Cartilaginous Differentiation in Peritoneal Tissues: A Report of Two Cases and a Review of the Literature

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Two cases of cartilaginous differentiation of the peritoneum not associated with an intraabdominal malignancy are described. This is the first detailed report of cartilaginous metaplasia of the peritoneum. The patients were female, ages 53 (Patient 1) and 77 years (Patient 2). Prior medical histories were significant for a culdotomy (to drain pelvic abscesses associated with pelvic inflammatory disease) in Patient 1 and for an open abdominal surgery in Patient 2. The peritoneal lesions were incidental findings in both cases. In Patient 1, surgery was performed for a septated ovarian cyst; the other patient underwent surgery to relieve obstructive bowel symptoms. In Patient 1, multiple firm, white lesions ranging from 2.0 to 7.0 mm were present on the serosal surfaces and the mesenteries of the small and large bowel. In Patient 2, a single firm, white lesion measuring 2 cm in maximum dimension was removed from the mesentery of the ileum. Microscopically, the lesions consisted of small nodules of mature hyaline cartilage surrounded by nondescript fibrous tissue and covered by mesothelium. There was no foreign body giant cell reaction, inflammation, or other reactive changes in the surrounding adipose tissue. These may represent metaplastic lesions of the secondary mullerian system, or a unique peritoneal response to previous surgical manipulation. Alternatively, these may represent benign neoplastic lesions (chondroma) of the submesothelium.

KEY WORDS: Cartilage, Cartilaginous metaplasia, Heterotopic cartilage, Peritoneum.

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REPORT OF CASES

Case 1

Patient 1 was a 53-year old Caucasian female who presented with complaints of low back discomfort. She gave a medical history of self-induced abortion at 6 months' gestation, complicated by pelvic inflammatory disease and pelvic abscesses, approximately 30 years before presentation. Those abscesses reportedly were drained through a culdotomy, although the specific details were unavailable for review. An ultrasound at current presentation revealed a septated right ovarian mass. At surgery, several firm, white nodules ranging from 2 to 7 mm were noted throughout the peritoneal cavity and were excised from several locations along the serosal surfaces and mesenteries of the small and large bowel. The patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy and has had no recurrence of pleural, peritoneal, or gynecologic diseases after a 9-year follow-up.

Case 2

Patient 2 was a 77-year-old Caucasian female who presented with abdominal distention, diarrhea, and abdominal pain. She gave a medical history of a total abdominal hysterectomy and bilateral salpingo-oophorectomy approximately 28 years before presentation for pelvic pain caused by uterine leiomyomata. Radiographic studies revealed an obstruction in the small bowel. During an exploratory laparotomy, a single firm, white nodule measuring 2.0 cm in maximum dimension was identified and excised from the mesentery of the ileum, just lateral of midline. There were significant adhesions involving the small and large bowel that were lysed. The last recorded follow-up was 1 year after presentation, at which time there had been no development of any peritoneal or pleural diseases.

PATHOLOGIC FINDINGS

Macroscopically, the peritoneal nodules from Case 1 consisted of several firm, glistening, white tissue fragments ranging from 2 to 7 mm. The left ovary measured 10.0 × 8.5 × 6.0 cm and was replaced by a unilocular cyst filled with clear fluid. The internal lining was smooth and without papillae. No lesions were identified in the uterus, fallopian tubes, or right ovary. The specimen from Case 2 consisted of a single firm, glistening, white tissue fragment measuring 2.0 cm in maximum dimension. The central portions were yellow and gritty. The specimens from both cases were processed routinely for microscopic examination. Microscopically, Case 1 consisted of lobulated nodules of perichondrium-lined mature hyaline cartilage that were surrounded by adipose tissue and overlined by benign mesothelium (Fig. 1). The left ovary was replaced by a serous cystadenoma. Sections obtained from the uterus showed weakly proliferative endometrium and adenomyosis. A focus of endometriosis was identified in the left fallopian tube; the cervix and the right adnexa showed no pathologic changes. The nodule from Case 2 had a microscopic appearance similar to Case 1, but in addition displayed calcific rimming of some individual chondrocytes in the central portions (Fig. 2). Neither case had any associated inflammation, fat necrosis, or foreign-body giant cell reaction in the surrounding fibrous and adipose tissue.

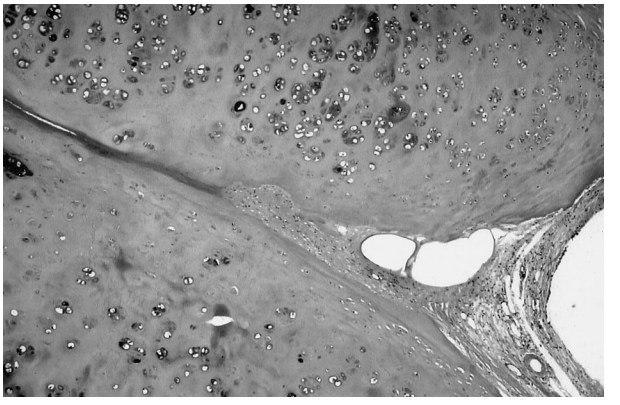

FIGURE 2. Case 2 showing nodules of mature hyaline cartilage similar to Case 1, with calcific rimming of some chondrocytes.

