# PSEUDOMYXOMA PERITONEI ARISING FROM PAPILLARY ADENOMATOUS TUMOUR OF THE APPENDIX

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Pseudomyxoma Peritonei or mucous ascites is a condition characterized by an accumulation of gelatinous material in the free peritoneal cavity. It is not a single entity of consistent origin and prognosis, but is the result of intraperitoneal extravasation of mucoid material from any origin.(10) This disorder was first described in 1884 by Werth in a patient following rupture of pseudomucinous cysts of the ovary(11). Since then approximately 500 cases of peritoneal pseudomyxoma have been reported. More than four-fifth of these, the condition was thought to be of ovarian origin.(11) Fraen kel reported a case of pseudomyxoma peritonei after rupture of mucocele of theappendix in 1901.(20) Appendiceal mucocele is an uncommon disorder and its association with pseudomyxoma peritonei is even more of a rarity(17,18). It has been estimated by Weaver(17) that only 0.11 per cent of mucocele of the appendix are followed by pseudomyxoma peritonei.

To the best of our knowledge, pseudomyxoma peritonei have never been reported in Thailand. Only one case of unruptured mucocele of the appendix has thus far been published (13). Another two cases of simple mucocele were recorded in the surgical pathology file of Chulalongkorn Hospital. Because of the rarity of this disease, we are presenting 2 patients with pseudomyxoma peritonei of appendiceal origin.

## Case Reports

**Case 1:** (H.N. 72377/12)

A sixty-one year old Thai farmer was admitted to the hospital because

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of swelling of the abdomen of two years duration. At that time he noted a gradual and painless increase in abdominal girth. He denied fever, loss of appetite, nausea, vomiting and change in bowel habit.

A year later he was treated at a provincial hospital without any improvement. Diagnosis was cirrhosis of the liver. The patient had been an alcoholic for about 30 years. Abdominal paracenthesis was attempted twice without success. During the last three months before admission the abdominal enlargement increased and he noticed some weight loss.

Physical examination revealed a chronically ill man with marked abdominal swelling (Fig 1). There was no jaundice, spider angiomata or liver pain. The heart and lungs were normal. The abdomen was bulging and tense, with dilatation of superficial veins. The liver and spleen were not palpable. The entire abdomen was dull on percussion without shifting dullness. There was no lymphadenopathy or peripheral edema. Sigmoidoscopy was normal.

Complete blood count and urinalysis were within normal limits. Stool was negative for occult blood. Serum bilirubin, thymol turbidity, alkaline phosphatase, and SGOT were normal. Serum albumin was 5.4 gm. and globulin, 1.9 gm. per 100 ml; BSP showed 8 per cent retention at 45 minutes. Abdominal film showed no abnormal calcification. Chest x-ray, upper G.I. and small bowel series revealed no abnormality. Barium enema showed deformed cecum with pressure from inside by a round soft tissue mass (Fig. 2). Abdominal tap after admission produced five ml of jelly like fluid which was sterile and negative for malignant cell.

Patient was explored with preoperative diagnosis of pseudomyxoma peritonei resulting from ruptured mucocele of the vermiform appendix. At operation the entire abdominal cavity and its contents were covered with gelatinous material. The greater omentum was markedly thickened and filled with nodules. The appendix was found imbedded in large gelatinous mass attached to the cecum.

Appendectomy and omentectomy were performed with removal of about five litres of the mucinous material. The patient made an uneventful recovery.

Gross Examination : The specimen consisted of a vermiform appendix which measured 6.0 cm. in lenght. The diameter of the proximal portion is 0.4 cm. and the distal portion, 1.5 cm. The serosa and periappendiceal fat were studded with multiple cysts containing mucinous material. These cysts varied in size, measuring from 0.5 to 1.5 cm. in diameter. On dissection, the appendix showed dilated lumen. The wall was thickened, measuring 0.4 cm. in average thickness. The mucosal surface was not smooth but grossly was free from the mass. (Fig. 3).

