

Sebaceous adenoma arising in mature cystic teratoma of the ovary. Case report

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SUMMARY

We report the case of a 44-year-old female with sebaceous adenoma arising in mature cystic teratoma of the ovary. The patient had a tumor in the left ovary; 125 x 90 x 70 mm. Microscopically, the tumor consisted of structures typical of dermoid cysts. However, large areas of sebaceous proliferation were found. These areas were comprised of sebaceous nodules with features similar to a sebaceous adenoma of the skin. Immunohistochemically, the tumor showed "wild-type" expression of p53 and low proliferative activity (Ki-67 index < 5%). To verify the possibility of Muir-Torre syndrome we performed immunohistochemical examination of DNA mismatch repair proteins expression. However, all four proteins examined (MSH2, MSH6, MLH1, PMS2) were positive. Sebaceous adenoma arising in mature teratoma of the ovary is rare. To the best of our knowledge, only six cases have been reported in the literature to date.

Keywords: sebaceous adenoma – mature cystic teratoma – ovary

Sebaceous adenom vzniklý ve zralém cystickém teratomu ovária. Kazuistika

SOUHRN

Prezentujeme případ 44 leté ženy se sebaceous adenomem vzniklým ve zralém cystickém teratomu ovária. Nádor lokalizovaný v levém ovariu byl velikosti 125 x 90 x 70 mm. Mikroskopicky se jednalo o nádor tvořený typickými strukturami dermoidní cysty, nicméně s poměrně rozsáhlými oblastmi sebaceous proliferace. Tyto oblasti byly tvořeny sebaceous noduly vykazujícími obdobné znaky jako sebaceous adenom kůže. Imunohistochemicky jsme prokázali „divoký typ“ exprese proteinu p53 a nízkou proliferativní aktivitu (Ki-67 index < 5%). K ověření možnosti, že jde o syndrom Muir-Torre, jsme provedli imunohistochemické vyšetření exprese "DNA mismatch repair" proteinů. Vyšetření s protilátkami proti všem 4 analyzovaným proteinům (MSH2, MSH6, MLH1, PMS2) vyznělo pozitivně. Sebaceous adenom vznikající ve zralém teratomu ovária je vzácný, doposud bylo popsáno pouze 6 takových případů.

Klíčová slova: sebaceous adenom – zralý cystický teratom – ovarium

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We report the case of a 44-year-old patient with sebaceous adenoma arising in mature cystic teratoma of the ovary. Sebaceous tumors arising in mature cystic teratomas are rare and to the best of our knowledge, there have been only six prior reports of sebaceous adenoma (1-4). In one of the previous cases, association of ovarian sebaceous adenomas with Muir-Torre syndrome, a variant of Lynch syndrome, was described (2). In our case this possibility was not confirmed by immunohistochemical examination with antibodies against mismatch repair (MMR) proteins.

MATERIALS AND METHODS

Sections from formalin-fixed, paraffin-embedded tissue blocks were stained with hematoxylin-eosin. Selected sections were analyzed immunohistochemically using the avidin-biotin complex method with antibodies directed against the following

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antigens: p53 (clone DO7, 1:50, Immunotech, Quebec, Canada), MLH-1 (clone G168-15, 1:50, Zytomed Systems, Berlin, Germany), MSH-2 (clone FE11, 1:50, Zytomed Systems), MSH-6 (clone Fe 11, 1:50, Zytomed Systems), PMS-2 (clone EPR3947, ready-to-use, Zytomed Systems), and Ki-67 (clone MM1, 1:50, Diagnostic BioSystems, Pleasanton, California). Antigen retrieval was performed. This was comprised of pretreatment in 0.01 M citrate buffer (pH 6.0) for 40 min in a water bath at 98°C for p53, MSH-1 and MSH-6. Heat-induced epitope retrieval was performed in 0.01M citrate buffer (pH 9.0) for PMS-2 and MLH-1. Only nuclear staining was regarded as positive for all antibodies.

RESULTS

Grossly, the left adnexal tumor measured 125 x 90 x 70 mm. The dissection of the tumor revealed a cavity filled with fatty material similar to normal sebum, and hair surrounded by a firm capsule of varying thickness. The inner lining of the cyst was predominantly smooth, with only one yellowish tumorous mass measuring 40 x 30 x 10-15 mm.

