EJGO European Journal of Gynaecological Oncology

Coexistence of mature cystic teratoma and adenocarcinoma in situ within atypical proliferative mucinous tumour of ovary – a case report of 35-year-old woman

A. Wincewicz[1,2], P. Lewitowicz[1,2], O. Adamczyk-Gruszka[3], S. Sulkowski[4], L. Kanczuga-Koda[5], M. Koda[4]

[1] Departments of Anatomy and Pathology, Faculty of Health Sciences, Jan Kochanowski Memorial University of Kielce, Kielce
[2] NZOZ Zaklad Patologii, Department of Pathology, Kielce
[3] Department of Gynaecology, Faculty of Health Sciences, Jan Kochanowski Memorial University of Kielce, Kielce
[4] Department of General Pathomorphology, Medical University of Bialystok, Bialystok
[5] Department of Pathology, Bialystok Oncology Centre, Bialystok (Poland)

Summary

Combined ovarian tumors are found in common pathologic practice due to amazing potential of ovarian tissue to copy almost every tissue of human body and imitate many neoplasms of various other organs in a very flexible way. A multicystic tumor is presented in this case report of 35-year-old woman. It consisted of a cyst with sebum and hair and cavities with papillomatous projections and mucus. The ovarian tumor was diagnosed a mature cystic teratoma presenting mainly as dermoid cyst and mucinous adenocarcinoma in situ, arising within atypical proliferative mucinous tumor. This report demonstrates how histoformative properties are reflected in ovarian tumorigenesis. Such a stunning histoformativity makes ovaries the possible site of primary origin for malignant tumors that mimic extra ovarian differentiation. In the authors' point of view, the diagnosis of primary ovarian mucinous tumor within cystic teratoma is firm, whenever simultaneous extraovarian involvement by mucinous neoplasm is excluded.

Key words: Adenocarcinoma in situ; Atypical proliferative mucinous tumor; Dermoid cyst; Mature cystic teratoma.

Introduction

Combined ovarian tumors are found in common pathologic practice due to amazing potential of ovarian tissue to copy almost every tissue of human body and imitate lots of neoplasms of various other organs in a very flexible way. Among them, teratomas are the most educative examples of neoplastic histoformativity. They can form many histological structures that develop from all three germ layers and could appear as unique for certain organs that are distinct from ovary. Teratomas can coexist with mucinous neoplasm of ovary [1]. Although mature cystic teratomas (MCTs) are the most frequent ovarian germ cell tumors, such a malignant transformation is a rare event in their course [2]. It is estimated that adenocarcinoma comprises approximately 5.8% of all cases of malignant transformation of ovarian teratoma, while large majority of such malignancies are squamous cell carcinomas [3]. Indeed, squamous cell carcinoma is the most common malignancy growing from cystic teratoma with quite a poor prognosis affected by histopathological grading and extend of invasion [4]. Mucinous adenocarcinomas are described as uncommon transformation of mature cystic teratoma. Nevertheless, they have quite favorable prognosis with one reported case of woman who survived five years after operation without recurrence of the disease [2] and the other report of female patient whose three-year-long follow-up was free of disease [5].

Here the authors present a case of dermoid cyst and adenocarcinoma in situ within atypical proliferative mucinous tumour of 35-year-old woman.

Materials and Methods

A 35-year-old woman underwent unilateral salpingo-oophorectomy and excision of subserosal uterine leiomyoma due to abdominal pain and discomfort in the pelvic region. Right adnexa with tumor and a conventional subserous leiomyoma were sent to histopathological examination. Tissues were fixed in 10% buffered formalin solution. The representative samples were dissected and embedded in paraffin blocks at 56˚C according to standard procedures. The material was sliced into three-µm thick specimens that were routinely stained with hematoxylin-eosin. Histopathological examination was done by two independent pathologists with determination of conventional histopathological parameters of diagnosed entities.