Microscopic Examination : A sec-

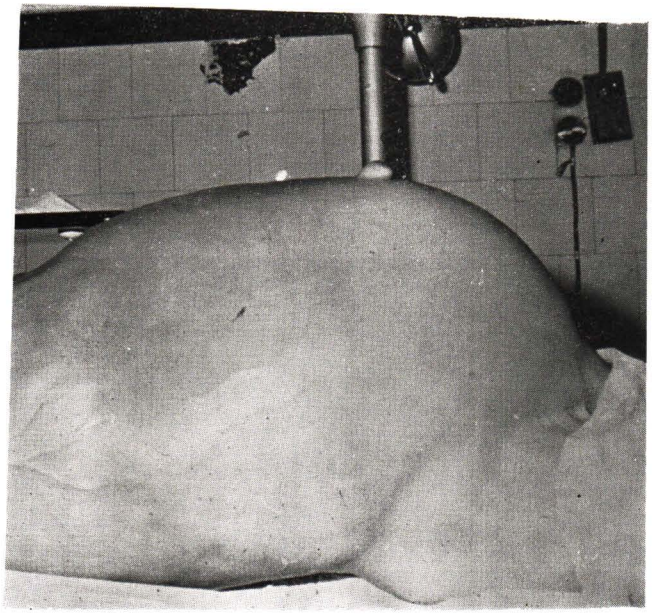

Fig. 1. The distended abdomen with prominent veins (case 1)

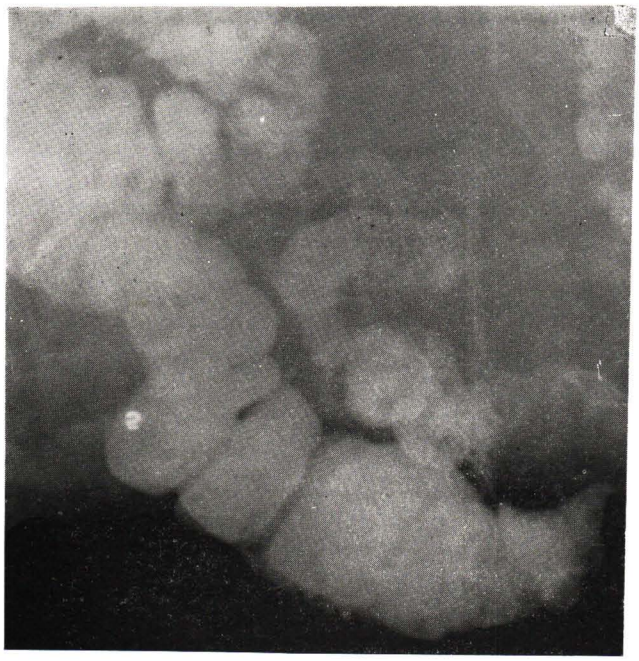

Fig. 2. Barium enema showing, wide separation of cecum from distal ileal loops due to appendiceal mass. (case 1)

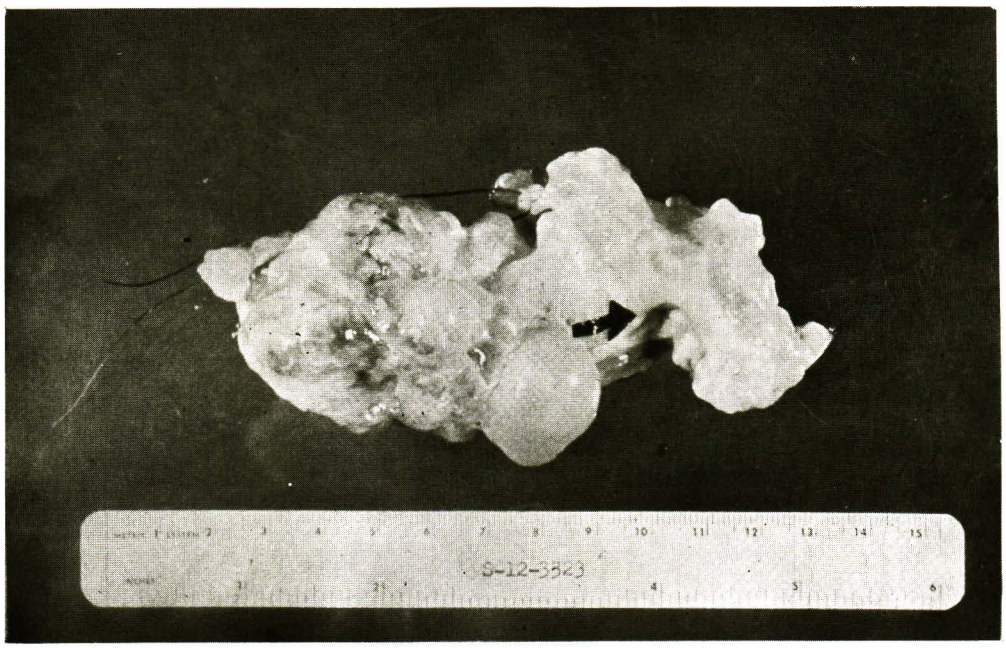

Fig 3. The Vermiform appendix with periappendiceal mucinous cyst. (Note:Stump is ligated by suture material). (case 1)

