腹膜偽粘液腫（pseudomyxoma peritonei）における中皮下リンパ管系の形態的変化

三浦真弘[1]　紀　瑞成[1]　米村　豊[2]

[1]大分大学医学部生体構造医学講座（解剖学 1）　[2]NPO 法人腹膜播種治療支援機構

緒　言

腹膜偽粘液腫（以下 PMP）は，腹腔内に多量の腫瘍性粘液が播種すると同時に大量の粘液性腹水が貯留する比較的稀な病態を示す[1]．PMP 発症に伴い経リンパ腹水吸収動態が急激に変化することが予想されるが，同現象と中皮下リンパ管網（以下 SMLN）との関係を論じた研究は存在しない．本研究では，PMP の腹膜播種進展に応じた SMLS の形態的変化ついて組織化学的に解析し，両者の関係について検討した．

材料と方法

検索材料は，4 名の PMP 患者の peritonectomy から得られた横隔膜腹膜を用いた．リンパ管の解析には，Whole-mount 伸展試料及び OCT 凍結切片に酵素二重（5′-nucleotidase-alkaline phosphatase：以下 5′-Nase, ALPase）染色[2]と D2−40免疫染色を用いた．SMLN の発達した腹膜領域について SEM を用いて中皮ならびに膠原線維板の微細構築と脈管外通液路（以下 PLC）との関連性についても観察した．

結　果

1．伸展試料：腫瘍嚢胞が小さく疎な腹膜領域では横隔膜全域に lymphatic lacunae（LL）を含む 5′-Nase 陽性の密性 SMLN が描出された（Fig. 1）．SMLN は，ALPase 陽性血管を基軸とした典型的な樹状形態を呈さず盲端部の少ない網工を呈した．SMLN 発達領域では lymphatic islands[2]の出現も認められた．横隔膜では SMLN と中皮下結合組織層との間にリンパ小孔（lymphatic stomata）を想起させる染色所見（Fig. 2）も観察された．腹膜表面に増殖した腹膜小突起（PP）や小粘液嚢胞壁には既存の SMLN から伸展したリンパ管（Fig. 3）が侵入した．

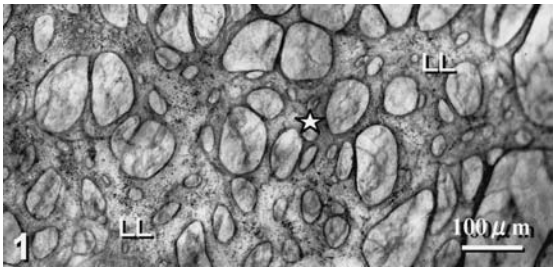


Fig. 1　Light micrograph of a whole-mount preparation of the subserosal lymphatic networks（☆）in the diaphragmatic peritoneum stained with 5′-Nase
LL: lymphatic lacunae

2．凍結切片試料：小型腫瘍辺縁には SMLN の発達と腫瘍内へのリンパ管侵入が認められた．一方，大型粘液嚢胞が密集する腹膜では嚢胞壁間が狭小でリンパ管数が激減した．5′-Nase・D2−40陽性リンパ管は，中皮下組織の浅層に広がる浸潤リンパ球（以下 IL）集族内およびその深層領域に新生リンパ管として多数認められた（Fig. 4）．

3．SEM 試料：横隔膜・モリソン窩腹膜において mesothelial stomata と中皮下膠原線維板に散在して篩状斑構造（以下 MC）が多数認められた．

考　察

著者らはこれまでサル SMLN の微細構築の解明を試みてきた[3]．今回，ヒト腹膜において PMP の病態に応じた SMLN の形態的変化について検討を行った．

本検索結果から，PMP 初期病態では，SMLN は新生リンパ管の出現を含めて顕著に発達することで経リンパ腹水吸収能の亢進が示唆された．一方，腫瘍嚢胞が密集・巨大化した後期病態では，腫瘍周囲を中心に既存および発達した SMLS は消失または減少することで，粘液性腹水の増加に経リンパ腹水吸収能が適応できない非生理的不均衡が生じることが示唆された．PLC に関しては，横隔膜・モリソン窩腹膜において，中皮下膠原線維板に多数の MC が確認されたことから，これらの腹膜では PLC を介する経リンパ腹水吸収能が他の腹膜領域より極めて高いことが推測された．

文　献

1）Yan H, Pestieau SR, Shmookler BM, Sugarbaker PH. 2001. Histopathologic analysis in 46 patients with pseudomyxoma peritonei syndrome: failure versus success with a second-look operation. Mod Pathol 14: 164–171

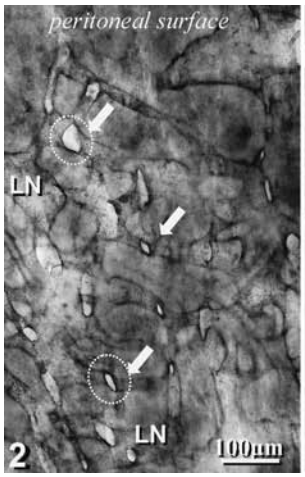
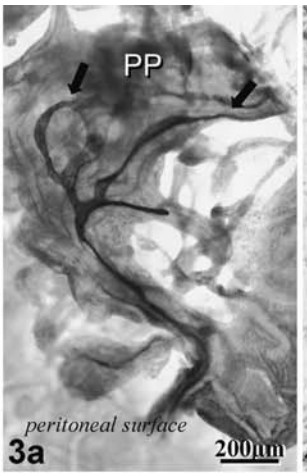


Fig. 2 Light micrograph of a whole-mount preparation of the diaphragmatic peritoneum stained with 5′-Nase. *Arrows* indicate lymphatic stoma-like structure between the lymphatic networks (LN) and submesothelial gap (*dotted circles*) on peritoneal surface.



