Ovarian Mucinous Cystadenocarcinoma with Mural Nodule of Anaplastic Carcinoma and Synchronous Cervical Squamous Carcinoma

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Souhrn

Mucinózní cystadenokarcinom ovaria s murálním uzlem anaplastického karcinomu a současný dlaždicobuněčný karcinom děložního hrdla

Solidní murální tumorózní uzel v mucinózním cystickém nádoru ovaria je častější než se běžně předpokládá. Je prezentován jeden případ se současným karcinomem děložního hrdla.
Třicetiosmiletá žena byla operována pro nádor pravého ovaria. Po peroperační diagnóze ovariální malignity byla provedena oboustranná salpingo-ooforektomie a hysterektomie. Nádor ovaria byl tvořen unilokulární cystou s murálním uzlem. Uzel měl charakter nediferencovaného karcinomu. Imunohistochemicky byly atypické buňky uzlu pozitivní pro cytokeratin, CEA a vimentin, což potvrzuje jejich anaplastický charakter. Histologicky byl nalezen i současný invazivní dlaždicobuněčný karcinom děložního hrdla. Pacientka byla léčena chemo- a radioterapií. Patnáct měsíců po operaci je v dobrém stavu, bez známek nádoru.
V literatuře jsme nenašli podobný případ mucinózního cystadenokarcinomu ovaria s murálním uzlem anaplastického karcinomu a současný dlaždicobuněčný karcinom děložního hrdla.
Klíčová slova: ovarium – mucinózní cystadenokarcinom – murální uzel – anaplastický karcinom – cervikální karcinom

Summary

Solid mural nodule within a mucinous cystic ovarian tumor occurs more often than generally presumed. One especially interesting case involving coincidental cervical carcinoma is presented.
A 38-year-old woman underwent exploratory laparotomy for a right ovarian tumor. After ovarian malignancy had been diagnosed from frozen section, the bilateral salpingo-oophorectomy and hysterectomy was performed. The tumor had a unilocular cystic cavity and a mural nodule. The nodule showed undifferentiated carcinomatous features. The immunohistochemical examination revealed atypical cells in the nodule which were positive for cytokeratin, CEA, and vimentine, establishing its anaplastic nature. A synchronous cervical invasive squamous carcinoma was documented. The patient was treated with chemotherapy and radiotherapy. Currently, at 15 postoperative months, she is well and free of disease.
The occurrence of ovarian mucinous cystadenocarcinoma with mural nodule of anaplastic carcinoma and cervical squamous cell carcinoma is evidently very uncommon, because we have not found a similar case in the literature.
Key words: ovary – mucinous cystadenocarcinoma – mural nodule – anaplastic carcinoma – cervical carcinoma

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Mural nodules have been reported to occur in mucinous cystic tumors of the ovary and pancreas (8, 12). A single case has been reported to be associated with a mucinous tumor of the gallbladder (14) and a few cases associated with cysts in the cerebral hemispheres (7). Mural nodules can be associated with benign, borderline or malignant mucinous cystic ovarian tumors (24). These mural nodules may be malignant (anaplastic carcinoma, sarcoma or carcinosarcoma) or benign (sarcoma - like) (24).

To our knowledge, nineteen cases of ovarian

mural nodules composed of anaplastic carcinomas have been reported, and one additional case is presented: 18 with mucinous tumors (11 cystadenocarcinomas, 4 borderline and 3 benign) and 2 with serous borderline tumors (1, 3–5, 13, 15, 17, 18, 23).

Several cases with multiple coexistent or subsequent primary gynecological cancers are reported in the literature (10, 21).

We present a case of ovarian mucinous cystadenocarcinoma with a mural nodule of anaplastic carcinoma and simultaneous cervical carcinoma.

Case report

A 38-year-old woman was admitted to the hospital because of a painless pelvic mass. Her gynecologic and obstetric histories were silent. She had regular 30-day menstrual cycles. Physical examination revealed a large, fixed, painless right ovarian mass. She had a normal-sized left adnexa and uterus.

A transabdominal ultrasound study demonstrated a 12-cm round mass with mixed cystic and solid echogenicities in the right lower abdomen. Computer tomography showed a right cystic lesion with a mural nodule. The cyst had a smooth, thin wall with focal wall thickening and minimal edema. Serum CA125 was elevated (48.36 U/ml). The other laboratory data were normal.

A staging exploratory laparotomy was performed. A large cystic mass in the right ovary was confirmed. A bilateral salpingo-oophorectomy, Hartmann's operation, and hysterectomy were performed. A malignant tumor was diagnosed in the right ovary during the operation by frozen section. The FIGO stage of ovarian tumor was IA.