Microscopically, the majority of the tumor was composed of mature cystic teratoma structures, including skin and skin adnexa, and also contained respiratory-type epithelium. However, the whole yellowish tumorous mass showed an abnormal proliferation of sebaceous cells forming nodules with features similar to a sebaceous adenoma of the skin (Fig. 1). This part of the lesion had a lobular growth pattern and a pushing border with ad-

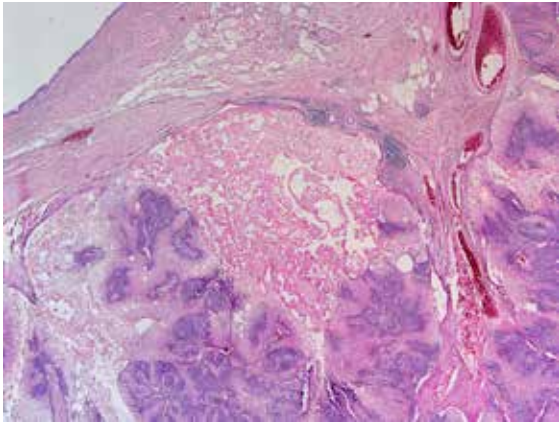


Fig. 1. Sebaceous adenoma surrounded by a connective tissue capsule of varying thickness (H&E, original magnification 20x).

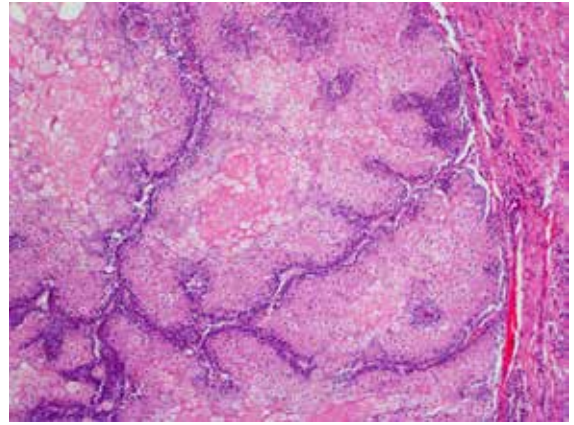


Fig. 2. Sebaceous adenoma composed of nodules of sebaceous cells (H&E, original magnification 100x).

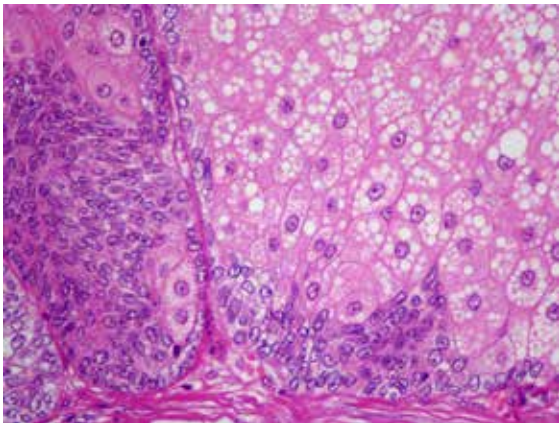


Fig. 3. Two cell types, peripheral germinative cells and central mature sebaceous cells, are present (H&E, original magnification 400x).

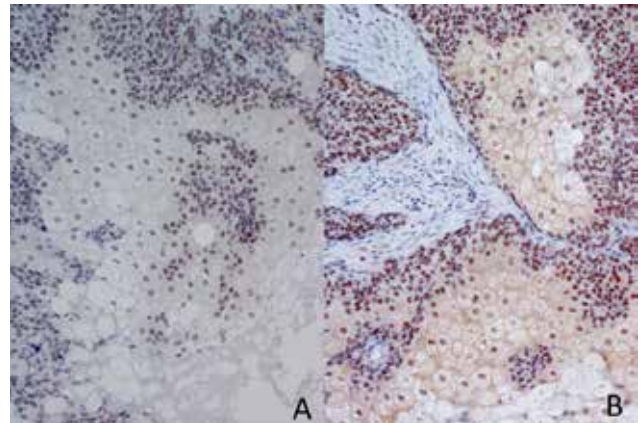


Fig. 4. Immunohistochemical examination of MMR proteins showed nuclear positivity with antibodies against all four proteins examined. **A:** MLH1. **B:** PMS2 showing nuclear positivity (original magnification 200x).