tion from the proximal portion of the appendix showed normal pattern of the mucosa and submucosa. The mucosa of the distal half showed papillary projections. The cell lining the papillary projections were tall columnar with hyperchromatic nuclei and prominent nucleoli. Abnormal mitotic figures were occasionally present. The submucosa or muscular invasion was not present. Sections of periappendiceal fat and omentum revealed mucin producing glandular epithelium in the hyalinized connective and fatty tissue. (Fig. 4, 5).

**Case 2** : (H.N. 98240/12)

A 34 year old Chinese woman was adimitted to the hospital because of increased swelling of the abdomen of 8 months duration.

The patient had experienced vague pain in the abdomen during the past 5 years. She was not an alcoholic and history of hematemesis, melena and alterations in bowel habit was denied. Lately she had been treated for pulmonary tuberculosis. She had 7 children, her youngest child was 3 years old. Her menstruation had been normal up to the time of admission.

Physical examination showed an apparently healthy woman despite the presence of marked abdominal swelling. An umbiliical hernia was evident (Fig. 6). The liver and spleen could not be palpated. Fluid thrill and shifting dullness were detected. No intraabdominal mass was found. Pelvic examination was also negative. Complete blood count, urine analysis, stool examination, and liver function tests were within normal limits. Chest X-ray revealed only minimal scar in both apices without pulmonary infiltration. Barium enema showed the small bowel being pushed up by a mass in the right lower quadrant of abdomen (Fig. 7). On abdominal paracenthesis, a small amount of fluid with gelatinous contents was obtained. Diagnosis of pseudomyxoma peritonei was made; celiotomy was performed. Four litres of fluid with mucinous material was evacuated. The appendix had been changed into a mucocele which had ruptured. Cystic masses of various sizes were found deposited on the omentum, peritoneum, wall of the intestine and right ovary. Appendectomy, omentectomy and right salphingo-oophorectomy were performed. Ten milligrams of nitrogen mustard was injected intraperitoneally. The patient made an uneventful recovery and discharged.

Gross Examination : The specimen consisted of a vermiform appendilx measuring 4.0 cm. in lenght. The praoximal portion was 1.0 cm. in diameter. The distal portion revealed a diverticulum-like structure, located at 0.5 cm. from the tip of the appendix, measuring 2.0 cm. in diameter. This punch-out saccular lesion showed a small perforation, 0.5 cm. in diameter. The serosa of the appendix and periappendiceal tissue were diffusely infiltrated by cysts containing mucous substance. These cysts va-