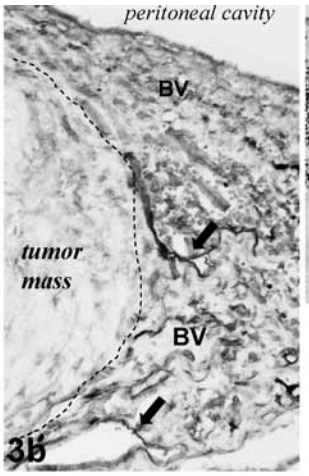


Fig. 3 Light micrographs of the whole-mount preparation of peritoneum with peritoneal projection (a) and cryostat section of peritoneum with a mucinous tumor in the early pathological stage
3a: 5′-Nase staining. Newly formed lymphatic vessels (*arrows*) extend in the peritoneal projection (PP).
3b: 5′-Nase-ALPase double staining. Well-developed 5′-Nase-positive lymphatics (*arrows*) are seen in the peritumoral tissue layer.
BV: blood vessels ×100

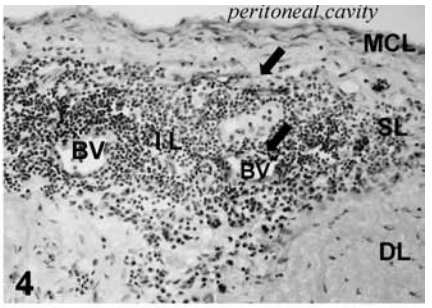


Fig. 4 Light micrograph of cryostat section of non-mucinous cystic peritoneum stained with D2–40 immunostaining for lymphatic vessels (*arrows*). ×200
BV: blood vessels, DL: deep layer of submesothelial tissue, IL: infiltrating lymphocytes, MCL: mesothelial cell layer, SL: superficial layer of submesothelial tissue

2) Miura M, Ji RC et al. 2002. Demonstration of lymphatic networks in monkeys pelvic peritoneum during pregnancy: an enzyme-histochemical observation. Lymphology 35(Suppl): 17–75

3) Miura M, Kato S. 2000. Distribution and organization of peritoneal lymphatics: enzyme-histochemical observation. Jpn J Lymphology 23: 23–32

The morphological changes in the submesothelial lymphatic vessel system in the pseudomyxoma peritonei

Masahiro MIURA[1], Rui-Cheng JI[1], Yutaka YONEMURA[2]
[1]*Department of Human Anatomy, Faculty of Medicine, Oita University,* [2]*Organization to support Peritoneal Dissemination Treatment*

Pseudomyxoma peritonei (PMP) exhibits a relatively rare pathogenesis in that a massive amount of tumorous mucus is mucinous tumor disseminated on the peritoneal surface and a large amount of mucinous ascites is retained at the same time. As for the mechanism of dissemination, it has been generally considered that mucinous substances, are accumulated in the primary lesion and tumor cells are scattered in the peritoneal cavity by the serosal perforation and floating cells form metastatic lesions with the proliferative region of subperitoneal lymphatic vessels as their center. In this study, morphological changes in the submesothelial lymphatic networks (SMLN), which are predicted to show alterations in the dynamics of absorbing ascites via the lymphatic system with the onset of PMP, were mainly examined enzyme-histochemically with light and electron microscopy. Peritoneum from different peritoneal zones was removed by peritonectomy techniques in five patients with PMP. Whole-mount preparations of each peritoneum and cryostat sections were stained with 5′-Nase-ALPase double staining and D2–40 immunostaining. In the peritoneal region with well-developed lymphatic networks, the fine structure related to the prelymphatic channel was observed by SEM. In whole-mount preparations, 5′-Nase-positive lymphatic networks and the tumor disseminated pathway on the peritoneum, were widely observed in small tumor cases. In particular, dense SMLN with lymphatic lacunae and islands locally appeared in the diaphragmatic region and Morrison's pouch. Some apical parts extending from preexisting SMLN were seen in the proliferating small peritoneal projection and single small mucinous cystic wall. No typical milky spots were observed on the peritoneum except for the greater omentum. In cryostat sections, infiltration of lymphatic vessels was widely detected in the periphery of small tumor. In the dense and proliferative region of mucinous cystic lesions, developed SMLN with tumor lymphangiogenesis were observed to be obviously reduced or even disappeared. The submesothelial cell layer on the disseminated peritoneum had infiltrating lymphocytes and tumor cells, especially at its central portion. Numerous 5′-Nase and D2–40–positive lymphatic vessels were also distributed widely in the same deep layer. In the SEM observation, stomata with oval shapes and various sizes were seen in the diaphragmatic subperitoneal connective tissue layer. In conclusion, it was suggested that the SMLN are markedly developed in the periphery of tumors, which may greatly contribute to ascites absorption at the early stage of PMP. However, the SMLN were less developed mostly in the peritumor region, which caused an imbalance between ascites production and absorption via the lymphatic system at the later stage.

Key words: submesothelial lymphatic vessels, peritoneum, enzyme-histochemical staining, pseudomyxoma peritoni