After the peritoneal cavity was opened, a thorough inspection and palpation of the peritoneal cavity was made to exclude evidence of metastasis. There was no ascitic fluid, adhesion or other suspicious findings.

The postoperative course was without complication. She was treated with adjuvant chemotherapy with cisplatin, adriamycin and cyclophosphamide; also adjuvant external pelvic radiation and brachytherapy for treatment of the cervical carcinoma. Upon completion of six cycles of chemotherapy the value of CA125 returned to normal (< 35 U/ml). Currently, 15 months later, the patient is well. She was given a pelvic examination (including the inguinal region), vaginal cytology and tumor marker follow-up every three months.

Pathologic examinations

All surgical specimens were fixed in 10% buffered formalin and embedded in paraffin for routine histopathologic examination. Five-micrometer tissue sections were stained with hematoxylin and eosin (H&E), periodic acid Schiff (PAS) and alcian blue (pH 2.5).

Representative formalin-fixed paraffin-embedded sections from the mural nodule were studied with indirect immunoperoxidase techniques (avidin-biotin complex) (11). The reaction was developed with 3-amino-9-ethylcarbazole substrate-chromogen (DAKO). The primary monoclonal and polyclonal antisera used were as follows: (a) anti-cytokeratin AE1/AE3 (DAKO); (b) anti-desmin (Signet Laboratories); (c) anti-vimentin (Signet Laboratories); (d) antimyoglobulin (Signet Laboratories); e) carcinoembryonal antigen-CEA (DAKO) and f) epithelial membrane antigen - EMA (DAKO).

Gross pathology findings

The right ovarian cystic mass measured 15.5 cm in diameter. The outer tumorous surface was lobular. The cut surface of the right ovarian tumor showed an unilocular cyst with focal thickening of the wall. There was a large protruding solid nodule, measuring 11x11x5 cm. The nodule was firm, grey-yellow with focal haemorrhage and necrosis on the cut surface. The cystic space was filled by dark-brown bloody fluid. The left adnexa and uterus was of a normal size. Carcinoma of the cervix was not seen.

Microscopic findings

Hematoxylin-eosin-stained slides from the wall of the right ovarian mucinous tumor revealed mucin producing tumorous cells, which formed microcysts and papillae. There were cellular atypias, mitoses and stratification on multiple sections (fig. 1).

The nodule was composed of a bizarre, pleomorphic, densely cellular population with a sarcomatous appearance (fig. 2). Numerous clusters of neoplastic cells had oval or spindle-shaped hyperchromatic nuclei with prominent nucleoli and abundant eosinophilic moderately granular cytoplasm. Many of the atypical

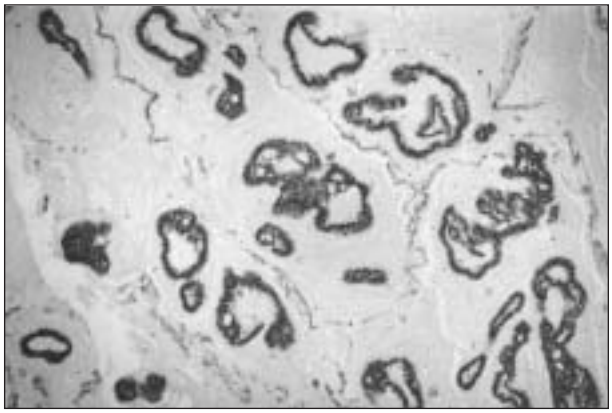

Fig. 1. Mucinous ovarian cystadenocarcinoma. H&E staining, x200

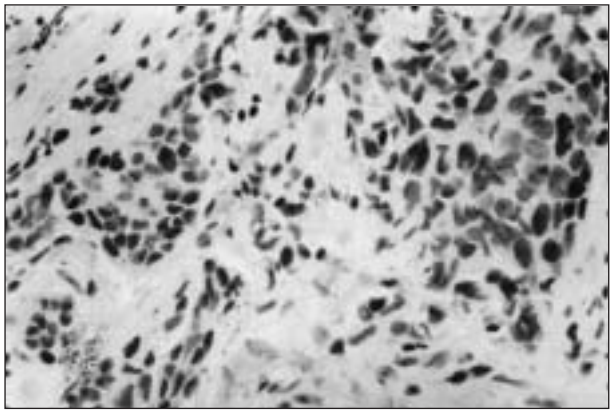

Fig. 3. Mural nodule composed of anaplastic carcinoma. Neoplastic cells positive for CEA. Immunostaining, x200