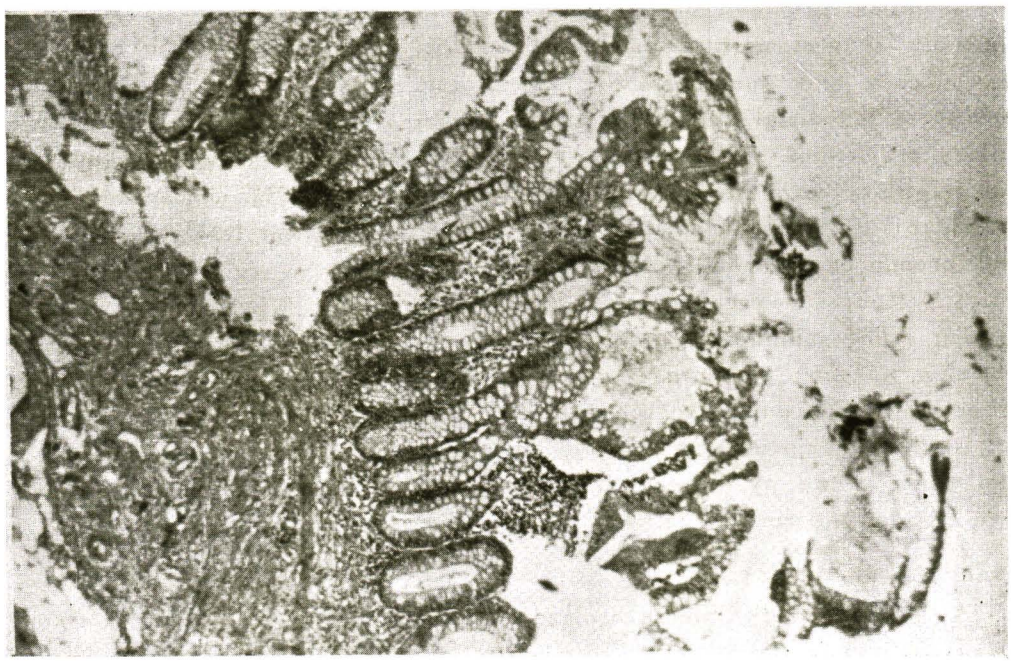

Fig. 4. The Appendix showing normal mucosa adjacent to area of papillary projection. H & E x 50

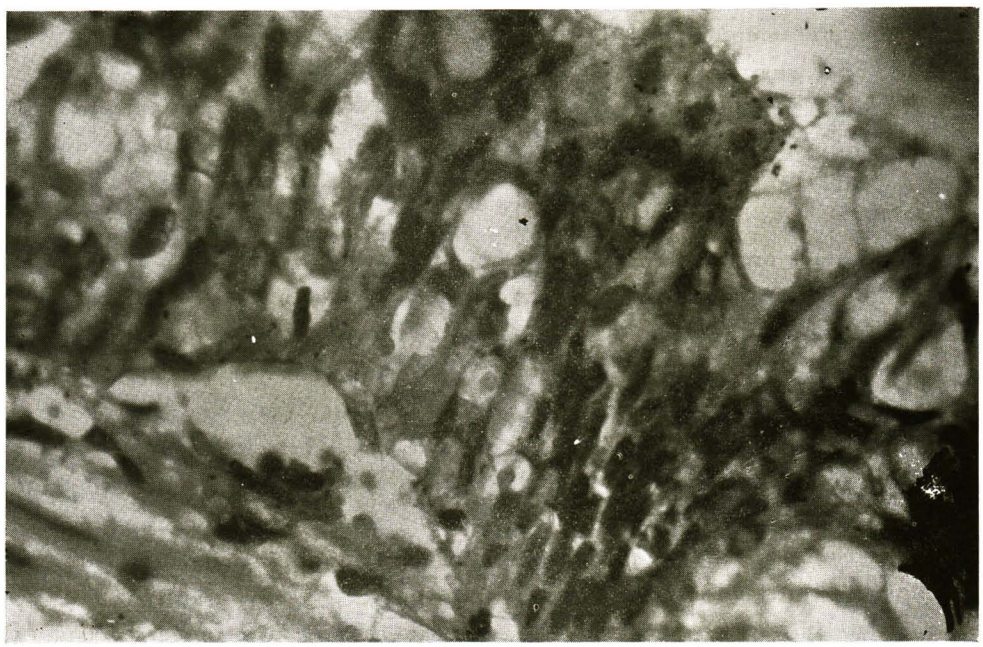

Fig. 5. Mucosa of the appendix showing loss of polarity of cell, with enlarged hyperchromatic nuclei. H & E x 400

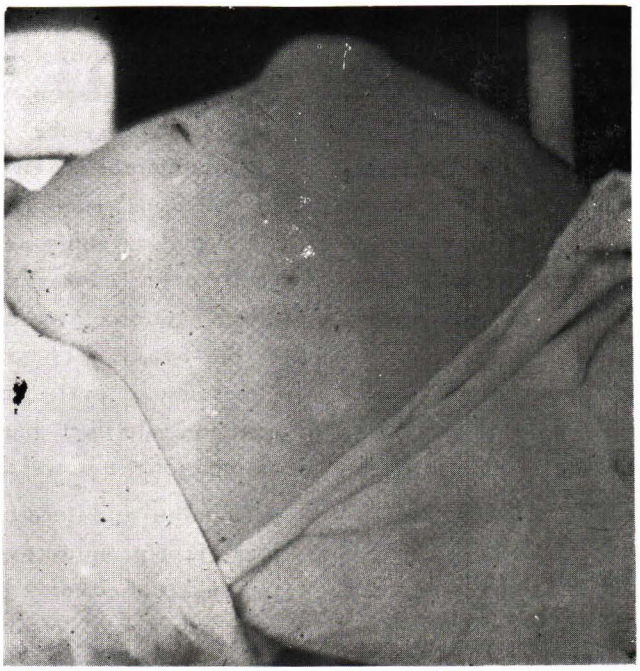

Fig. 6. The abdominal swelling with umbilical hernia (case 2)

