Epidermoid cyst and primary trabecular carcinoid of the ovary: case report

A. Azzena, M. Zannol, M. Bertezzolo, T. Zen, S. Chiarelli[1]

Department of Gynaecological Sciences and Human Reproduction
[1]Department of Oncological and Surgical Sciences, Section of Pathology, Padua University (Italy)

Summary

In the literature and in our experience epidermoid cysts and carcinoids of the ovary are rare benign pathologies which occur more frequently in younger women. They probably are a one-sided development of a teratoma, which arise from germ cells after the first meiotic division due to either a meiosis I or a meiosis II non dysjunction. Diagnosis is possible only with histological examination and immunohistochemistry which allow us to differentiate carcinoids from sex-cord tumors and ependymomas. Prognosis is very good because the rate of malignant transformation is 1.4%-2% and the rate of complications is 14%. Thus conservative surgical therapy associated with long-term follow-up is the treatment of choice.

Key words: Ovarian epidermoid cyst; Ovarian trabecular carcinoid.

Introduction

Mature cystic teratoma is one of the most common benign ovarian tumors (10-20% of the ovarian tumors) and, although it may occur at any age, the peak incidence is between 20-40 years of age. The most frequent are typical dermoid cysts, while the pure epidermoid cyst is extremely rare; it is reported in the literature in less than 30 cases and its origin is still debated. Furthermore association with primary trabecular carcinoids of the ovary is highly uncommon.

We report a case of a coexistent epidermoid cyst of the ovary associated with a nodular trabecular carcinoid in a 59-year-old woman in menopause since 1990. We also review our case series of 200 ovarian mature cystic teratomas observed at our Institute.

Case Report

The patient was 59 years old, gravida 2, para 2. She had been in menopause since 1990 and she did not complain of any symptoms. She referred only hypertension lasting 20 years, stable and unchanged. Her three brothers were also affected by hypertension and her father died of an acute cardiac infarct.

Diagnosis was possible due to incidental ultrasonographic evidence of an asymptomatic cyst. The patient underwent a laparotomic left ovariosalpingectomy. At laparotomy the uterus appeared atrophic, the right ovary seemed normal and the left one was completely substituted by a cyst measuring 4 x 3 x 2 cm. The cyst had a smooth surface and contained white solid material. The wall was thin with a nodular ovoid solid area extending 1.5 cm and 0.5 cm thick.

The postsurgical period was regular with no evidence of hormonal dysfunction and only a slight anemia (hb 109 g/l, RG 3.48 x 10.12/l, sideremia 7,3 umol/l) and piastrinopenia (149 x 10.9/l) was found.

The patient was examined one month later: a serological search for neurohormonal peptides was done together with magnetic resonance imaging (MRI) to exclude multifocality, possible in carcinoids, and to confirm stage IA of the disease. We also requested further cardiologic evaluation. Hematochemical tests and MRI resulted negative. The cardiological exam did not point out any other abnormality except for known and unchanged hypertension.

Histological findings

At histological examination the cyst showed a very thin wall (0.5 mm thick) of ovarian stroma covered by squamous epithelium with granular cells directly lining the basal cell layer and superficially desquamative laminated keratin (Figure 1). A normal stratification pattern of parabasal, intermediate and superficial cells was absent. No dermal adnexa, no inflammatory reaction and no atypia were noted.

The nodular area was composed of ribbons, nests and trabeculae of cuboidal-columnar cells, with pale or eosinophilic cytoplasm, typical of neuroendocrine-type cells, and with hyaline irregular fibrous stroma. Cells had regular round-ovoid nuclei with finely granular chromatin, lacking mitosis and atypia.