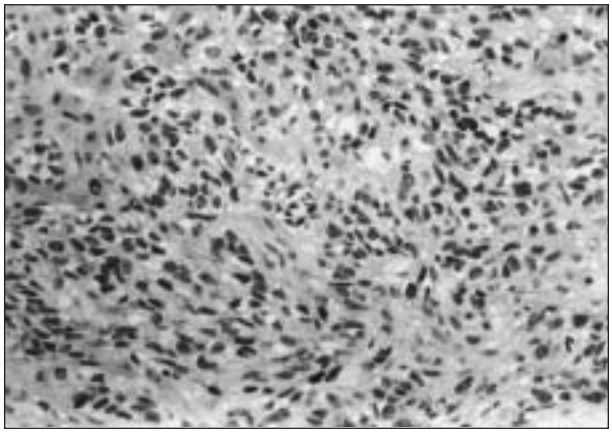

Fig. 2. Mural nodule composed of anaplastic carcinoma. H&E staining, x200

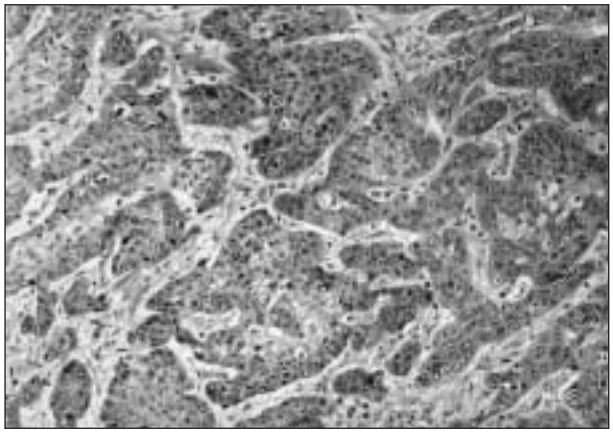

Fig. 4. Squamous cervical carcinoma. H&E staining, x100

tumorous cells were multinucleated and showed several large nucleoli. Mitotic figures were frequently seen. Small areas of necrosis, haemorrhage, foam cells accumulation, and diffuse mixed inflammatory infiltrate were also seen. Histochemically, the neoplastic cells were alcian blue-positive and PAS-negative.

Immunohistochemically, the pleomorphic tumor cells showed diffuse cytoplasmic positivity for cytokeratin, CEA (fig. 3), and EMA, and focal positivity for vimentin. Desmin, and myoglobin were negative.

Flow cytometry revealed that the neoplastic cells of the mural nodule anaplastic carcinoma were DNA diploid.

On the microscopical level, an invasive squamous, well - differentiated carcinoma was found in the cervical stroma (fig. 4). Immunohistochemically, the neoplastic cells showed a strong reactivity for cytokeratin (fig. 5). There was no invasion in the vaginal stump and the parametrium. The FIGO staging of carcinoma of the cervix uteri was I B.

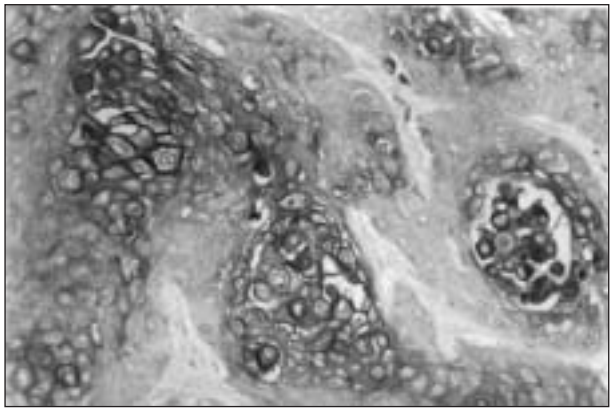

Fig. 5. Squamous cervical carcinoma. Neoplastic cells positive for cytokeratin. Immunostaining, x200

Discussion

The occurrence of mural nodules in mucinous tumors of the ovary and pancreas is well documented (2, 3, 6, 16-20, 22). As the term

implies, the nodules usually occur in the walls of cystic mucinous tumors. These mural nodules are classified according to WHO (24).

Although it is important to distinguish between the mural nodule subtypes, they are frequently difficult to separate by histologic methods alone because of their overlapping morphologic features. Several authors (3, 13, 15, 23) have pointed out the usefulness of immunohistochemistry in characterising mural nodules. Nichols et al. (15) reported that immunohistochemical study of the mural nodule revealed strong coexpression of cytokeratin and vimentin, supporting a diagnosis of anaplastic carcinoma. The carcinomatous nature of the nodule in the presented case was also confirmed by immunohistochemistry.