Revised manuscript accepted for publication December 30, 2013

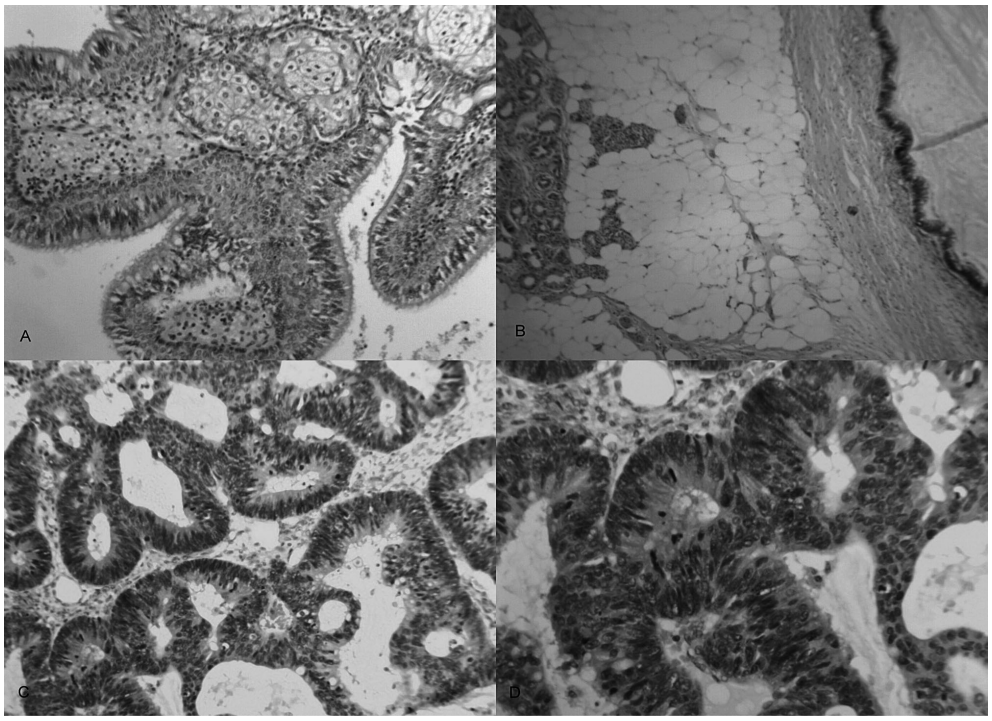

Figure 1. — Mature teratoma, adenocarcinoma in situ, and mucinous atypical proliferative tumor of ovary. A: Metaplastic, ciliated pseudostratified epithelium of respiratory tract with sebaceous glands in dermoid cyst (magnification x100). B: Mucinous epithelial lining of the cyst in a separation from other teratomatous components (magnification x 40). C and D: Adenocarcinoma in situ with morphology of intestinal type (magnification x 100 and x 200, respectively).

Results

Clinical data and macroscopic findings

No other tumor masses were detected in the body of the patient. The ovarian tumor measured 7 x 5 x 4cm. On cut surface it was composed of a few cysts which were filled with sebum, hair, and semi-fluid viscous content. Internal surfaces of the cysts were mostly smooth but focally there were prominent papillomatous projections into cystic lumen. The adjacent fallopian tube was four cm long and accompanied by perisalpingeal cysts up to one cm in diameter. On endoscopic investigation and imaging there was no neoplastic involvement of intestines and lungs of the patient. There was no trace of neoplasm in material that was obtained from uterine abrasion as well.

