CLINICAL CASE

A CASE OF OVARIAN CARCINOID TUMOUR

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Abstract

Primary ovarian carcinoid tumours are rare neoplasms. Carcinoid tumours mostly occur in the gastrointestinal tract and the lungs. Ovarian carcinoid tumours constitute only 0.5% of all carcinoid tumours and <0.1% of all ovarian carcinomas. Conventional tumour pathology criteria and DNA cytometry have limited value in assessing the malignancy of a neuroendocrine tumour. Hence, the detection of substances that are more specific for carcinoid tumours can facilitate a more exact diagnosis. Two markers are primarily used to diagnose and follow carcinoid tumours: 5-hydroxyindoleacetic acid (5-HIAA) and chromogranin A (CgA).We present the case of a 35-year-old female without personal pathological antecedents, diagnosed with right ovarian tumour at an ultrasound examination, without any clinical symptoms, for which she underwent right ovarectomy in January 2015, with histopathological diagnosis of stromal carcinoid (well differentiated neuroendocrine tumour) and immunohistological result of well differentiated G1 ovarian tumour. At present, the patient is under periodical endocrinological monitorization. 5-hydroxyindoleacetic acid, serotonin and chromogranin A levels are in normal ranges currently. Preoperatively there was no endocrinological evaluation or specific blood test examination with biochemical markers.

Keywords*: ovarian carcinoid tumour, neuroendocrine tumour*

Introduction

Primary ovarian carcinoid tumours are rare neoplasms. Carcinoid tumours mostly occur in the gastrointestinal tract and the lungs [1]. Ovarian carcinoid tumours constitute only 0.5% of all carcinoid tumours and <0.1% of all ovarian carcinomas. Primary ovarian carcinoid tumours are rare and make up less than 0.1% of all ovarian carcinomas [2]. They are commonly seen in perimenopausal and postmenopausal women. Primary carcinoids of the ovary are invariably unilateral. They form a solid nodule within a cystic teratoma, or form a pure solid hypervascular mass. They can be indistinguishable from other solid neoplasms of the ovary [3]. Lesions can markedly vary in size and metastatic carcinoids are nearly always bilateral with scattered tumour deposits present throughout both ovaries.

Conventional tumour pathology criteria and DNA cytometry have limited value in assessing the malignancy of a neuroendocrine tumour. Hence, the detection of substances that are more

specific for carcinoid tumours can facilitate a more exact diagnosis. Two markers are primarily used to diagnose and follow carcinoid tumours: 5-hydroxyindoleacetic acid (5-hiaa) and chromogranin A (CgA) [4].

5-HIAA: Serotonin released by carcinoid tumours is metabolized by monoamine oxidases in the liver, lungs, and brain to 5-HIAA. When measured in a 24-hour urine sample, 5-HIAA level has a sensitivity of 73% and a specificity of 100% for diagnosing carcinoid [5]. The normal range for urinary 5-HIAA is 3–15 mg/24 h, but the figure may vary depending on the laboratory. Up to 45 mg/24 h is considered normal by some laboratories. Levels of 5-HIAA have no clear correlation with symptoms, but they do fluctuate with symptomatology. Additionally, 5-HIAA levels reflect the actions of somatostatin analogues, with a 50% reduction from pretreatment levels being indicative of a biochemical response. However, some patients with carcinoid tumour have symptoms of flushing with low or normal levels of 5-HIAA [6].

Chromogranin A is found in the wall of synaptic vesicles that store serotonin and glucagon. Levels of CgA tend to correlate with large tumour size, but not with symptoms. In general, CgA levels are elevated in 85%–100% of patients with carcinoid tumour, regardless of whether the tumour is functional or nonfunctional. The specificity of CgA has been found to be 98.4%, and the sensitivity, 62.9% [6].

In classical midgut neuroendocrine tumours, CgA levels are elevated to 100–1000 times normal [7]. Measurements of CgA can be helpful, particularly if 5-HIAA is negative, but they are not as specific as measurements of 5-HIAA. Inflammatory conditions and renal insufficiency can cause elevations of CgA and, in rare cases, the cause cannot be identified. Type A gastritis and treatment with proton pump inhibitors can raise CgA levels. Change over time may be more useful than a single CgA value, because CgA levels are independent of symptoms. Practical problems, such as availability of the test, may hinder its use. Furthermore, several different methods for determining CgA are available, and the choice of method may affect the results. Chromogranin A appears to undergo a process of fragmentation, and the fragments detected by particular tests influence the resulting sensitivity.

Ki67 antigen is a nuclear protein expressed by proliferating cells; it is absent in resting cells. Expression can be tested in resected tissue specimens. Antibodies against Ki67 are a reliable marker of cell proliferation [8]. Assessment of Ki67 expression or antibody levels can be useful if chemotherapy is a consideration. High values (>2%) have some prognostic value for proliferation; patients with low values (<2%) are unlikely to benefit from chemotherapy [9]. Expression or antibody levels of Ki67 should be tested in all patients.

Material and Methods

We present the case of a 35-year-old female without personal pathological antecedents, diagnosed with right ovarian tumour of about 4/2.5/2.5 cm at an ultrasound examination after a recent childbirth, without any clinical symptoms, for which she underwent right ovarectomy in January 2015 with histopathological diagnosis of stromal carcinoid (well differentiated neuroendocrine tumour) – cystic wall of the ovarian stroma presenting thyroid tissue consisting in acini of different shapes and sizes (Figure 1).