In 1982, Prat et al. (18) reported a case of an ovarian mucinous tumor accompanied by 0.5 x 1.7-cm nodules of anaplastic carcinoma, in which the nodules developed rapidly into a widespread peritoneal metastasis; the patient died 4 months later. Our patient, who had ovarian mucinous cystadenocarcinoma with mural nodule of anaplastic carcinoma and squamous carcinoma of the cervix is in a good health 15 months after surgery.

As in the literature, the flow cytometry revealed that the neoplastic cells of the mural nodule anaplastic carcinoma were DNA diploid (9).

The pathogenesis of the nodule in mucinous tumors remains unclear, but there have been several hypotheses. Prat and Scully (16) proposed that the concept of a collision tumor, which is the result of a collision between 2 neoplasms that have arisen in adjacent areas, might be the best explanation for the pathogenesis. Czernobilsky et al. (5) reported a nodule developing as a result of progressive dedifferentiation of mucinous cells, with a concomitant loss of the ability to produce mucin. Both hypotheses are possible in our tumor. Further studies are necessary before the pathogenesis of this interesting type of lesion can be fully clarified.

Conclusion

Ovarian mucinous cystadenocarcinoma with mural nodule of anaplastic carcinoma is a very rare tumor. It is necessary to distinguish the types of mural nodules, as the prognosis depends on its structure. The occurrence of an ovarian mucinous cystadenocarcinoma with mural nodule of anaplastic carcinoma and a cervical squamous carcinoma is evidently very uncommon; we have not found a similar case in the literature.

References

1. **Baergen RN, Rutgers JL.** Mural nodules in common epithelial tumors of the ovary. Int J Gynecol Pathol 1994;13:62–72. – 2. **Baergen RN, Rutgers JL.** Classification of mural nodules in common epithelial tumors of the ovary. Adv Anat Pathol 1995;2:346–351. 3. **Chan YH, Ho HC, Ma L.** Ovarian mucinous tumor with mural nodules of anaplastic carcinoma. Gynecol Oncol 1989;35:112–119. – 4. **Clarke TJ.** Sarcoma-like mural nodules in cystic serous ovarian tumors. J Clin Pathol 1987;40:1443–1448. – 5. **Czernobilsky B, Dgani R, Roth LM.** Ovarian mucinous cystadenocarcinoma with mural nodule of carcinomatous derivation: a light and electron microscopic study. Cancer 1983;51:141–148. – 6. **Fujii S, Konishi I, Kobayashi F, Okamura H, Yamabe H, Mori T.** Sarcoma-like mural nodules combined with a microfocus of anaplastic carcinoma in mucinous ovarian tumor. Gynecol Oncol 1985;20:219–233. – 7. **Garg A, Suri A, Gupta V.** Cyst with a mural nodule: unusual case of brain metastasis. Neurology India 2004;52(1):136. – 8. **Guibeau C, Soubeyrand MS, Devillebichot C, Sage M, Collin F, Arnold L.** Mural nodules of anaplastic carcinoma in bilateral ovarian borderline mucinous cystadenoma: a case report. Ann Pathol 2003; 3(4):340–344. – 9. **Hellemans, H, Moerman, P, Timmerman, D, Vergote, I:** Anaplastic nodules in an ovarian mucinous tumor. Case report and literature review. Eur J Gynaecol Oncol, 1998; 19: 529–533. – 10. **Hemminki K, Aaltonen L, Li X.** Subsequent primary malignancies after endometrial carcinoma and ovarian carcinoma. Cancer 2003;97(10): 2432–2439. – 11. **Isu SM, Raine L, Fanger H.** Use of avidin-biotin-peroxidase complex (ABC) immuno-peroxidase techniques. A comparison between ABC and unlabelled antibody (PAP) procedures. J Histoch Cytochem 1981;29:177–80. – 12. **Kawai M, Uchiyama K, Tani M, Onishi H, Kinoshita H, Ueno M, Hama T, Yamane H.** Clinicopathological features of malignant intraductal papillary mucinous tumors of the pancreas: the differential diagnosis from benign entities. Arch Surg 2004; 139(2): 188–192. – 13. **Kessler E, Halpern M, Koren R, Dekel A, Goldman J.** Sarcoma-like mural nodules with foci of anaplastic carcinoma in ovarian mucinous tumor: clinical, histological, and immunohistochemical study of a case and review of the literature. Surg Pathol 1990; 3: 211–219. – 14. **Mizuno T, Eimoto T, Tada T, Tateyama H, Inagaki H, Murase T.** Mucinous tumor of the gallbladder with a separate nodule of anaplastic carcinoma. Arch Pathol Lab Med 1999;123:1280–1284. – 15. **Nichols GE, Mills SE, Ulbright TM, Czernobilsky B, Roth LM.** Spindle cell mural nodules in cystic ovarian mucinous tumors: a clinicopathologic and immunohistochemical study of five cases. Am J Surg Pathol 1991;15:1055–1062. – 16. **Prat J, Scully RE.** Sarcomas in ovarian mucinous tumors: a report of two cases. Cancer 1979; 44:1327–1331. – 17. **Prat J, Scully RE.** Ovarian mucinous tumors with sarcoma-like mural nodules: a report of seven cases. Cancer 1979; 44: 1332–1344. – 18. **Prat J, Young RH, Scully RE.** Ovarian mucinous tumors with foci of anaplastic carcinoma. Cancer 1982; 50: 300–304. – 19. **Rego JAG, Ruvira LV, Garcia AA, Freijanes MPS, Penaranda JMS, Soto JMR.** Pancreatic mucinous cystadenocarcinoma with pseudosarcomatous mural nodules: a report of a case with immunohistochemical study. Cancer 1991;67:494–498. – 20. **Sondergaard G, Kaspersen P.** Ovarian and extraovarian mucinous tumors with solid mural nodules. Int J Gynecol Pathol 1991;10: 145–155. – 21. **Studzinski Z, Filipczak A, Branicka D.** Coexistence of ovarian adenocarcinoma with tubal pregnancy and plano-epithelial cervical cancer of uterus. Ginekol Pol; 69(11):805–808. – 22. **Tsujimura T, Kawano K, Taniguchi M, Yoshikawa K, Tsukaguchi I.** Malignant fibrous histiocytoma coexistent with mucinous tumor of the pancreas.

