Primary mucinous carcinoid tumour of the ovary: a case report

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Summary

Primary ovarian carcinoid tumours of the ovary are rare and represent less than 0.1% of ovarian malignancy. The evidence to guide treatment and prognosis of these tumours is limited. We report a case of primary ovarian mucinous carcinoid tumour, of the atypical category, in a 34-year-old nulliparous woman. Only three such cases have previously been reported. At four years from presentation, she has no signs of metastatic disease, despite delayed primary surgery and then initial conservative management. At present surgical excision with close follow-up appears to be the management of choice. This case adds to the body of evidence and demonstrates a possible good prognosis with non-aggressive behaviour in the atypical mucinous carcinoid group.

Key words: Carcinoid; Ovary.

Introduction

Primary ovarian carcinoids are rare germ cell tumours that may be found in association with benign teratomas. They are divided into insular, trabecular, stromal and mucinous types [1]. Ovarian mucinous carcinoids are further subdivided into "well-differentiated", "atypical" and "carcinoma arising in mucinous carcinoid" on the basis of their microscopic features [2]. We report a case of a 34-year-old woman with primary mucinous carcinoid tumour of the ovary of the atypical subgroup who had no evidence of metastatic spread at 4-year follow-up after initial presentation.

Case Report

A 34-year-old nulliparous woman presented with progressive abdominal distension and urinary frequency. She had been seen two years previously at another institution where magnetic resonance imaging (MRI) suggested the mass was fibroids and she was advised to observe the situation. Her periods were normal and she had no other symptoms. Clinical examination revealed a firm pelvic mass up to the level of the umbilicus. A pelvic ultrasound scan detected a left-sided mass that again was thought to be a large fibroid uterus. Magnetic resonance imaging showed a normal main body of the uterus with a 10 cm multi-lobulated mass arising from the superior aspect of the uterine fundus, mainly on the left side. It appeared to have a mixed heterogeneity and an area of central scarring. The presumptive diagnosis was a pendunculated fundal uterine fibroid.

In view of her increasing symptoms, she was given monthly Zoladex® injections (3.6 mg) for three months in order to reduce the size of her fibroid, and an elective myomectomy was planned. At laparotomy, she was found to have a left sided mobile, irregular mass completely involving the left ovary. The right ovary was nodular with papillary excrescences. She had a normal size uterus with no fibroids present. There was no ascites or obvious metastases elsewhere in the pelvis. A left salpingo-oophorectomy was performed plus a biopsy from a right ovarian excrescence. The omentum, which appeared normal, was also excised.

The histopathology assessment demonstrated a left ovarian tumour measuring 190 x 130 x 135 mm and weighing 1610 g. It was firm, nodular and irregularly bosselated. The cut surface was cream and white in colour. No areas of necrosis or haemorrhage were seen. One small cystic structure measuring 11 x 6 x 5 mm and containing whitish keratinous material was identified.

The tumour had an unusual histological appearance (Figure 1). It had a glandular component with numerous small, well formed acini in which there were focal goblet cells, signet-ring mucin-containing cells, and cells with prominent eosinophilic granules consistent with argentaffin granules. There were also smaller clumps of cells and single cell infiltration in places. The epithelial nuclei showed variable mild to moderate pleomorphism and there was moderate mitotic activity [up to 6 mitoses per 10 high power fields (HPF)]. These glandular structures were set in a prominent but benign cellular stroma which in places was composed of smooth muscle fibres and in other areas resembled the stromal reaction to a Krukenberg tumour. Immunostaining showed the epithelial cells to be positive for cytokeratins (CAM 5.2, CK 20 and focally positive for CK 7) and carcino-embryonic antigen (CEA). The tumour cells immunostained for chromogranin and focally for gastrin and glucagon, but there was no staining for somatostatin, inhibin or alpha-fetoprotein. The proliferation marker MIB-1 showed about 30% of the epithelial cells to be in cycle. The cystic structure was seen to be an epidermoid cyst lined partly by keratinising stratified squamous epithelium and with a foreign body giant cell to keratin. The left fallopian tube and omentum showed no abnormality.

