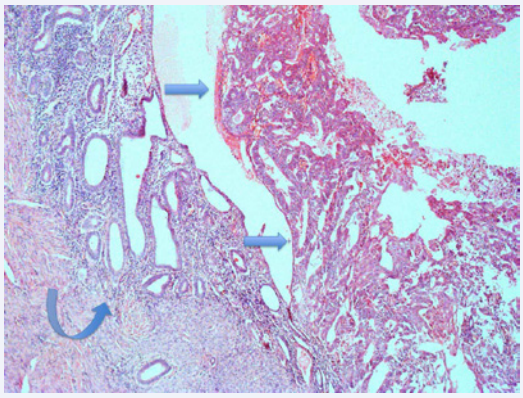

Figure 1a Original tumour in the endometrium was a grade 1 endometrioid carcinoma. This was an exophytic tumour involving the endometrium with no myometrial invasion. The tumour [straight arrows] grows above and within the endometrium [curved arrow].

evidence of myometrial invasion and no lymphovascular invasion (LVSI). Therefore, after discussion at the gynaecological oncology multidisciplinary team meeting (GO MDT), no adjuvant treatment was offered and regular follow up in the surgical clinic was planned.

Five years from her initial diagnosis of endometrial cancer, she presented to her general practitioner with upper abdominal pain. She had a laparoscopic cholecystectomy for gallstones in the previous year, which was complicated by post-operative deep vein thrombosis (DVT). Liver function test were requested, which revealed slight increase in serum alanine transaminase (ALT), 37unit/L. This prompted an ultrasound examination of the liver, which showed calcifications within liver parenchyma and she was referred to a Hepatologist. A triple-phase liver computed tomography (CT) scan suggested a lesion in the right liver dome. There was evidence of concentric wall thickening at the recto sigmoid junction and suspicion of malignancy was raised. Her case was discussed in the lower gastrointestinal tract multidisciplinary meeting. Further Positron Emission Tomography with 2-deoxy-2(fluorine-18) fluoro-D-glucose integrated with computed tomography (F-FDG PET/CT) scan and colonoscopy to investigate the recto sigmoid lesion was organised. Colonoscopy revealed a distal ulcerated polypoid sigmoid lesion 20 cm from the anus, biopsies of which were obtained. The F-FDG PET/CT scan revealed a metabolically active lesion along the right dome of the liver (Figure 2A) and a further metabolically active lesion extrinsic to the rectosigmoid junction (Figure 2B). Histopathology of the biopsy from the sigmoid lesion taken at colonoscopy was re-reviewed by our pathologist with interest in gynaecological malignancy and immunohistochemistry was strongly positive for estrogen receptor (ER) and progesterone receptor (PR) as well as CK7. Staining was negative for CK20 and CDX2. Paradoxically the background colonic crypts were CK20, CDX2 positive and ER, PR, CK7 negative which confirmed recurrent endometroid endometrial carcinoma. Immunohistochemistry Biopsy of the liver lesion under ultrasound guidance was performed which confirmed metastatic adenocarcinoma with strong estrogen receptor (ER) positivity and patchy CK7 expression. This was consistent with recurrence of endometrial carcinoma.

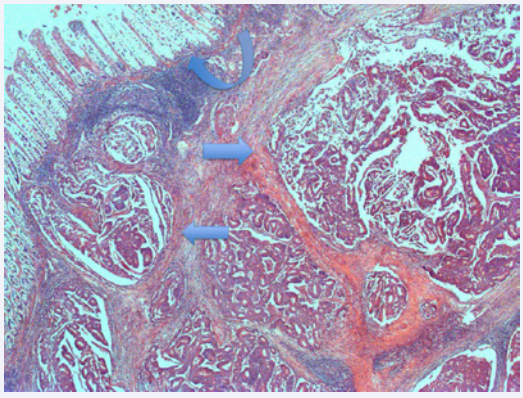

Figure 1b Tumour showing transmural infiltration of the bowel wall [straight arrows]. Normal large bowel mucosa is seen over the luminal surface [curved arrow].

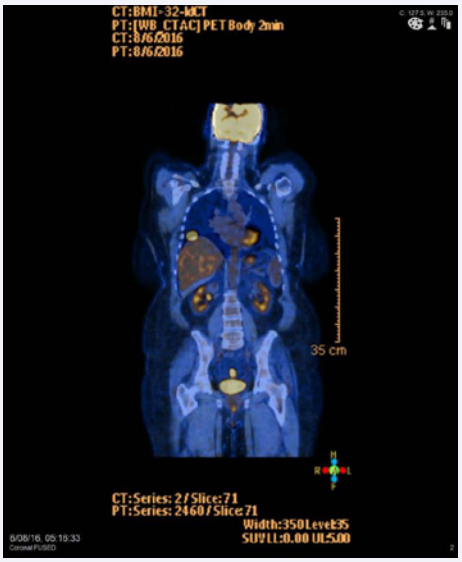

Figure 2a Coronal image of F-FDG PET/CT scan showing metabolically active lesion along the right dome of the liver.