At immunohistochemistry a differential diagnosis was made between trabecular carcinoid, Sertoli-Leidig tumour and ependymoma. In fact our node was positive for NSE, synaptophysin, chromogranin, keratin (Figure 2) and negative for vimentin, prostatic acid phosphatase, thyreoglobulin, calcitonin,

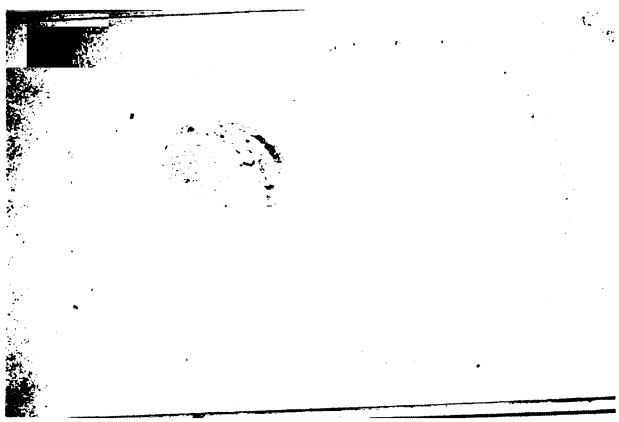

Figure 1. – The cyst and nodular trabecular carcinoid.

Revised manuscript accepted for publication February 14, 2002

Figure 2. – Nodular carcinoid positive for keratin at immunohistochemistry.

somatostatin, glucagon, serotonin and gliofibrillar acid protein (GFAP). Sex-cord tumors are usually positive for vimentin and almost always negative for GFAP while ependymomas are positive for GFAP and negative for synaptophysin and keratin.

Discussion

Our case report is particularly interesting because of the rarity of an ovarian epidermoid cyst in association with a trabecular carcinoid, the histogenetic uncertainty, and for the diagnostic problems and therapeutic choices.

In our experience ovarian teratomas are a frequent pathology presenting as dermoid cysts and occur most commonly during the reproductive period. In fact, among 200 women affected by ovarian teratomas the mean age was 35 with only 25 women over 50 years old and probably in menopause. We also observed that teratomas occurring in older patients were more often characterised by unusual and complex ectopic tissue (27%) than in younger patients (21%). Tumor size ranged from 0.3 cm to 10 cm in our patients.

In the literature epidermoid cysts have an incidence of 0.07 to 0.24% (1, 13) and in our case series we found only one among 200 ovarian teratomas.

The structure of an epidermoid cyst is defined as a cyst lined solely by mature squamous epithelium and containing only keratinized debris. There are two hypotheses on its histogenesis.

The most probable is the one-sided development of a teratoma (subtype of a dermoid cyst or monophyletic development of a teratoma). According to Niklas *et al.* [3] teratomas arise from germ cells after the first meiotic division due to failure of meiosis II or due to failure of meiosis I. Instead Deka *et al.* [4] suggest that there are five modes of origin for teratomas: failure of meiosis I or fusion of the first polar body with an oocyte (21.3%); failure of meiosis II or fusion of the second polar body with an ootid (39.3%); endoreplication of the genome of a mature ovum (6.3%); failure of meiosis I and II in a primordial germ cell; fusion of two ova [4]. They demonstrated that the majority of teratomas (65%) arose by either meiosis I or meiosis II non dysjunction [4].

Other hypotheses for the origin of epidermoid cysts are: a squamous metaplasia of the rete ovarii, of mesonephric tubules of the ovarian hilus, of endometrial, endocervical and transitional epithelium derived from differentiation of coelomic surface epithelium or of surface epithelial inclusion glands of the ovary [1].

In our case report presence of a trabecular carcinoid positive for NSE leads us to consider the first possibility appropriate.

Usually diagnosis of this pathology is incidental because it is asymptomatic and the rate of total complications (torsion, rupture) is 10.7% [3]. In our case series 14% of patients had complications such as torsion (wall pericystic xanthogranulomatous flogosis, areas with necrosis and haemorrhagic infiltration).

The rate of malignant transformation in these tumors is 1.4%-2%. Malignancy seems to be related to larger tumor size (median diameter 9 cm) and older age distribution (median 50 years) [3]. Furthermore Noumoff et al. found that in teratomas there seems to be an association between chromosome abnormalities (translocation (8;14) and (5;8), deletion [4]) and risk of malignant transformation. It means that genetic analysis could be a way to discover rare teratomas that seem benign but could become malignant.