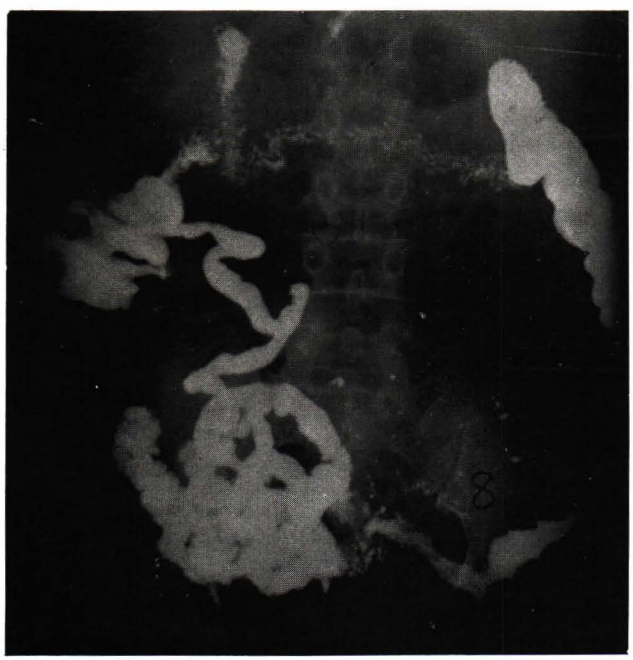

Fig. 7. Barium enema revealed small bowel being pressed upon by lower abdominal mass. (case 2)

ried in size from .0 cm. to 6.0 cm. in diameter. The mucosa of the appendix was grossly unremarkable. (Fig. 8).

Other specimens included a fallopian tube, an ovary and omentum, all of which were studded, on the surface with cysts containing mucous substance similar to the periappendiceal tissue.

Microscopic Examination: Sections of appendix showed a normal mucosa with an area of abrupt changes. The abnormal areas showed papillation of mucosal epithelial cells with lost of nuclear polarity and many abnormal mitotic figures. There was no area of tumor cell in the submucosa or muscular layer. The serosa and the peri—appendiceal fat were studded with glandular epithelium with mucin production. There were many areas showing collection of mucinous substance but there were no tumor cells surrounding it. The outer surface of the ovary and the fallopian tube also showed similar picture. There were no tumor cells within the ovarian tissue. (Fig. 9, 10).

## Discussion

### Pathogenesis

The general conception is that mucocele, a benign cystic dilatation of the appendix, is the result of stricture of the lumen which usually is caused by an inflammatory process[20]. The normal mucous cells continue to secrete mucous into this closed lumen and the wall of the appendix is gradually distended by the accumulation of gelatinous material. This cyst may become very large and may rupture with pouring some of its content into the abdominal cavity producing the so-called "Pseudomyxoma peritonei".

Pseudomyxoma peritonei may arise rarlly from causes other than appendiceal mucocele and mucinous cyst of the ovary. These include omphalomesenteric cyst, carcinoma of the common bile duct, mucinous adenocarcinoma of the bowel, ovarian fibroma, carcinoma and teratoma[8,10]. It is clear that pseudomyxoma peritonei is the result of either a benign or malignant process. Virchow believed that mucin which had escaped into the peritoneal cavity from the original lesion acted as an irritant and the peritoneum responded by secreting large amount of gelatinous material which he called pseudomucin.[20] Concerning the malignant process, Olshausen[17] believed that the epithelial cells from the lining of the ruptured cyst were able to transplant to the peritoneum, and that they then grew and continued to secrete the gelatinous material. The report by Waugh and Findley[16] that some mucoceles undergo "adenocarcinomatous degeneration" supported the malignant implantation nature in some cases of this condition. Woodruff and McDonald[20] found 6.6 percent of 146 cases of mucocele of the appendix to be malignant. They proposed that pseudomyxoma peritonei


Fig. 8. The Vermifrom appendix showing saccular dilatation of the distal portion with area of perforation (case 2)