The right ovarian biopsy showed a similar appearance and the same immunoprofile as the large left ovarian tumour. There was mild to moderate nuclear atypia and focally there was prominent mitotic activity (up to 13 mitoses per 10 HPF). These features were those of a primary mucinous carcinoid of the ovary, a very rare tumour.

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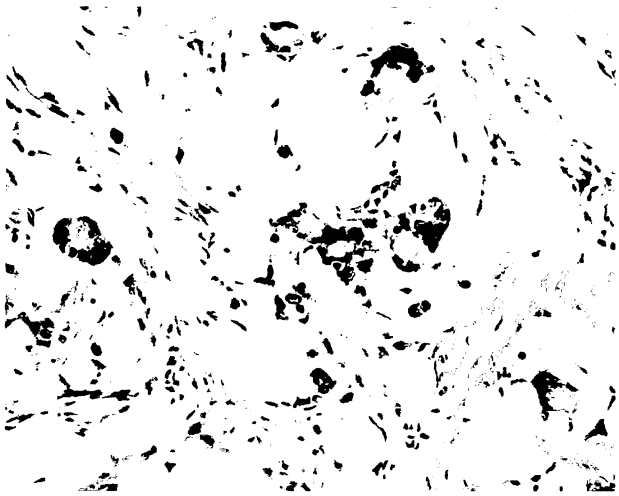

Figure 1. — Left ovary showing infiltration of stroma by acini of mucinous carcinoid tumour containing goblet cells.

A computerised tomography scan of the abdomen and pelvis was performed which showed a right ovarian cyst, consistent with the positive biopsy from the right ovary, but no lymphadenopathy or lesions in the abdomen. I^{123} metaidodobenzylguanidine (MIBG) and $Indium^{111}$ octreotide scans were performed to look for possible lesions outside the ovary. These showed no uptake of either scintographic agent. The abnormal right ovary did not demonstrate any tracer accumulation. Her urinary 5-HIAA was normal.

The patient had a repeat laparotomy to remove the residual carcinoid tumour from the right ovary, exclude alternative primaries and to stage the ovarian tumour. At laparotomy, examination confirmed that the appendix had been removed previously. The small bowel was examined carefully, and no abnormalities were found. The right ovarian lesion was excised. As the patient was nulliparous and wished to conserve her fertility, some ovarian tissue was preserved. A biopsy was taken from the residual ovarian tissue to ensure that no carcinoid tissue remained. Staging excision of the para-aortic lymph nodes was also performed.

The excised right ovarian lesion was 40 x 35 x 35 mm and contained a similar tumour to the previous specimen. MIB-1 staining showed 30-40% of the cells were in cycle. The omentum and paraaortic nodes were free of tumour. The biopsy of the preserved ovarian tissue was normal.

The histopathology slides of her previously removed appendix were reviewed and confirmed no carcinoid abnormalities.

No evidence of metastases or alternative primary lesions were found and a final diagnosis of stage Ic primary mucinous carcinoid of the ovary was made. Her postoperative course was uncomplicated. She was followed-up closely, with clinical examination, MRI abdomen and pelvis, and pelvic ultrasound scan being normal at 12 months following initial surgery.

A subsequent pelvic ultrasound scan showed a suspicious 5 cm lesion in the residual right ovary. The lesion was observed over four months. It increased in diameter to 6 cm and continued to look suspicious. The patient underwent a third laparotomy to remove the remaining right ovary. There were extensive adhesions, and it was necessary to excise an area of the small bowel. The ovary was enlarged to 5 cm and it was removed. There was no evidence of metastasis. Histopathology confirmed the same tumour as seen previously.

Subsequent follow-up was normal with normal MRI scan and octreotide scans. This follow-up was four years from her original presentation with a mass, two years from her first operation when the carcinoid tumour was diagnosed, and six months from her final operation.

Discussion

Primary carcinoid tumours of the ovary are rare and represent less than 0.1% of ovarian malignancies [3]. The most likely pathogenesis of these tumours is development from the totipotent cells of benign teratomas and they may be found in association with these tumours [1]. Ninety per cent of primary carcinoid tumours are found within the gastrointestinal tract [4-6]. The ovaries are rarely involved. The exclusion of a primary tumour in all extra-ovarian sites is necessary to make a diagnosis of primary carcinoid tumour of the ovary.