jacent ovarian stroma. The lobules were composed of two cell types, cuboidal peripheral germinative cells and central mature sebaceous cells (Fig. 2,3). Immunohistochemical analysis of p53 exhibited weak nuclear positivity of scattered cells and moderate nuclear positivity in sporadic cells, in keeping with “wild-type” expression. The Ki-67 proliferation index was low, less than 5% of all tumor cells revealed nuclear positivity, with only some sporadic foci of “hot-spots”, where positivity reached 25% of tumor cells. Immunohistochemistry of MMR proteins showed nuclear positivity with antibodies against all four proteins examined (MSH2, MSH6, MLH1, PMS2) (Fig. 4).

DISCUSSION

Mature cystic teratoma is the most common type of ovarian teratoma and the most common type of ovarian germ cell neoplasm. It comprises approximately 20% of all ovarian neoplasms (5). Tumors with sebaceous differentiation arising in mature cystic teratomas are rare, although sebaceous glands are almost always components of mature cystic teratomas. These tumors include sebaceous adenoma, basal cell carcinoma with sebaceous differentiation, and sebaceous carcinoma. There have only been six prior reports of sebaceous adenoma, nine reports of sebaceous carcinoma, and two reports of basal cell carcinoma with sebaceous differentiation arising in mature cystic teratoma of the ovary (1-4,6-9). The sebaceous adenomas were in all cases composed of nodules or lobules of proliferating sebaceous cells showing various degrees of maturity, with mature cells predominating.

The histologic spectrum of sebaceous lesions and tumors encompasses sebaceous hyperplasia, sebaceous adenoma, sebaceoma and sebaceous carcinoma (10). Sebaceous adenoma has to be differentiated from sebaceous hyperplasia, in which the sebaceous lobules are increased in number, but comparing with sebaceous adenoma have only two layers of peripherally located basaloid or germinative cells (11). There can be some histological overlaps between sebaceous adenomas and sebaceomas. Sebaceomas are irregularly shaped nodular lesions comprising undifferentiated basaloid sebocytes in more than half of the tumour cell volume, and to a lesser extent small groups of sebaceous cells and transitional cells. Sebaceous adenomas and sebaceomas, in contrast to sebaceous carcinoma, lack nuclear atypia and invasive growth patterns. However, there may be substantial mitotic activity present in the basaloid regions in these benign tumors. Sebaceous carcinomas are cytologically and/or architecturally malignant tumors with sebocytic differentiation and the grading of these carcinomas is based on growth patterns rather than on their cytological features (10). Regarding immunohistochemical expression, analysis of p53 and Ki-67 may be helpful in differential diagnosis between benign and malignant sebaceous proliferations. One study has shown that sebaceous hyperplasia, sebaceous adenomas, and sebaceomas tended to show low levels of p53 and Ki-67 positivity, whereas sebaceous carcinomas tended to show higher levels of nuclear p53 expression (50% versus 11%) and Ki-67 positivity (30% versus 10%) compared to the adenomas (12).

The outcome of sebaceous adenomas arising in ovarian teratoma is favorable; all patients were well and disease-free for peri-

ods ranging from 1.5 to 6 years postoperatively. Only one patient, who had in the same ovary sebaceous adenoma and squamous cell carcinoma, died of the disseminated disease 1 year after the diagnosis (1). Moreover, this patient also had well-differentiated endometrial carcinoma. In the last presented case report, the authors described sebaceous adenoma arising in an ovarian mature cystic teratoma in a patient with Muir-Torre syndrome, a variant of Lynch syndrome (2). The authors emphasized the possible association of Muir-Torre syndrome and cutaneous sebaceous adenomas highlighting that a single sebaceous neoplasm of the ovary could be a part of Muir-Torre syndrome (2,11,13). They suggest investigating patients with the sebaceous adenoma arising in an ovarian mature teratoma in the same way as patients with cutaneous sebaceous adenomas to rule out this

important genetic cancer predisposition syndrome. However, in our case all four investigated MMR proteins (MSH2, MSH6, MLH1, PMS2) showed nuclear positivity in both tumor and non-tumor tissue, which instead points against the possibility of association with Muir-Torre syndrome in this case.

In conclusion, we report a case of sebaceous adenoma arising in mature cystic teratoma of the ovary. To the best of our knowledge, only six cases of such a tumor have been reported in the literature to date.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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