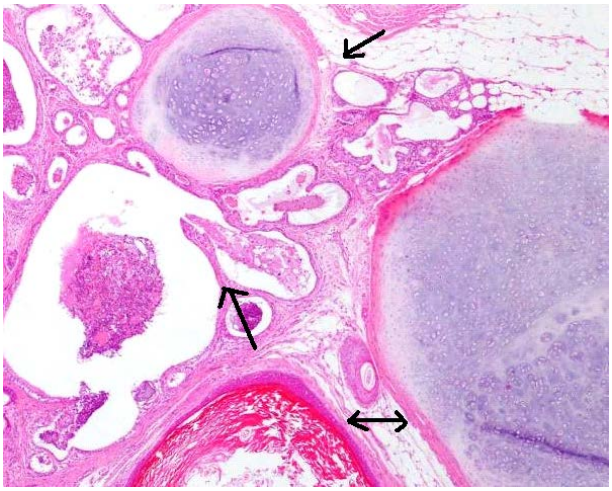

Figure 1 - Ovary teratoma; there is stratified squamous and respiratory epithelium, cartilage, fat and connective tissue in these photomicrographs

The immunohistological result of well differentiated G1 ovarian tumour – TIREO

positive, TTF positive, CROMO diffusely positive, Ki67 positive <2%. The histopathological picture, correlated with IHC tests and with anatomoclinical data support an ovarian tumoral proliferation of the monodermic teratoma type with aspect of stromal carcinoid/ G1 well differentiated neuroendocrine tumour.

Figure 2 - Scintigraphic thyroidian aspect

Figure 3 – Scintigraphic thyroidian aspect

Preoperatively there was no endocrinological evaluation or specific blood test examination with biochemical markers. Currently there are normal levels of 5-hydroxyindoleacetic acid (3.4 mg/24h; 2-9 mg/24h normal ranges), serotonin (plasma serotonin 181 ug/L; 80-400 ug/L normal ranges) and chromogranin A (31ug/L; 27-94 ug/L normal ranges).

Postoperatively CT exam shows right adnexectomy, and on the left ovary a cyst of about 2.4/2.4/3 cm was found, which we are periodically monitoring.

The thyroid scintigraphy examination reveals a normal situated thyroid, with normal I131 fixation, without pathologic aspect (Figures 2,3).

At present, the patient is under periodical endocrinological monitorization.

Discussions

Recommendations: Levels of 5-HIAA should be measured at baseline and at 3- to 4-month intervals in the first year. If the patient is unstable or symptomatic, if evidence of disease progression is found, or if a change in therapy is being considered, measurement of the 5-HIAA level should be repeated.

In the second year, the frequency of 5-HIAA measurements will depend on the patient's status. If the patient is stable, measurements at 6-month intervals may be appropriate. If the patient has had a complete macroscopic resection, a measurement every year may be adequate.

Where the test is available, CgA should be measured every 3 months in the first year. Elevated CgA in the absence of other altered parameters generally warrants further investigation. [4]

Conclusions

Primary ovarian carcinoid tumours are rare neoplasms [1]. Ovarian carcinoid tumours constitute only 0.5% of all carcinoid tumours and <0.1% of all ovarian carcinomas [2]. Primary ovarian carcinoid tumours are rare and make up less than 0.1% of all ovarian carcinomas and are commonly seen in

perimenopausal and postmenopausal women. Hence, the detection of substances that are more specific for carcinoid tumours can facilitate a more exact diagnosis. Two markers are primarily used to diagnose and follow carcinoid tumours: 5-hydroxyindoleacetic acid (5-HIAA) and chromogranin A (CgA) [4].

We present the case of a 35-year-old female without personal pathological antecedents, diagnosed with right ovarian tumour at ultrasonography examination, without any clinical symptoms, for which she underwent right ovarectomy in January 2015 with histopathological diagnosis of stromal carcinoid (well differentiated neuroendocrine tumour) and immunohistological result of well differentiated G1 ovarian tumour.

5-hydroxyindoleacetic acid, serotonin and chromogranin A levels are in normal ranges currently, and the patient is currently under periodical endocrinological monitorization.

References

[1]R. G. Robertson, W. J. Geiger, and N. B. Davis, "Carcinoid tumors," American Family Physician, vol. 74, no. 3, pp. 429–434, 2006.

[2]A. Talerman, "Germ cell tumors of the ovary", Current Opinion in Obstetrics and Gynecology, vol. 9, no. 1, pp. 44–47, 1997.

[3]Alenghat E, Okagaki T, Talerman A. Primary mucinous carcinoid tumor of the ovary. Cancer. 1986;58 (3): 777-83.

[4]J. Maroun, W. Kocha, R. Wong et al., Guidelines for the diagnosis and management of carcinoid tumours. Part 1: The gastrointestinal tract. A statement from a Canadian National Carcinoid Expert Group, Curr Oncol. 2006 Apr; 13(2): 67–76.

[5]Feldman JM, O'Dorisio TM, Role of neuropeptides and serotonin in the diagnosis of carcinoid tumors. Am J Med. 1986 Dec 22; 81(6B):41-8.

[6]Eriksson B, Oberg K, Stridsberg M, Tumor markers in neuroendocrine tumors. Digestion. 2000; 62 Suppl 1():33-8.

[7]Oberg K, Kvols L, Caplin M, Delle Fave G, de Herder W, Rindi G, Ruszniewski P, Woltering EA, Wiedenmann B, Consensus report on the use of somatostatin analogs for the management of neuroendocrine tumors of the gastroenteropancreatic system. Ann Oncol. 2004 Jun; 15(6):966-73.

[8]Sökmensüer C, Gedikoglu G, Uzunalimoglu B, Importance of proliferation markers in gastrointestinal carcinoid tumors: a clinicopathologic study. Hepatogastroenterology. 2001 May-Jun; 48(39):720-3.

[9]Oberg K, Diagnosis and treatment of carcinoid tumors. Expert Rev Anticancer Ther. 2003 Dec; 3(6):863-77.