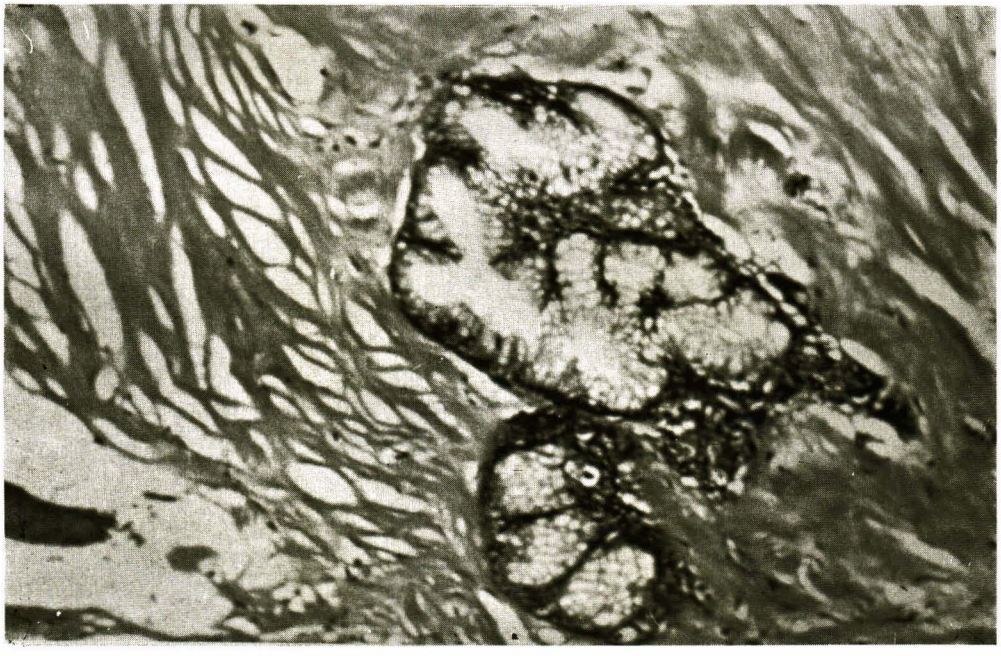

Fig. 9. Island of tumor tissue in the hyalinized connective tissue of omentum. H & E 2 x 100

