Review article

PSEUDOMYXOMA PERITONEI AND MUCINOUS OVARIAN TUMORS

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Pseudomyxoma peritonei (PMP) is a clinical condition characterized by copious amounts of mucinous ascites and mucinous peritoneal implants. Female patients with PMP often have synchronous ovarian and appendiceal tumors. Three pathohistological diagnostic categories of PMP are described as follows: peritoneal mucinous carcinomatosis (PMCA) which represents high-grade metastatic adenocarcinoma usually derives from the appendix or colon; peritoneal mucinous carcinomatosis with intermediate or discordant features (PMCA-I/D) which is characterized by peritoneal lesions composed of abundant extracellular mucus and epithelium showing focal proliferation and minimal atypia; and disseminated peritoneal adenomucinosis (DPAM) which represents an indolent proliferation of benign or minimally atypical neoplastic mucinous cells nearly always derive from a ruptured mucinous neoplasm of the appendix. The term PMP is not sufficiently specific to be used as a histopathological diagnosis. *Acta Medica Medianae 2009;48(1): 46-49.*

***Key words**: pseudomyxoma peritonei, mucinous tumors, ovary, appendix*

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Introduction

Pseudomyxoma peritonei (PMP) is a clinical syndrome characterized by copious amounts of mucinous ascites and mucinous peritoneal implants.

The incidence of PMP is approximately two per 10 000 laparatomies and about 75% of patients are female (1,2). The most common sites of origin of PMP are tumors of the appendix, colon and ovary (2-8). Other origins of PMP have been described, including the lung, fallopian tube, uterus, urachus, common bile duct, pancreas and stomach (9-14).

Approximately 44% of women with PMP have ovarian mucinous tumor (3,8). It is generally accepted that the ovarian involvement in women with PMP is secondary; PMP is nearly always of gastrointestinal origin, usually from a mucinous adenoma of the appendix (2,3,8,15). The most frequently observed symptoms of PMP are abdominal distension due to the progressive accumulation of mucinous ascites, presence of ovarian mass, and appendicitis-like symptoms (2,16,17).

Some investigators (8,18,19,20) have proposed that clinical presentation and gross appearance of PMP encompass three distinct histopathological entities: peritoneal mucinous carcinomatosis (PMCA), which is histopathologically a high-grade metastatic adenocarcinoma usually from the appendix or colon with a high early mortality rate; peritoneal mucinous carcinomatosis with intermediate or discordant features (PMCA-I/D), which is characterized by peritoneal lesions composed of abundant extracellular mucus, showing epithelium with minimal atypia or mitotic activity and with limited focal proliferation; and disseminated peritoneal adenomucinosis (DPAM), which is an indolent proliferation of histopathologically benign or minimally atypical neoplastic mucinous cells nearly always derived from a ruptured mucinous neoplasm of the appendix. The mucinous epithelium released from the appendiceal neoplasm implants on peritoneal surfaces and is capable of producing a large amount mucin. The mucinous epithelium has little capacity to invade tissue, but the mucin that accumulates in the peritoneal cavity is an irritant which induces fibrosis and adhesions.

Gross features

Pseudomyxoma peritonei is characterized by copious amounts of mucinous ascites and mucinous peritoneal implants (Figure 1).

Figure 1. Pseudomyxoma peritonei – gross appearance

Mucinous ovarian tumors associated with PMP are bilateral in 80% of cases with a mean diameter of 7 cm (3). When unilateral, there is a right-sided predominance. In DPAM, the ovaries are often cystic and usually display mucoid surface, surface nodules, or implants. In PMCA, the ovaries can appear similar but are more often solid (3,8). In 75% of patients with PMP, there is gross or microscopic evidence of rupture of the appendiceal tumor (3). Appendiceal rupture can be very small, can heal or can be overlooked as a result of inadequate sampling and these are the best explanations for most of the remaining 25% of apparently unruptured appendices (3).