The rate of bilateral mature teratomas is 8 to 15% but it is covert only in 1.1 % of cases [6]. Thus in the presence of a unilateral mature cystic teratoma a careful inspection and palpation of the controlateral ovary is very important to detect initial bilateral teratoma.

Because of the low rate of complications, malignancy and covert bilaterality the therapeutic choice should be based on age, fertility desire or presence of another pelvic pathology. In fact, cystectomy or monolateral adnexectomy is favored for younger patients with lower gravidity and parity in order to preserve as much ovarian tissue as possible, while older patients in menopause should undergo monolateral or bilateral adnexectomy. Moreover, the lack of recurrence may confirm the appropriateness of these approaches. Incidence of ovarian carcinoids is 0.52% of all carcinoids and they can occur isolated or in association with teratomas (57.4%). The age of diagnosis ranges between 16 and 83 years with an average of 50.8 years.

Ovarian carcinoids have been classified on an embryological basis into three groups namely, foregut, midgut and hindgut carcinoids and can be subdivided, according to the histological aspect, into insular (midgut derivation), strumal (endodermal derivation and evidence of thyroid and C-cell differentiation), mucinous (goblet or adenocarcinoid) and trabecular (foregut and hindgut derivation). Trabecular carcinoid tumors of the ovary are less frequent than insular and strumal tumors which are more easily found in the bronchi, pancreas and rectum [7, 8, 9].

A review of the literature shows that diagnosis is often incidental; in fact only 7.8% of cases have evidence of the carcinoid syndrome, typical of the insular pattern, and usually they are so small that they do not cause symptoms of compression.

Long-term prognosis is favorable. Soga et al's case series showed a 5-year survival rate of carcinoids associated with teratoma of 93.8%, and they observed a metastasis rate of 5.8%, probably related to the size of the carcinoids [11]. Davis *et al.* reported an overall survival for carcinoids confined to one ovary of 100% at five years, but a bad prognosis for patients with advanced stage at diagnosis (33% 5-year survival) [8]. Robboy et al observed an actuarial survival of 95% at five years and 88% at ten years [12]. These data confirm that ovarian carcinoids and ovarian teratomas confined to one ovary should be treated only with surgery and a conservative approach in younger fertile women.

However for a correct diagnosis and realistic prognosis, primary trabecular carcinoids must be histologically differentiated from other types of ovarian carcinoids and from trabecular carcinoids metastatic to the ovary. Usually metastatic carcinoids affect both the ovary and other organs or structures, while the primary type is found to affect only one ovary. The presence of teratomatous elements helps exclude a metastatic lesion. Nonetheless in diagnosing and staging of this pathology a total body CT or MRI is important to detect any other focal metastatic or primitive lesions.

Trabecular carcinoids must also be differentiated from Sertoli-Leydig cell tumors of the ovary. The cords of trabecular carcinoids are usually longer, more uniform and numerous. Carcinoid cells are larger, contain more cytoplasm and neurosecretory granules which are round and homogeneous while Sertoli-Leydig cell tumors do not have these granules [9]. Differential diagnosis from ependymoma is also necessary and it is possible through immunohistochemistry since only ependymoma is positive for both vimentin and GFAP.

Conclusion

Epidermoid cysts and carcinoids of the ovary are rare benign pathologies which occur more frequently in younger women but with a wide age distribution. The histological origin is well defined as the development of a teratoma but it would be interesting to better understand how they can arise in postmenopausal women with no proliferating oocytes.

Diagnosis of carcinoids and teratomas is dependent only on histological examination and immunohistochemistry.

Prognosis is very good and overall survival is 93-100% at five years for primary carcinoids at stage IA and 100% for epidermoid cysts.

Thus, younger patients with a mobile monolateral tumor may be treated by cystectomy or unilateral adnexectomy, while in menopausal patients salpingo-oophorectomy is the treatment of choice. Nevertheless long-term follow-up is advisable.

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Address reprint requests to:
S. CHIARELLI, M.D.
c/o Istituto di Anatomia Patologica
Via Gabelli, 61
35100 Padova (Italy)