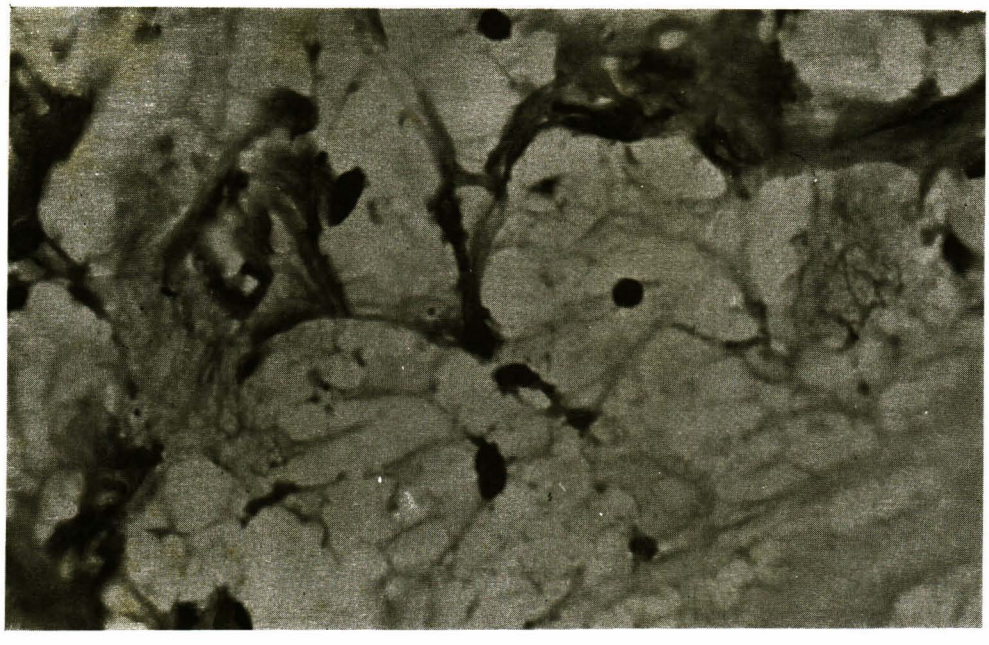

Fig. 10. Mucinous substance in the omental tissue. H & E x 400

of appendiceal origin occurs only in those patients in whom the formation of mucoceles are associated with grade I adenocarcinoma, the so called "malignant mucocele". This contention has been denied by many authors[3,12]. Sluiter[6] stated that there are many reports of mucoceles which gave rise to pseudomyxoma peritonei in which no malignant cells could be demonstrated. Bernhardt and Young[1] proposed that pseudomyxoma peritonei from rupture of mucocele of the appendix is a term to cover a spec trum of disorders. At one end of the spectrum is the passive transfer of cell free mucous into the peritoneal cavity from rupture of a benign mucocele. At the other end is rupture of appendix having the appearance of a mucocele but whose epithelium shows malignant potentialities by the ability to implant and produce mucous in association with the passive transfer. of mucous trom the diseased appendix.

Because of the well differentiated, papillary, and mucous producing character of the appendiceal lesions, our two cases should be classified, as grade I adenocarcinoma of the appendix or the so called "cystic or malignant mucocele" type of adenocarcinoma, according to Uihlein and McDonald[14]. However, by the classification of Sieracki and Tesluk[7,12], they should fall in the group of noninvasive adenocarcinoma of the appendix. The hypothesis proposed by Woodruff and McDonald[20] was that the grade I adenocarcinoma in the appendiceal cyst is the result of malignant change which takes place somewhere in the pathogenic cycle of the simple mucocele, and that this, in turn, is the result of an obstructive process in the lumen of the appendix. This type of tumour does not spread through lymphatic channels or blood vessels. Only peritoneal implantation by seeding of malignant cells has been found and mesenteric nodes are rarely involved. Distant metastasis has not been conclusively demonstrated. Bernhardt and Young[1] reported two cases with presumed distant metastasis. In one case mucinous material was found between muscle bundles, in the perineural lymphatics and around nerves, but no epithelial cells were found in the mucous. In another case one axillary lymph node was replaced by mucous filled cystic spaces with innocent looking columnar epithelium. It would be more appropriate to call this papillary, noninvasive, mucous producing,

potentially malignant lesion "papillary adenomatous tumour" of the appendix.

**Diagnosis:** Simple mucocele gives very little evidence to warrant a clinical diagnosis. An occasional patient may complain of pain in the right lower quadrant of abdomen resembling appendicitis. A few large cysts may be palpable through the abdominal wall. The diagnosis was usually not made preoperatively. Diagnosis however may be made by radiography. (7,15) In the plain film of the abdomen, superficial calcium deposits within the right lower quadrant mass may be seen. And from barium enema, the, appendix usually fails to fill and around sharply outlined soft tissue mass is seen in the cecal region. Differential diagnosis includes appendiceal abscess, carcinoid tumour, caecal carcinoma, ovarian cysts, retroperitoneal tumour and occasionally urinary calculi (7,15).

The diagnosis of pseudomyxoma has been made preoperatively in few cases. Mekhedko stressed clinically the indefinite contour of the abdominal mass, the unpainful slowly developing enlargement of the abdomen, the absence of cachexia, the small fluctuation and lack of change in percussion note on change of position of the patient, the engorged abdominal veins, the history of recurrent attacks of abdominal pain, and the terminal symptoms of intestinal obstruction and perforation. (11)

Gelatinous material in the peritoneal fluid "Jelly belly" is pathognomonic of pseudomyxoma peritonei. When it is discovered, the source of the mucinous material should be determined. Usually celiotomy is indicated to determine the definite cause.

In males, pseudomyxoma peritonei usually is due to ruptured mucocele of the appendix. In females, cystadenoma of the ovary is the leading cause (8). However, the appendix still may be the site of origin of pseudomyxoma even in the presence of an ovarian cystadenoma or cysadenocarcinoma. A normal appendix has never been reported or documented in a case of pseudomyxoma peritonei in which the patient was a woman, and in at least 25 per cent of the reported cases of pseudomyxoma peritonei in woman, a dual origin has been found (11).

**Prognosis and Treatment:** Malignant mucocele is not always fatal. There is a chance that the patient may be completely cured by aggressive surgical approach, even in the presence of extension or recurrence (4).