Histopathology

Histopathologically, DPAM is characterized by pools of mucin with mucinous epithelial cells without significant cytologic atypia or mitotic activity (Figure 2) and without invasion of tissues. In PMCA, pools of mucin contain mucinous epithelial cells showing moderate to marked cytologic atypia and significant mitotic activity. Mucinous epithelial cells display invasive growth pattern (2,3).

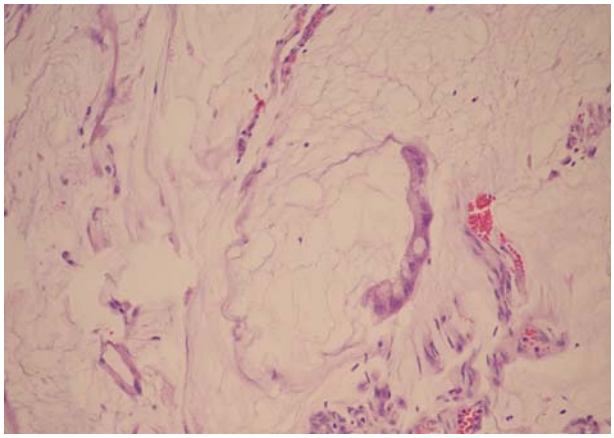

Figure 2. Pseudomyxoma peritonei – histopathological appearance (HE, x200)

The majority of tumors associated with PMP display mucoid nodules or implants involving the ovarian surface. Superficial or deep cortical involvement is seen in more than 50% of cases, and about 25% are confined to the ovarian stroma (3). Pseudomyxoma ovarii, an appearance characterized by dissection of acellular lakes of mucin throughout the ovarian stroma, is presented in two-thirds of cases and is usually multifocal or extensive.

In DPAM, the ovarian tumor is composed of pools of mucin with simple or focally proliferative mucinous epithelium displaying minimal cytologic atypia and rare mitotic figures. The mucinous epithelium contains mucin and basally located nuclei, and closely resembles the gastric foveolar-type epithelium. The ovarian tumors of this morphology are nearly always associated with appendiceal adenomas without significant atypia (3). Histopathologically, the ovarian mucinous tumor closely resembles to the peritoneal mucinous lesions as well as the appendiceal adenoma (3).

In PMCA, the ovarian mucinous tumor is characterized by epithelial proliferation and moderate to marked cytologic atypia or presence of signet-ring cells, significant mitotic activity, and obvious stromal invasion (2,3).

Immunohistochemistry

Immunohistochemical and molecular biologic studies have provided evidence that the bland appearing mucinous tumors associated with PMP involving the ovaries are secondarily and derived from the associated appendiceal mucinous tumor (20-25). The immunohistochemical profile of these ovarian tumors is similar to the associated appendiceal mucinous adenoma in the majority of cases. The ovarian mucinous tumors associated with PMP display diffusely positive staining for cytokeratin 20 and negative staining for cytokeratin 7 (Figures 3 and 4).

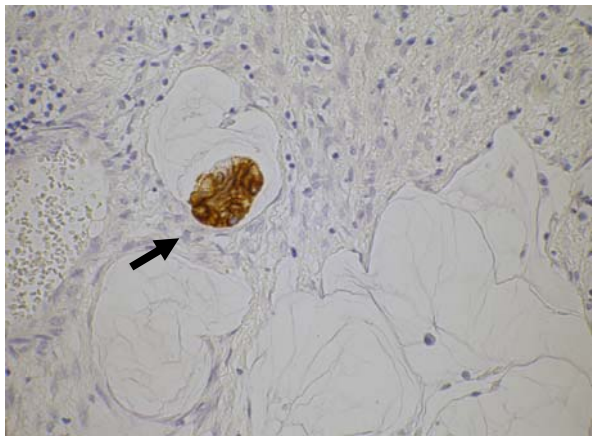

Figure 3. Mucinous ovarian tumor – positive reaction for cytokeratin 20 (LSAB, x200)

