MUCOID DISEASE OF THE APPENDIX*

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AS THE VESTIGIAL REMAINS of an ancestral colon and of similar structure the vermiform appendix, with the notable exception of primary malignancy, is subject to the common diseases of the colon. The nature and the course of disease, however, are affected by the size, shape and position of the appendix, by the blood supply which is terminal, and by stasis which is a natural state. Chronic obstruction of the lumen with retention of its contents produces morbid changes in the anatomy and in the physiology of the appendix which, with their complications, are known as mucoid disease. Because of its chronicity and comparative rarity this condition has not received the attention that it merits.

In the stomach mucus is a protective mechanism, in the colon it is an agent for the lubrication of feces that become solid from loss of water by absorption. In both the colon and the appendix mucus is secreted by columnar cells lining simple tubular glands in the mucosa. Spastic colon,[18] so-called mucous colitis, is a disease caused by a disturbance of the vegetative or autonomic nervous system that is marked by hypersecretion of mucus and by the passage of mucous casts of the colon. In it there are no symptoms referable to the appendix and it has no etiologic relationship to mucoid disease, although both the appendix and the colon are under autonomic nerve influence.

Chronic obliterative fibrosis from long-continued low grade inflammation converts the appendix throughout its length into a fibrous cord with loss of gland and of muscle structure. Chronic localized obstruction from stenosis, however, if of sufficient degree, is followed by cystic distention of the distal lumen. For distention to occur, secretion into the lumen must exceed fluid loss from it by drainage and by absorption. If enlargement is slow the resulting mucocele or hydrops may ultimately approach the size of the gravid uterus at full term.[8, 9, 12, 21] Rapid growth precipitates rupture. Fortunately, under modern conditions, most cases of chronic obstruction are operated upon as appendicitis before cystic change has become apparent. Increasing intraluminal pressure causes thinning of the appendiceal wall with the formation of diverticula. Diverticula occurring in the antemesenteric portion of the wall tend to rupture early; those developing into the meso-appendix grow more slowly and may themselves become secondary mucoceles. Bailey,[17] before this Association, has reported a case of a massive mucoid cyst of the meso-appendix, missed at appendicectomy, being removed at subsequent operation. Mucoceles produce indefinite symptoms and preoperative diagnosis is difficult.

Atrophy of the glands from intraluminal pressure may result in reduction of secretion into a mucocele. Growth stops when fluid loss by absorption

*Read before the Fifty-sixth Annual Meeting, Southern Surgical Association, December 5–7, 1944, Hot Springs, Va.

balances fluid gain from secretion. Continued secretion into a mucocele with loss of fluid content by absorption results in the deposit of mineral salts as granules on the mucosa (Case 2) or as calculi (Case 4) in the lumen.

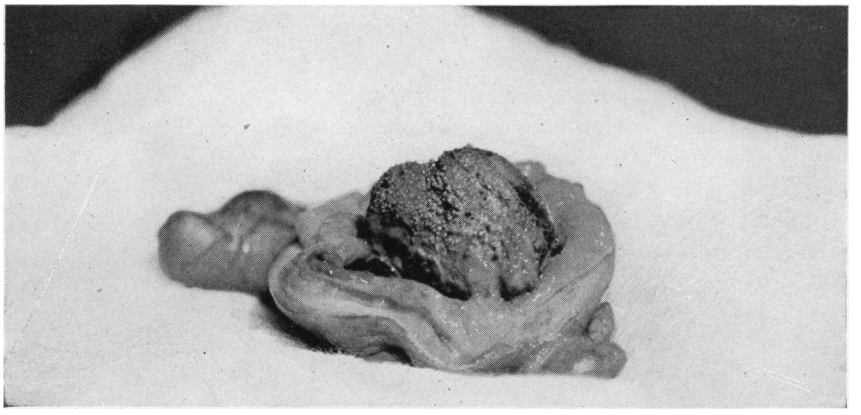

FIG. 1.—Photograph of the appendix opened. Giant faceted calculus of the appendix.