DISCUSSION

Non-mesothelioma–associated cartilaginous differentiation of the human peritoneal tissues has never been fully described in the literature to the best of the authors' knowledge, although a single case is cited in a surgical pathology text (1). That case was interpreted as a probable metaplastic lesion of the submesothelium. Although osseous and/or cartilaginous differentiation in pleural malignant mesotheliomas have been described in several reports (2–8), Kiyozuka *et al.* (9) reported the only case of a peritoneal malignant mesothelioma with osseous and cartilaginous differentiation. In animal models (rats), however, Rittinghausen and colleagues (10) were able to induce peritoneal malignant mesotheliomas with cartilaginous and osseous differentiation after intraperitoneal injections of asbestos fibers.

The histogenetic explanation for cartilaginous differentiation in peritoneal tissues has been the source of some controversy. This differentiation has customarily been explained by the theory that there exists a population of submesothelial multipotent cells with ability to differentiate along mesenchymal and mesothelial lines, a concept originally suggested by Klemperer and Rabin in 1932 (11). This was supported by the electron microscopic studies of Raftery (12), who observed the ultrastructure of rat peritoneum after mechanical injury and described a mesenchymal cell that "appeared intermediate in form between primitive mesenchymal cells on one hand and proliferating fibroblasts or mesothelial cells on the other." The cells eventually differentiated into mesothelium, which covered up the defect. Perhaps the best support for the multipotent cell theory came from the studies of Bolen *et al.* (13). Using light microscopic, ultrastructural, and immunohistochemical studies, those investigators demonstrated that normal surface mesothelium expressed both low molecular weight cytokeratins (LMWK) and high molecular weight cytokeratins (HMWK), whereas submesothelial cells expressed vimentin only while at rest. However, when reactive, these submesothelial cells displayed a loss of vimentin immunoreactivity and progressively acquired LMWK and HMWK immunoreactivity as the cell differentiated towards the mesothelial surface. Other investigators believe that desquamated mesothelial cells in the peritoneum

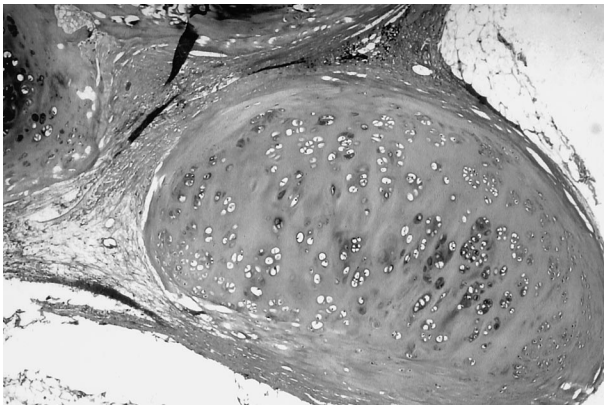

FIGURE 1. Case 1 showing nodules of mature hyaline cartilage surrounded by perichondrium and adipose tissue.

are the primary source of mesothelial regeneration (14). Donna and Betta (5) thought that the mesothelial cell was not only totipotent but represented real mesoderm that retained the potential to differentiate along embryonic developmental lines, including toward cartilage and bone. Hence, they suggested the term *mesodermoma,* instead of *mesothelioma*, to emphasize the mesodermal origin of associated tumors (5).

In the human peritoneum, at least seven well-documented cases of mesenteric heterotopic ossification (or osseous metaplasia) have been reported (15–17). The fact that 6 of those 7 cases were associated with a history of abdominal surgery underscores the ability of the peritoneal tissues to differentiate into heterologous tissues in response to injury.

Cartilaginous heterotopia has been reported in several organs, including such unlikely sites as the prostate (18), tonsils (19), and thyroid gland (20). In the uterus and cervix, cartilaginous heterotopia is a rare but well-recognized phenomenon. Remmele and colleagues (21) reported two cases and extensively reviewed the literature on the subject. Nodules of cartilage are typically identified in the endometrium, myometrium, and endocervix, and in two cases (22, 23), a cartilaginous nodule was present in the anterior uterine subserosa. In the first patient (22), a bar of cartilage was noted beneath the uterine serosa of a 32-year-old gravida 1, abortus 1 female during a salpingectomy for hydrosalpinx. A similarly located cartilaginous nodule in the anterior uterine subserosa of a second patient, a 36-year-old gravida 17, para 7, abortus 10, was reported by Jakubowitz (23). These cases are similar to our Case 2, who had a single nodule of cartilage on a peritoneal surface. However, in our case, the excised nodule was in the mesentery of the ileum and was not in close proximity to the previous location of the uterus (history of hysterectomy, see report of cases). The possibility of a benign cartilaginous neoplasm (chondroma) also warrants some consideration in these cases. In contrast, the diffuse presence of the cartilaginous lesions in our Case 1 would seem to argue against a neoplastic pathogenesis. The diffuse occurrence of seemingly heterologous tissues in the peritoneum is well recognized when such tissues are smooth muscle (*leiomyomatosis peritonealis disseminata*) or glial tissue (*gliomatosis peritonei*). The latter is of particular interest because some authors have suggested that the glial nodules are implanted into the peritoneum from capsular defects in ovarian teratomas (24), and a similar mechanism might explain the diffuse cartilaginous lesions in Case 1. However, as previously indicated, no teratomatous lesion was identified in either ovary. Given the gynecologic history of self-induced abortion (approximately 30 y before presentation), these lesions may also represent organized products of conception showing cartilaginous differentiation. However, the presence of the nodules in the entire peritoneal cavity and the lack of involvement of the pelvic peritoneum or gynecologic organs argues against that possibility.

We share these cases for the benefit of surgeons who might encounter these lesions and for pathologists who would be making their intraoperative evaluation.

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