Treatment of unruptured mucocele is simple appendectomy. With ruptured mucocele and pseudomyxoma peritonei, removal of the appendix and as much of the cystic masses and mucous as possible should be attempted. Peritoneal pseudomyxoma may disappear following removal of the ruptured mucocele Reaccumulation of intraperitoneal fluid may be troublesome. Radiotherapy [9], radioactive gold [1], hyaluronidase [1], and activated trypsin [5] have been tried without much success. Multiple excisional procedures, combined with the use of alkylating agents intraperitoneally, appeared to be beneficial. One patient with mid-differentiation adenocarcinoma of the appendix and pseudomyxoma peritonei treated with Thio-Tepa as reported by Long et al [9], was alive and well 4 years after initial treatment. Three patients with ruptured mucocele of the appendix and peritoneal pseudomyxoma described by Byron et al [2], also were well 19 to 52 months after treatment which consisted of aggressive surgery and irrigation of the peritoneal cavity with 10 gm. of mechlorethamine (nitrogen mustard).

## Summary

Two cases of pseudomyxoma peritonei resulting from ruptured appendiceal tumour were described. Preoperative diagnosis of the condition was made from the gelatinous character of the aspirated peritoneal fluid. In one case the radiological evidence of soft tissue mass in the cecal region suggested that the appendiceal lesion was the cause of pseudomyxoma peritonei. The nature of the appendiceal tumour was discussed.

## References

1. Bernhardt, H. and Young, J.M. : Mucocele and pseudomyxoma peritonei of appendiceal in origin. Clinicopathological aspects. Am. J. Surg., 109 : 235; 1965.

2. Byron, R.L., Jr., Yonemoto, R.H., King, R.M., Lamb, E.J., Aromin, G.D., Solomon, R.D., and Gildenhorn, V.B. Management of pseudomyxoma peritonei secondary to ruptured mucocele of the appendix. Surg. Gynec. & Obst., 122 : 509; 1966.

3. Carleton, C.C. : Mucoceles of the appendix and peritoneal pseudomyxoma. Arch. Path., 60 : 39; 1959.

4. Das Gupta, T.K. and Paglia, M.A.: Primary malignant tumors of appendix. N.Y. State, J. Med., 66:890; 1966.

5. Denize, A. and Laufman, H. : Pseudomyxoma peritonei. Failure of activated trypsin to modify the course of the disease. Arch. Surg., 96 : 127; 1968.

6. Early, K., Stephenson, D.V., and Davis, W.C. : Giant retroperitoneal mucocele simulating pseudomyxoma peritonei and mucinous adenocarcinoma. Am. J. Surg., 116 : 439; 1968.

7. Elson, M.W.: Cecal invagination by mucocele of the appendix. Radiology., 71 : 90; 1958.

8. Jones, D.H. : Pseudomyxoma peritonei. Brit. J. Clin. Pract., 19:675; 1965.

9. Long, R.T.L., Spratt, J.S., Jr. and Dowling, E. : Pseudomyxoma peritonei. New concepts in management with a report of seventeen patients. Am. J : Surg., 117 : 1962; 1969.

10. Malpas, P. : Pseudomyxoma peritonei. J. Obst. & Gynaec. Brit. Emp., 66 : 247; 1959.

11. Rosenfield, E.D. : Peritoneal pseudomyxoma. Arch. Path., 48 : 255; 1949.

12. Sieracki, J.C. and Tesluk, H.: Primary adenocarcinoma of the vermiform appendix. Cancer., 9:997; 1956.

13. Sukhupragarn, S. : Mucocele of the appendix. J. Med. Ass. Thailand., 52:460; 1969.

14. Uihlein, A. and McDonald J.R.: Primary carcinoma of the appendix resembling carcinoma of the colon. Surg. Gynec. & Obst., 76:711; 1943.

15. Unger, H.M. and Paradny, R.: Ruptured mucocele of appendix with pseudomyxoma peritonei. Ann. Surg., 143 : 280; 1956.

16. Waugh, T.R. and Findley, D. : Mucocele with peritoneal transplantation in adenocarcinoma of the appendix. Am J. Surg., 37:518; 1937.

17. Weaver, C.H. : Mucocele of appendix with pseudomucinous degeneration. Am. J. Surg., 36:523; 1937

18. Wesser, D.R. and Edelman, S. : Experiences with mucocele of the appendix. Ann. Surg., 153:272; 1961.

19. Wilson, R. : Primary carcinoma of the appendix. Am. J. Surg., 104 : 238; 1962.

20. Woodruff, R. and McDonald, J.R.: Benign and malignant cystic tumors of the appendix. Surg. Gynec. & Obst., 71 : 750;1940.