Ogilvie[7] has reported a case of cyst of the appendix, two and one-half by one and one-half inches in size, with calcification of the walls, in a railroad brakeman who complained of something solid "tapping him on the inside while he followed his daily work." Calculi may be multiple but as a rule are single. They vary in size; the largest reported[14] was in a man aged 61, which weighed 13.5 Gm. It consisted mainly of calcium and magnesium phosphates. Mucoceles rarely occur before middle age. We have seen, by invitation, a boy, age four, with a hard mass in the lower right abdomen which was shown roentgenographically to be a stone.[13] The preoperative diagnosis was verified at celiotomy. The stone, weighing 33 Grains, was contained in a mucocele that had recently perforated.

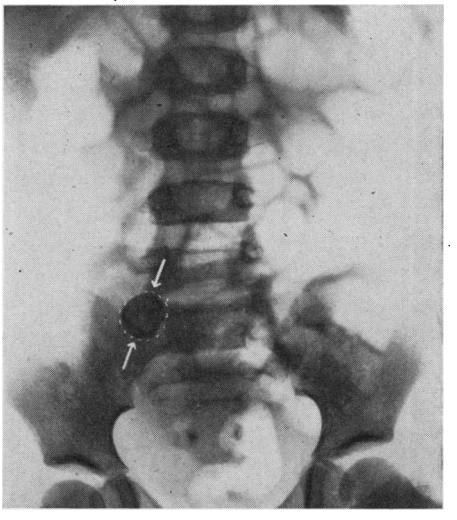

FIG. 2.—Roentgenogram of pelvis of four-year-old boy showing stone in mucocele of the appendix. Case of Dr. Adcock.

The viscid contents of a mucocele, like the white bile of a cholecystic hydrops or the clear fluid of a gonorrheal hydrosalpinx is practically sterile, and septic peritonitis does not follow rupture of a mucocele as its does perforation in acute appendicitis. The opaque material that escapes from a mucocele is not absorbed from the peritoneal cavity but blocks the lymphatics and remains as a foreign body to accumulate and produce ascites or "jelly-

belly," a bizarre disease that is termed pseudomyxoma peritonei. Due to chronic obstruction and inflammation the secretion into a mucocele becomes changed from mucin to pseudomucin by metaplasia rather than by degeneration of the goblet cells. The great increase in the volume of pseudomucin that accumulates in the abdomen after perforation of a mucocele makes it certain that, although transplants may not occur, secreting cells do escape from the appendix to live and to function in the peritoneal cavity. It is not logical to assume that the foreign body serositis which follows perforation activates the endothelial cells of the peritoneum to secrete pseudomucin.

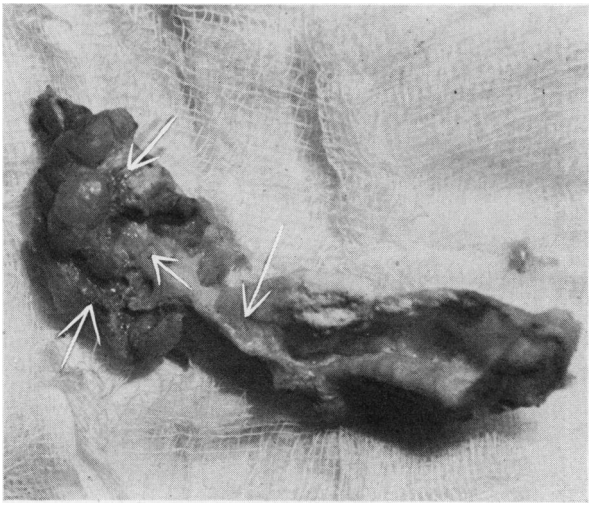

FIG. 3.—Photograph of mucocele of the appendix opened, showing deposit of mineral salts on mucosa. Case 2.