Microscopic findings

In samples from a cyst with sebum and hair, there were quite a few histological structures and tissues that originated from all three germ layers. There was classical pattern of dermoid cyst that was lined by epidermis with well developed skin adnexa. Within the cyst there was a focal growth of ciliated pseudostratified epithelium of respiratory tract as well (Figure 1A). In close vicinity of these elements of mature cystic teratoma, there were cysts lined by relatively tall mucinous epithelial cells that varied in a degree of atypia from none to prominent (Figure 1B). This neoplastic counterpart was diagnosed as atypical proliferative mucinous tumor (APMT) with morphological features of intestinal type of epithelium. The cuboidal glandular mucinous epithelium with atypia presented with epithelial stratification, micropapillary projections, and a compact assembly of carcinomatous tubes that coalesced into cribriform pattern in papillomatous excrescences of cysts with viscous, mucinous content (Figures 1B, 1C). There was also budding of this epithelium into cyst wall but no evident stromal invasion of ovary. These foci were consistent with adenocarcinoma in situ. The cancer cells were relatively tall with basally oriented highly atypical nuclei. Moreover goblet cells were present in better differentiated areas of this atypical mucinous tumor (Figure 1D). Careful analysis revealed that walls of teratoma and APMT showed distinct borders with teratoma tissues and fibrous wall of APMT. No extension through the ovarian capsule was noted corresponding with pT1a (FIGO Stage 1A). No recurrence was noted after surgical resection. The ovarian tumor was diagnosed a MCT with atypical proliferative mucinous tumour with foci of adenocarcinoma in situ.

Discussion

Whenever adenocarcinoma and cystadenoma is encountered within teratoma, some questions could appear as follows: Are adenocarcinoma, cystadenoma, and teratoma synchronous tumors or are they parts of one combined entity? What is the origin of malignant component? Is the prognosis different for adenocarcinoma arising from intestinal type epithelium in comparison to adenocarcinoma growing from ciliated epithelium of respiratory type? and so on.

The prognosis of adenocarcinoma arising within teratoma is still not precisely estimated but staging and grading seem to affect prognosis in the similar way as in other adenocarcinomas. In the present authors' opinion the mode of spreading is going to be different for adenocarcinoma no matter from which teratomatous epithelium such a malignancy comes from. Not only the epithelial origin of teratomatous adenocarcinoma could play a role, but also the primary location certainly affects prognosis, for example adenocarcinoma arising from respiratory or intestinal epithelium of teratoma. In such a case, mode of spreading and prognosis could be totally different from conventional lung adenocarcinoma or colon adenocarcinoma which grow at quite different sites and face different histological barriers at their primary sites of origin.

Immunohistochemistry sometimes helps to elucidate an origin of malignant tumors that are found in ovarian dermoid cysts [6]. For example p63 and CK5/6 stainings were strongly positive in squamous carcinoma and this immunoreactivity was preserved in stratum of basal cells that covered the inner surface of the mucinous cyst in a case of monodermal teratoma. That distribution of immunostain suggested that these basal cells could be a site of origin of diagnosed malignancy [6]. Moreover, such a basal-cell pattern of staining was thought to be quite characteristic for mucinous cysts of mature teratomas and was completely lost in ovarian benign and borderline cystic mucinous cystadenomas, giving a clue for eventual differential diagnosis in doubtful cases [6]. MCT-derived mucinous borderline-like tumor was predominantly positive for cytokeratin 20 [7]. However, immunohistochemistry results were not straightforward because there was also a little intriguing partial immunoreactivity for cytokeratin 7. Besides this, MUC5AC was also partially positive with only residual immunoreactivity for MUC2 and MUC6. This mixed pattern of staining was a ground to support an idea that mucinous borderline tumor was originating from gastrointestinal epithelium of teratoma [7].

However, sometimes nor immunohistochemistry nor molecular biology methods fail to explain a coexistence of various ovarian tumors as in case of synchronous rhabdomyosarcoma arising in a MCT and contralateral serous carcinoma [8]. Other types of sarcomas were also reported in association with MCT as rhabdomyosarcomatous transformation and contralateral serous carcinoma [8].

Carcinomatous and sarcomatous component can arise not only on the basis of mature teratoma but also from immature teratomas [9]. Namely, a malignant mixed Müllerian tumor (MMMT) of nasopharyngeal teratoid carcinosarcoma type was accompanied with malignant neuroectodermal foci that resembled ganglioneuroblastoma with pronounced immunoreactivity for synaptophysin, S-100 and neuron-specific enolase [9]. Mucinous adenocarcinoma and teratoma were reported in quite unusual settings as in coexistence with a large cell neuroendocrine carcinoma [10].