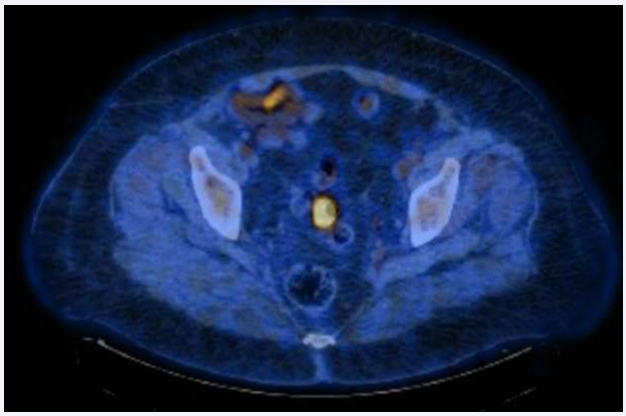

Figure 2b Axial image of F-FDG PET/CT scan showing metabolically active lesion extrinsic to the rectosigmoid junction.

Her case, including imaging and histopathology, was reviewed at the GO MDT and decision to offer surgical resection of the recurrent disease was made. She underwent a laparotomy with recto sigmoid resection with division of large bowel 10 cm above and below the visible tumors, primary colorectal anastomosis with defunctioning ileostomy and non-anatomical liver resection from the right dome of the liver, after complete liver mobilization and pringle manoeuvre (Figure 1B). This was a joint surgical procedure between the gynaecological oncology, colorectal and hepatobiliary surgical team. She had an uncomplicated post-operative recovery.

A post-operative review was completed in the GO MDT. Pathology confirmed presence of grade 2 metastatic endometroid carcinoma in both the recto sigmoid and liver resection specimens. She was reviewed by the clinical oncology team and is to receive six cycles of adjuvant chemotherapy with carboplatin and paclitaxel.

DISCUSSION

Our case report highlights an unusual pattern of recurrence, both in relation to the time interval from the initial treatment and the sites of involved recurrence. After her initial surgery, our patient was deemed to be in the low risk group for recurrence as per the clinical and pathologic prognostic factors defined by European Society of Medical Oncology (ESMO), including the age at diagnosis, FIGO stage, depth of myometrial invasion, tumour differentiation grade, tumour type and LVSI [7-9]. Following evidence from large randomized control trials including PORTEC, ASTEC and EN.5 it is clear that patients with low-risk endometrial cancer have no benefit from adjuvant vault brachytherapy, likely because the risk of recurrence after surgery alone is < 5%. Therefore, current recommendations are that no adjuvant treatment is indicated for patients with low-risk endometrial cancer [10-14]. Our patient was initially diagnosed with a grade 1 stage 1A endometroid carcinoma and therefore had surgery alone as curative treatment without any adjuvant treatment.

A large multicentre study from France reported 9% recurrence rate in 256 patients with low-risk endometrial cancer group. Most recurrences were either the vaginal vault or nodal (either pelvic and/or para-aortic). The mean time interval to regional recurrence was 28 months [15]. In literature, the reported rates of loco-regional, distant and mixed recurrences vary widely from 2.1 to 14% in the background of a low-risk endometrial carcinoma [16,17]. Our patient had unusual sites of recurrence potentially causing minimal symptoms and hence the dilemma in diagnosis. Moreover, the time interval between the initial diagnosis and recurrence was more than five years, which is when patients of low-risk endometrial cancer are discharged from routine follow up in the surgical clinic. There is much controversy in literature regarding optimal postoperative follow up strategies. Some have suggested intensive and prolonged follow up regimens to aid early diagnosis of recurrence [18-20]. It is worth noting that the ESMO-ESGO-ESTRO guidelines do not suggest specific follow up regimen whilst the NCCN guidelines recommend physical examination every 3 to 6 months for 2-3 years and then every 6 months or annually [21,22]. Moreover, there is now evidence that a nurse-led telephone follow up is as effective as hospital follow up with equivalent patient satisfaction for patients following surgery for low-risk endometrial carcinoma [23].

For patients with recurrent disease, surgery is recommended only if optimal cyto reduction (no residual disease) can be achieved. Retrospective data from 14 publications including 672 patients with advanced or recurrent disease who underwent surgical resection had overall survival benefit which was positively associated with an increasing proportion of patients with no residual disease (each 10% increase improved survival by 9.3 months). Exenteration is considered for central pelvic relapse [24]. Our GO MDT suggested surgical resection for recurrence in this patient as after careful evaluation it was thought that complete cyto reduction was achievable.

Thus, we have managed an unusual case of recurrence of a low-risk endometrial carcinoma with a multidisciplinary approach.

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