Largely because most cases of pseudomyxoma peritonei develop from rupture of adenomatous cysts of the ovary rather than from the appendix the disease is more common in women. It is not known why mucocele of the appendix is found as an associated lesion in a high percentage of women who have developed pseudomyxoma peritonei from ovarian cystadenoma. In some cases the cystadenoma and the mucocele have both ruptured and are found at operation to be discharging pseudomucin into the peritoneal cavity (Cases 3 and 4). Cystadenoma of the ovary is often malignant. Pseudomyxoma developing after the rupture of such a malignant cyst, although the cells are not invasive, is potentially carcinomatosis, which terminates in death. Metastases from pseudomyxoma peritonei of ovarian origin have been found in the chest.[11]

Woodruff and McDonald,[15] reviewing 43,000 appendices removed at the Mayo Clinic, found dilatation in 146 cases, an incidence of 0.3 per cent. In ten of the appendices they found adenocarcinoma, and in four of the ten cases there was an associated malignancy of the ovary. They believe that fatal cases of pseudomyxoma peritonei which develop after rupture of

mucoceles all originate in carcinomatous cystadenomas of the appendix. Although they do not state that any of the 146 cases of mucocele ruptured and developed fatal pseudomyxoma peritonei, their findings strongly suggest that peritoneal pseudomyxoma of *appendiceal as well as of ovarian origin* may be benign or malignant in type, depending upon the tissue from which it springs Possibly cells originating in a benign lesion may assume malignant characteristics after they reach the peritoneum. Primary cancer of the appendix is rare, of low grade malignancy, and requires microscopic identification. Norment[1] estimates that the relation of carcinoma of the appendix to carcinoma of other parts of the intestinal tract is as 1 to 250. I have never seen a case recognized by the surgeon at operation. Boyd[20] says true primary carcinoma of the appendix very rarely occurs. The condition commonly called primary carcinoma is really carcinoid tumor. It resembles carcinoma microscopically but is a benign lesion and is without symptoms.

Adenocarcinoma of the ovary is of frequent incidence and of high malignancy. Pseudomyxoma peritonei of appendiceal origin has a lower mortality rate. However, death in pseudomyxoma from either source may be mechanical and independent of cell structure, for it is most often due to intestinal obstruction. From serositis, pseudomucin in the free peritoneal cavity becomes enveloped into cystic masses of mucoid material which adhere to each other and to the viscera. Segments of small intestine may be bound in a colloid cast of the abdomen. Either condition results in chronic intestinal obstruction of varying degree. In late cases, that are operated upon after the intestine has become fixed, surgical treatment is futile.

Pseudomyxoma peritonei of appendiceal origin is a rare disease, less than 100 cases having been reported. The symptoms are those of a progressive, painless ascites which, untreated, results in death from intestinal obstruction. According to Seelig[3] the disease may run a benign or a malignant course clinically without furnishing any differentiating criteria, macroscopically or microscopically.

Mucoceles of the appendix should be removed before rupture occurs and pseudomyxoma peritonei develops. After rupture, if the mucocele, with all the pseudomucin that has escaped, is removed, the prognosis, in our experience, is good. Late cases, in which pseudomucin has become encysted and cannot be removed, tend to become obstructive. Drainage should not be employed. Cases that were drained by Ries[5] to allow the escape of masses which could not be completely removed at operation all died. All cases should be reported in order that authoritative factual information may be obtained. At operation upon females there are often associated adenomatous cysts of the ovary which should be removed. In cases originating in carcinomatous lesions of either the appendix or the ovary, maximum dosage of deep roentgenotherapy should be administered postoperatively.

CASE REPORTS

Case 1.—G. P. W., male, age 75, was seen July 2, 1937, with large bilateral inguinal herniae of long duration. At the repair of the right hernia, which was

strangulated, a perforated mucocele of the appendix, the size of an adult thumb, was removed with 500 cc. of brilliant amber jelly that was found free in the hernial sac and in the pelvis. Closure was without drainage. Radiation was not administered. On September 25, 1937, three months after dismissal, he returned for operation upon the left hernia, which had become strangulated. At this time the peritoneum was grossly normal and without pseudomucin or evidence of pseudomyxoma. He is reported to have died early in 1938 of hypertension.