If both appendix and ovary are involved with borderline mucinous tumor, the determination of primary site of the tumor is quite challenging, particularly if mucinous tumors give a clinical picture of pseudomyxoma peritonei (PMP) and morphology and immunoprofile overlap with characteristics of the secondary neoplasms of appendiceal origin [11]. If adenocarcinoma is encountered within ovarian cystic teratoma, both respiratory and gastrointestinal epithelium could be considered as a potential tissue of neoplastic origin [12, 13]. If epithelium that lines cysts of teratoma is a ciliated, pseudostratified columnar epithelium that contains ciliated cells, goblet cells and basal cells its respiratory type could be unequivocally elucidated [12, 13]. The adenocarcinoma in multicystic teratoma gives a quite mixed pattern of staining. The crucial cytokeratins are CK7 that is predominantly positive in case of primary origin from gynecological tract and CK20 that is strong in tumor of gastrointestinal type [14]. To examine utility of immunhistochemistry, CK7, CK20, CDX2, and villin stains were studied in a largest so far group of 44 ovarian mucinous adenomas and adenocarcinomas ex-MCTs without extraovarian presentation of mucinous tumor [14]. In this report, 15 cystadenomas without pseudomyxoma ovarii showed the same intensity both for CK7 and CK20 [14]. If so, whenever appendix is involved, it is truly impossible to judge what the origin of the mucinous neoplasm is only on the ground of immunohistochemistry. Eight proliferative mucinous cystadenomas without pseudomyxoma ovarii exhibited much stronger CK7 staining than CK20 immunoreactivity, while all cystadenomas with Meigs syndrome lacked CK7 and CK20 immunoexpression. To make immunohistochemistry more puzzling, adenocarcinomas manifested presence or lack of CK7 and CK20 expression in all three following combinations (CK7-/CK20+, CK7+/CK20+, or CK7+/CK20-) [14]. Meigs syndrome was accompanied with CK7-/ CK20+ immunophenotype with CDX2 and villin expression in adenocarcinoma [14]. Such a mixed immunohistochemistry with positive immunoreactivity to CK20 suggested teratomatous origin of at least a subgroup of described ovarian tumors [14]. In the present authors' point of view, the diagnosis of primary ovarian mucinous tumor within cystic teratoma is firm,if only simultaneous extraovarian involvement by mucinous neoplasm is excluded, as in the presented case. Indeed in described example immunohistochemistry would not add anything essential to diagnosis in perspective of prognosis of this patient especially because the authors did not diagnose invasive adenocarcinoma. We conclude that although this mucinous tumor presents morphologic features of intestinal type epithelium, it is still primary tumor of ovary. In this case, careful clinical information

was more useful than additional performance of immunohistochemistry. Namely any suspected extraovarian masses were not present on clinical inspection that included imaging, bronchial, and gastrointestinal endoscopy and uterine abrasion. Thus, a successful cooperation with clinician always goes first before performance of any additional staining in routine pathologist's practice.

To sum up, the present report is one of few that present quite a rare coexistence of dermoid cyst and adenocarcinoma in situ within atypical proliferative mucinous tumour of 35-year-old woman with emphasis that in such cases clinical data are so useful that limit the need of performance of additional histopathological stainings.

Acknowledgement

This publication is institutionally affiliated to Medical University of Białystok, Poland.

References

[1] Kotsopoulos I.C., Xirou P.A., Deligiannis D.A., Tsapanos V.S.: "Coexistence of three benign and a borderline tumor in the ovaries of a 52-year-old woman". *Eur. J. Gynaecol. Oncol.*, 2013, *34*, 186.

[2] Takai M., Kanemura M., Kawaguchi H., Fujiwara S., Yoo S., Tanaka Y., *et al.*: "Mucinous adenocarcinoma of the intestinal type arising from mature cystic teratoma of the ovary: a rare case report and review of the literature". *J. Ovarian Res.,* 2012, *5*, 41.