Ovarian carcinoid tumours are similar to those that occur in the gastrointestinal tract, but do not often present with typical carcinoid characterised by episodic flushing, diarrhoea and evidence of right-sided cardiac failure [4]. It is unusual for ovarian carcinoids to cause raised 5HIAA [5, 7].

Primary carcinoid tumours of the ovary are divided into insular, trabecular, stromal and mucinous types [1]. Among the different types, insular carcinoid appears to be the most common, followed by the trabecular and strumal types. Mucinous carcinoid is the least common type of primary carcinoid tumour occurring in the ovary with only 19 cases having been reported in the literature worldwide [2, 8-11].

Baker *et al.* [2] described 17 cases of ovarian mucinous carcinoids. The cases were classified into three groups based on their histopathological characteristics. Six tumours designated "well-differentiated" contained small glands floating in pools of mucin. Three tumours designated "atypical" were composed of small nests of cells, some of signet ring cell type, in a hypocellular fibrous stroma. Eight tumours designated "carcinoma arising in mucinous carcinoid" were characterised by closely packed islands of tumour cells, mainly of the signet ring cell type. The features of the tumour we describe here fit best with the "atypical" category since it had no solid epithelial cell masses, areas of necrosis or abnormal mitotic figures.

In atypical or highly proliferative carcinoids, as evidenced by the mitotic and MIB-1 indexes, it is not unusual for the MIBG and octreotide scans to be negative

as these tumours are relatively more de-diffentiated and hence have less peptide receptor expression.

To diagnose a primary carcinoid tumour of the ovary, a primary lesion in another site such as the gastrointestinal tract, especially from the small bowel or appendix, must be excluded. Features suggestive of metastatic disease are bilateral ovarian involvement, multiple ovarian nodules and vascular invasion within the ovary. In our case, it was not possible that the ovarian lesions had spread from a primary tumour of the appendix, since the patient had an appendicectomy when 12 years old. The pathology of the appendix was reviewed and there was no evidence of carcinoid tumour. There was no evidence of a primary tumour in the small bowel on the MIBG and octreotide scans, nor at laparotomy. Typically, small bowel carcinoid tumours have liver metastases and display the carcinoid syndrome. This was not the case in our patient. Furthermore, the epidermoid cyst, which was associated with the left ovarian tumour, was in keeping with a cystic teratoma and primary ovarian carcinoid is thought most likely to arise from a teratoma.

Treatment of mucinous carcinoid tumours for young women who wish to preserve their fertility and have an early stage tumour is with unilateral salpingo-oophorectomy and close follow-up. Hysterectomy with bilateral salpingo-oophorectomy should be performed in older patients. In both age groups, it is important to exclude metastases to the ovary from a primary elsewhere, since these have a poor prognosis [1]. Ovarian carcinoid tumours are thought to have only limited sensitivity to radiation therapy and chemotherapy. Thus there is no evidence-based role for adjuvant therapy. The concern in this patient was the high proliferative index of the tumour which may be associated with risk of recurrence. Therefore, this patient needed rigorous follow-up.

The experience concerning the behaviour of primary mucinous carcinoid tumours of the ovary is very limited [2]. Although they have been supposed to exhibit aggressive behaviour and predilection to lymphatic spread, one patient with Stage I disease had no evidence of metastases after three years of follow-up [11], while 15 of 17 patients reported by Baker *et al.* [2] survived an average 4.7 years of follow-up. Our patient had an atypical mucinous carcinoid of which there are only three previously reported cases. At four years from presentation, she had no signs of metastatic spread, despite delayed primary surgery and then initial conservative management.

In conclusion, we report a rare case of primary mucinous carcinoid tumour of the ovary of the atypical category. The evidence to guide treatment and prognosis is limited. At present surgical excision with close follow-up appears to be the management of choice. This case adds to the body of evidence and demonstrates possible good prognoses with non-aggressive behaviour in the atypical mucinous carcinoid group.

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