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Case Report

Primary ovarian carcinoid: A report of two cases and a decade registry

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KEYWORDS

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Registry;
Carcinoid heart

Abstract *Objectives:* This study aims at reporting 2 cases of primary ovarian carcinoid tumor, and providing an adequate registry of such cases and how they were managed.
Methods: 2 female patients with primary ovarian carcinoid were diagnosed and treated in our center. Discussion of their presentation, pathology and treatment is entitled. Also a thorough search of all published registries and case reports of ovarian carcinoid was done with analysis of reported data.
Results: 164 cases of primary ovarian carcinoid tumor were detected since 2005 with the predominance of the insular variant. Carcinoid syndrome occurs in nearly 14% of these cases. Most of the cases were treated with hysterectomy. Unfortunately, the prognosis was not documented in most series.
Conclusion: Primary ovarian carcinoid is a relatively rare disease with an indolent course and excellent outcome. Carcinoid syndrome, especially carcinoid heart disease may worsen the prognosis. Total abdominal hysterectomy with bilateral salpingo-oophorectomy has been commonly used as the treatment of choice of primary ovarian carcinoid tumors.

Background

Ovarian carcinoid tumors may be primary or metastatic (mostly from GIT origin). Differentiation is usually difficult, but bilaterality, peritoneal deposits, absence of teratomatous element, and lymphovascular invasion are signs of metastatic carcinoid [1]; more recent studies suggested that immunohistochemistry with CDX2 may be of value in differentiating carcinoids of GIT origin [2]. Primary carcinoid tumor of the ovary represents less than 1% of all carcinoid tumors and less than 0.1% of all ovarian neoplasms. Two thirds of these tumors manifest as a localized lesion, while about one third presents with distant spread [3]. Most tumors are seen in perimenopausal women, commonly presenting with ovarian heterogeneous mass, or as an incidental finding in abdominal

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radiology done for other purpose. Histologically, according to WHO, there are four major variants of primary ovarian carcinoid: insular, trabecular, strumal, mucinous and mixed (insular and trabecular) [4]. 30% of patients with carcinoids have symptoms of the carcinoid syndrome, mainly affecting patients with insular type, while it rarely occurs with trabecular type. Extremely rare cases presented with an intractable constipation mainly due to peptide YY which inhibits intestinal motility [5,6]. Primary ovarian carcinoid may occur on top of teratoma or in an otherwise normal ovary. Surgery remains the cornerstone for treatment of localized cases with excellent prognosis.

Methods

This study reports 2 different cases of primary ovarian carcinoid who attended the Oncology Center Mansoura University (OCMU) in 2014, and aims to review and register all published cases since 2005 till March 2016.

Case report one

Malignant ovarian carcinoid on top of teratoma.

Female patient 59 years old, postmenopausal with 5 offspring, hypertensive and hepatic (HCV + ve) with no surgical history, presented with abdominal pain, enlargement and bloating to her gynecologist, who recommended computerized tomography. CT revealed right ovarian mass $9 \times 11 \times 7.3$ cm mostly cystic with irregular outline with omental metastasis and moderate ascites.

The patient was referred to our center (OCMU) where revision of CT suggested ovarian cancer, and after multidisciplinary panel discussion the decision was exploration.

Exploration was done on March 2014 under general anesthesia with a midline incision where about one liter of ascites was aspirated and sent for cytology, followed by right salpingo-oophrectomy and frozen section. The frozen pathology revealed malignant ovarian neoplasm, so complete staging laparotomy in the form of total abdominal hysterectomy, contralateral salpingo-oophrectomy, omentectomy, bilateral iliac lymphadenectomy and random peritoneal biopsies was done.

Postoperative pathology showed a malignant carcinoid tumor of the right ovary mostly on top of teratoma (insular variant) with no lymphovascular emboli with Ki67 $<2\%$ (Fig. 1). Left ovary, omentum and peritoneal biopsies were free with reactive hyperplasia of 14 dissected lymph nodes.

Patient was sent home at 4th day postoperative with drain output of 300c.c serous discharge.

The patient was readmitted one week later to the ICU with wound infection, low grade fever and disturbed conscious level. Investigations showed mildly elevated liver enzymes (SGOT = 65), mild deterioration of renal function (Cr = 2.3), leucocytosis (20,000) mainly neutrophilia, thrombocytosis (620), hyperbilirubinemia (1.5), respiratory alkalosis (PH = 7.42, CO_2 = 35 and HCO_3 = 21), hypernatremia (160), hypocalcemia (Ca = 6.5) and normal potassium (K = 5). The condition was recognized as severe sepsis leading to hepatic pre-coma and unusual electrolyte disturbances. The patient was managed by wound drainage, liver supports, IV fluids and electrolyte replacement.

The patient was re-discharged 5 days latter with good general status.

No chemotherapy was given and patient was scheduled for follow up every 6 months in 1st two years. No evidence of recurrence was detected in radiology after two years of follow up.

Case report two

Pure ovarian carcinoid tumor.

Female patient was aged 48 years with liver cirrhosis and surgical history of splenectomy followed by hernioplasty for incisional hernia one year later. CT (pre-excision) was done revealing large, well defined, bilobed solid and cystic mass in the right adenexal region with multiple areas of calcifications contacting and compressing right psoas muscle 6×11 cm suggestive of dermoid cyst. Left simple ovarian cyst 3 cm was also detected.

Unilateral right salpingo-oophrectomy was done outside our center. Postoperative pathology revealed a carcinoid tumor (trabecular variant) with positive chromogranin and synaptophysin, and Ki67 $<2\%$ (Fig. 2). CT after the operation was free. Serum 5-HIAA = 8.9.

Multidisciplinary panel at OCMU decision was completion hysterectomy, omentectomy and appendectomy which was done at November 2014 with postoperative pathology free of tumor tissue. Patient remains disease free after one and half year of follow up.

Registry

Although population based registries of primary ovarian carcinoid tumors are deficient, multiple researchers had made efforts on registering and analyzing reported cases of these tumors. The last of this published registry up to our knowledge was Modlin et al. [3] at 2003. A thorough search on pubmed, medline and google was done with headings (primary ovarian carcinoid, carcinoid on top of teratoma and malignant transformation of teratoma) and all reported cases since 2005 till March 2016 were registered (Table 1).

From the collected data we recognized 52 cases with insular variant (commonest pathology), 21 cases with trabecular variant, 20 cases with strumal variant, mixed variant in 4 cases and mucinous in 1 case with the remaining 66 case non-specified (Fig. 3). The mean age was 50 years. The average tumor size was about 11 cm. Most of the cases were pure carcinoid (68 cases) while carcinoid transformation of a benign teratoma occurs in 45 cases (51 cases were unreported) (Fig. 4).

Functioning ovarian carcinoid causing endocrine symptoms occurs rarely (only 25 cases). 14 cases manifested with carcinoid heart disease (2 of which were diagnosed in postmortem pathology). Another 9 cases manifested with constipation, which was related to polypeptide secretion. Only one case presented with Cushing syndrome and one with hyperinsulinemia (Fig. 5). More interestingly all cases documented with constipation were strumal variant and none of the cases with trabecular variant were functioning.

Associated tumors occur in only 16 cases (mucinous cystadenoma = 5, contra-lateral ovarian epithelial cancer = 1, liver metastasis = 2, strumal thyroid cancer + breast cancer = 1, endometrial cancer + gliomatosis peritonii = 1,

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