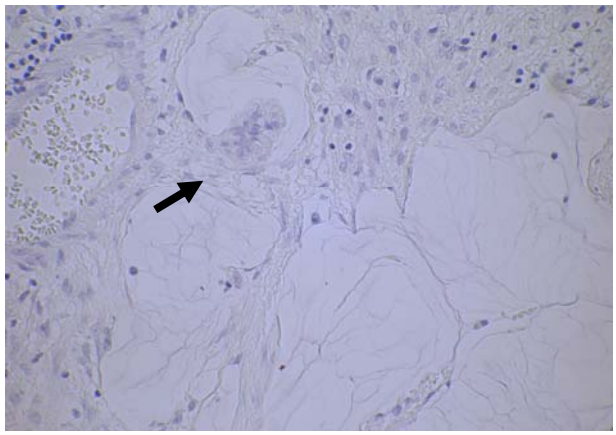

Figure 4. Mucinous ovarian tumor – negative reaction for cytokeratin 7 (LSAB, x200)

In contrast, primary ovarian mucinous tumors are all diffusely positive for cytokeratin 7 (20-22). They can also be positive for cytokeratin 20, but the distribution of positivity is often patchy, in contrast to PMP cases in which cytokeratin 20 staining is strong and diffuse. Molecular studies have demonstrated identical K-ras mutations or the lack of them in both the appendiceal and the simultaneous ovarian tumors (23,24). A discordant pattern of allelic loss was demonstrated in few

cases, characterized by loss of heterozygosity in the ovarian tumors but not in the appendiceal adenomas; this reflects the acquisition of additional genetic alterations in ovarian tumors as a part of tumor progression but can indicate that some simultaneous tumors of the appendix and the ovary are independent primaries (24,25).

Clinical behavior

Cases of PMP designated DPAM are nearly always associated with appendiceal mucinous adenomas and constitute the classic description of PMP found in the older literature, in which behavior of PMP is characterized as slow progressive, reaccumulation of mucinous ascites, and compatible with prolonged survival if treated symptomatically by periodic evacuation of the ascites (2-4,8,19). In contrast, those cases of PMP designated PMCA are metastatic mucin-secreting carcinomas from the appendix or colon and they are associated with an aggressive clinical course (more 90% of patients die within 3 years) (2-4,8,19).

Conclusion

The term pseudomyxoma peritonei, although useful as an operative and gross description, lacks sufficient specificity for use as a histopathologic diagnosis.

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PSEUDOMYXOMA PERITONEI I MUCINOZNI TUMORI JAJNIKA

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Pseudomyxoma peritonei (PMP) je kliničko stanje koje se karakteriše obilnim mucinoznim ascitesom i mucinoznim peritoneumskim implantatima. Bolesnice sa PMP često imaju sinhroni mucinozni tumor jajnika i apendiksa. Opisane su tri histopatološke forme PMP i to: peritoneumska mucinozna karcinomatoza, koja predstavlja metastatski adenokarcinom visokog gradusa, koji obično potiče iz apendiksa ili kolona; peritoneumska mucinozna karcinomatoza sa intermedijarnim ili neodređenim obeležjima, koju karakterišu peritoneumske lezije sastavljene od obilne ekstracelularne sluzi i epitela koji pokazuje fokalnu proliferaciju i minimalnu atipiju; diseminovana peritoneumska adenomucinoza, koja predstavlja indolentnu proliferaciju benignih ili minimalno atipičnih neoplastičnih mucinoznih ćelija koje gotovo uvek potiču od rupturirane mucinozne neoplazme apendiksa. Termin pseudomyxoma peritonei nije dovoljno specifičan da bi se koristio kao histopatološka dijagnoza. *Acta Medica Medianae 2009;48(1):46-49.*

Ključne reči: *Pseudomyxoma peritonei, mucinozni tumori, jajnik, apendiks*