[3] Güney M., Oral B., Demir F., Ozsoy M., Kapucuoğlu N.: "Mucinous adenocarcinoma arising from the gastrointestinal epithelium in benign cystic teratoma of the ovary—case report". *Eur. J. Gynaecol. Oncol.*, 2006, *27*, 304.

[4] Comerci J.T. Jr., Jones J.G., Fields A.L., Runowicz C.D., Goldberg G.L.: "Squamous cell carcinoma in mature cystic teratoma in a young woman: a diagnostic and management dilemma". *Eur. J. Gynaecol. Oncol.*, 1996, *17*, 501.

[5] Levine D.A., Villella J.A., Poynor E.A., Soslow R.A.: "Gastrointestinal adenocarcinoma arising in a mature cystic teratoma of the ovary". *Gynecol. Oncol.*, 2004, *94*, 597.

[6] Baughn M.R., Plaxe S.C., Weidner N.: "Primary squamous carcinoma of the ovary likely arising from a monodermal cystic mucinous teratoma". *Ann. Diagn. Pathol.*, 2011, *15*, 446.

[7] Nakatsuka S., Wakimoto T., Ozaki K., Nagano T., Kimura H., Nakajo K., Ito K.: "Mucinous borderline-like tumor of the gastrointestinal type arising from mature cystic teratoma of the ovary and its immunohistochemical cytokeratin and mucin phenotype". *J. Obstet. Gynaecol. Res.*, 2012, *38*, 471.

[8] Kefeli M., Kandemir B., Akpolat I., Yildirim A., Kokcu A.: "Rhabdomyosarcoma arising in a mature cystic teratoma with contralateral serous carcinoma: case report and review of the literature". *Int. J. Gynecol. Pathol.*, 2009, *28*, 372.

[9] Matsuura Y., Kitajima M., Hachisuga T., Tanimoto A., Okura N., Kihara I.: "Malignant mixed müllerian tumor with malignant neuroectodermal components (teratoid carcinosarcoma) of the ovary: Report of a case with clinicopathologic findings". *J. Obstet. Gynaecol. Res.*, 2010, *36*, 907.

[10] Chênevert J., Bessette P., Plante M., Têtu B., Dubé V.: "Mixed ovarian large cell neuroendocrine carcinoma, mucinous adenocarcinoma, and teratoma: a report of two cases and review of the literature". *Pathol. Res. Pract.*, 2009, *205*, 657.

[11] Hwang J.H., So K.A., Modi G., Lee J.K., Lee N.W., Lee K.W., et al.: "Borderline-like mucinous tumor arising in mature cystic teratoma of the ovary associated with pseudomyxoma peritonei". *Int. J. Gynecol. Pathol.*, 2009, *28*, 376.

[12] Song Y.J., Ryu S.Y., Choi S.C., Lee E.D., Lee K.H., Cho S.Y.: "Adenocarcinoma arising from the respiratory ciliated epithelium in a benign cystic teratoma of the ovary". *Arch. Gynecol. Obstet.*, 2009, *280*, 659.

[13] Cobellis L., Schürfeld K., Ignacchiti E., Santopietro R., Petraglia F.: "An ovarian mucinous adenocarcinoma arising from mature cystic teratoma associated with respiratory type tissue: a case report". *Tumori*, 2004, *90*, 521.

[14] Vang R., Gown A.M., Zhao C., Barry T.S., Isacson C., Richardson M.S., *et al.*: "Ovarian mucinous tumors associated with mature cystic teratomas: morphologic and immunohistochemical analysis identifies a subset of potential teratomatous origin that shares features of lower gastrointestinal tract mucinous tumors more commonly encountered as secondary tumors in the ovary". *Am. J. Surg. Pathol.*, 2007, *31*, 854.

Address reprint requests to:
A. WINCEWICZ FEBP, M.D., PhD,
Department of Anatomy,
Faculty of Health Sciences,
Jan Kochanowski Memorial University,
Kielce IX Wieków Kielc St 19,
25-317 Kielce (Poland)
e-mail: ruahpolin@yahoo.com
andwinc@gmail.com