Case 2.—Mrs. W. R., age 58, giving the history of having had gallbladder trouble for 20 years, was seen April 11, 1941, suffering from acute cholecystitis, with stones. At operation, the gallbladder containing pus and faceted stones was removed. The uterus and the ovaries were atrophic. A mucocele at the distal end of the appendix had ruptured, and about 750 cc. of yellow colloid material was found free in the peritoneal cavity. This, with the appendix, was removed. The surface of the mucosa of the mucocele was rough and granular like sandpaper from the deposit on it of mineral salts. The gallbladder region was drained. Recovery was without complication. No radiation therapy was administered. After three and one-half years she is in good health.

Case 3.—Mrs. W. M. S., age 61, has known she had had a slowly enlarging pelvic tumor for several years. She was suffering with abdominal pain of one week's duration. On examination, March 3, 1943, a cystic mass was found filling the pelvis and extending above the umbilicus. At operation, this proved to be a multilocular gelatinous cyst of the left ovary. Much yellow mucoid material from a ruptured loculus of it was free in the peritoneal cavity. There was a large mucocele of the appendix with a small rupture through which jelly, similar to that coming from the ovary, was being discharged into the abdomen. After the peritoneum had been freed of pseudomucin, the left ovary, the appendix and the gallbladder, with stones, were removed. The wound was closed without drainage. The patient did not receive deep roentgenotherapy, and after 20 months is in good health. *Pathologic Diagnoses* (Dr. Kenneth Lynch): Mucous cyst adenoma of the ovary. Mucocele of the appendix. Pseudomyxoma peritonei. Cholecystitis, chronic, with cholelithiasis.

Case 4.—Mrs. J. O., age 79, was admitted, March 3, 1944, complaining of difficulty in breathing and of progressive abdominal enlargement which began one year ago. Blood pressure and laboratory findings were normal. At operation, seven and one-half liters of thick yellow jelly were removed from the peritoneal cavity, much of it being contained in a massive papillomatous cyst of the right ovary that had ruptured. It was impossible to remove masses of jelly that were encysted in the great omentum and between coils of intestine. The left adnexa and the uterus were atrophic. There was a mucocele of the appendix with a small perforation at the tip. The appendix and the right adnexa were removed. *Pathologic Findings:* Cystic adenocarcinoma of the right ovary with rupture. Ruptured mucocele of the appendix which contained a small calculus. Pseudomyxoma peritonei.

Convalescence was uneventful. Deep roentgenotherapy was administered. On examination, September 25, 1944, her condition was good, with no evidence of ascites.

COMMENT

We have reported two cases of pseudomyxoma peritonei of appendiceal origin, one in a man, age 75 (Case 1), the other in a woman, age 58 (Case 2). In both the condition was symptomless and was found incidentally at operation, in one for strangulated hernia and in the other for cholecystitis with stones. No pseudomucin was found in the abdomen of the man at a second operation performed three months subsequent to the first. We also report two cases (Cases 3 and 4) of pseudomyxoma peritonei in women, age 61 and 79, respectively, in both of whom there were muoceles of the appendix with small perforations. In both, the disease had apparently originated in

cysts of the ovary that had ruptured in one (Case 3), a benign cystadenoma; in the other (Case 4), an adenocarcinoma. In Case 4 the fact that the mucocele of the appendix complicating adenocarcinoma of the ovary was itself without gross or microscopic evidence of malignancy, proves that malignancy was not a factor in its development. In Case 2 there was a deposit of mineral salts on the mucosa, and in Case 4 there was a small calculus in the mucocele—so that all phases of mucoid disease of the appendix except the late obstructive stages of pseudomyxoma peritonei have been illustrated in the four cases. All the patients have been white.

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