Cancer 1992;70:2792–2796. – 23. **Tsuruchi N, Kaku T, Kinoshita H. et al.** Ovarian mucinous cystadenocarcinoma with sarcoma-appearing mural nodule of anaplastic carcinoma. Gynecol Oncol 1993;50:259–263. – 24. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press: Lyon 2003, s. 117–145.

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RECENZE

Josef Závada: **Syndrom multiorgánové dysfunkce**. Praha, Grada 2001, 254 s., ISBN 80-7169-781-8

S rozvojem lékařství se postupně podařilo zvládat jednotlivé situace ohrožující život. Pacienta je dnes možno úspěšně převádět přes ty fáze onemocnění, ve kterých dříve umíral. U části nemocných se však daří smrt pouze oddálit. Ta nakonec nastává za postupného selhávání jednotlivých orgánových systémů (plíce, játra, ledviny, hemokoagulace aj.). Pro tyto situace byl posléze zaveden termín „Multiple Organ Failure" – MOF. Hlavním spouštěcím mechanismem MOF jsou šokové stavy a sepse.

K rozvoji MOF však dochází i u pacientů s neinfekčním onemocněním (pankreatitida, trauma), v období před bakteriální infekcí. Takoví pacienti mohou mít příznaky sepse, ač žádné infekční ložisko u nich není přítomné. Nemocní však přitom vykazují všechny klasické příznaky zánětu, jako horečku, vazodilataci, povšechný edém i porušení funkcí několika systémů. To vedlo k názoru, že podstatným mechanismem MOF je systémový zánět, označený posléze jako „Systemic Inflammatory Respiratory Syndrome" – SIRS.

SIRS může být vyvolán jak infekcí, tak i jiným fyzikálním či chemickým poškozením (např. hypoxií). Zánět v takových případech ztrácí obranný či reparativní charakter a nabývá autoagresivní povahu.

Samotná sepse je potom definovaná jako SIRS v důsledku pokročilého infekčního procesu.

Uvedená monografie rozebírá velmi přehledně etiologii a patogenezi SIRS/MOF. V přehledu zmiňuje úlohu hemokoagulace, buněk zúčastněných v zánětlivém procesu a cytokinů. Rozebírá význam ischémie – reperfuze a dále průvodní hormonální a metabolické změny. Významným faktorem je stále infekce.

V druhé polovině knihy autor rozebírá průběh selhávání jednotlivých životně důležitých orgánů a příslušné léčebné postupy. Vychází přitom z vlastních zkušeností, které doplňuje literárními poznatky.

Publikace, která vyšla před třemi lety, zpracovává písemnictví jen do roku 2000 a je zaměřena, až na dvě stránky s morfologickými údaji, převážně patofyziologicky a klinicky. Zdánlivě jsou tedy její údaje zastaralé. Její přínos pro patology však spočívá v tom, že jednotícím způsobem shrnuje poznatky, k nimž jsme se sami léty propracovávali ve své autoptické praxi.

L. Peychl, Kolín