Case Presentation

A 49-year-old woman with a recent history of a pelvic mass was referred for an oncology consult.

Six months prior: The patient presented to her family physician with lower abdominal discomfort and bloating. The patient had normal energy, and did not complain of weight loss, nausea, vomiting, fever, night sweats, or change in appetite. However, over the next few months, she experienced increasing abdominal girth with associated fullness and abdominal pain.

Over the next several months, several ultrasound (U/S) examinations were performed. The first U/S of the abdomen revealed ascites and the radiographic appearance of peritoneal carcinomatosis. Twelve days later, a repeat abdominal U/S and a trans-pelvic U/S revealed the presence of a large mass on the left ovary. The mass appeared cystic in nature, with associated peritoneal carcinomatosis and two solid tumour implants on the serosal surface of the liver. There were no discernible intrahepatic metastases and the remainder of the study was unremarkable.

The patient had a past medical history of mild cervical dysplasia that had resolved without treatment. She has had two uncomplicated vaginal deliveries, has been post-menopausal for one year, and was not receiving hormone replacement therapy. She had no prior history of breast or ovarian cancer. The patient is a non-smoker, married with two children, and had worked as a fitness instructor until the time of her illness. Her maternal family history is positive for cancer; her aunt was diagnosed in her fifties with ovarian cancer, and her grandmother had colon cancer.

What is the differential diagnosis to explain the clinical findings of ascites and a pelvic mass?

Differential Diagnosis

Ascites. Ascites is defined as the accumulation of excess fluid within the peritoneal cavity. Historically, ascites was typically classified as either transudative or exudative, however, the serum-ascites albumin gradient (SAAG) has been proven to categorize ascites better than total protein concentration or other parameters. The difference between the serum and ascitic fluid concentration of albumin correlates directly with portal pressure. The SAAG does not explain the source of albumin, nor can it be used to explain the pathogenesis of ascites formation. However, ascites resulting from disorders associated with portal hypertension is typically characterized (97% accuracy) by a high SAAG (>1.1g/dL), while other disorders (usually non-hepatic) can generally be characterized by a low albumin gradient. Causes of ascitic fluid accumulation include both hepatic and non-hepatic disorders. Table 1 provides a basic classification of ascites based on the SAAG.

Malignancies account for less than 10% of ascites, but should remain an important consideration in the differential diagnosis of ascites accumulation. When abnormal cells are discovered in an ascitic fluid sample (obtained by paracentesis), ascites may be classified as either malignant or inflammatory. Peritoneal carcinomatosis is a prominent malignant cause. Other malignancy-related sources of ascites include: massive liver metastases, hepatocellular carcinoma, and malignant lymph node obstruction. The mechanism of malignant ascites has not been fully characterized. Peritoneal carcinomatosis is believed to produce ascites fol-
lowing exudation of proteinaceous fluid from tumour cells lining the peritoneum. Other common explanations for malignant effusions are lymphatic/venous obstruction and a tumour-irritant effect on normal serous membranes.

Peritoneal carcinomatosis is generally attributed to one of two major origins: the ascites of ovarian cancer or that of ruptured or metastatic appendiceal cancer. Ascitic fluid derived from carcinoma of the ovary is generally clear and watery, while that of appendiceal origin tends to be mucinous or jelly-like in nature. Therefore, most experienced clinicians can recognize the presence of mucinous malignant ascites based on surgical presentation alone and do not require further sampling for cytological confirmation.

The radiographic findings in this patient suggest that an ovarian tumour and associated peritoneal carcinomatosis were most likely responsible for the development of ascites.

Pelvic Mass. A pelvic mass may originate in the uterus, ovaries, fallopian tubes, bladder, bowel, or soft tissues of the abdomen. Table 2 outlines some conditions in which a pelvic mass may be found upon physical examination. The differential diagnosis is narrowed significantly given the age of the patient, the likelihood of malignant ascites, and the presence of disease affecting the ovary as well as other peritoneal structures. The most likely diagnosis would be ovarian carcinoma, either primary or secondary.

Presumptive Diagnosis
The patient was referred for a same-day surgical consult. On examination, the vitals were normal and the abdomen

---

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Classification of Ascites by Serum-Ascites Albumin Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH GRADIENT (≥1.1 g/dL)</td>
<td>LOW GRADIENT (&lt;1.1 g/dL)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Peritoneal carcinomatosis</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Fatty liver</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Cardiac ascites (i.e. CHF)</td>
<td>Postoperative lymphatic leak</td>
</tr>
<tr>
<td>Budd-Chiari syndrome</td>
<td>Bowel obstruction/infarction</td>
</tr>
<tr>
<td>Myxedema</td>
<td>Infection</td>
</tr>
<tr>
<td>Veno-occlusive disease/thrombosis</td>
<td>Tuberculous peritonitis</td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Differential Diagnosis of Pelvic Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>SITE</td>
<td>CONGENITAL</td>
</tr>
<tr>
<td>UTERUS</td>
<td>Imperforate Hymen</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>OVARIES</td>
<td>Congenital cyst</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>FALLOPIAN TUBES</td>
<td></td>
</tr>
<tr>
<td>GENITO-URINARY</td>
<td>Full bladder</td>
</tr>
<tr>
<td>GASTRO-INTESTINAL</td>
<td>Diverticular disease Appendiceal abscess</td>
</tr>
<tr>
<td>SOFT TISSUES</td>
<td></td>
</tr>
</tbody>
</table>
was soft and slightly distended with ascites. There was evidence of intra-abdominal masses consistent with an 'omentum cake' and pelvic examination demonstrated a mobile cervix and a large left pelvic mass, 13-14 cm in size.

Based on the consistency of the mass and other abnormalities on physical examination, the responsible surgeon made a presumptive pre-surgical diagnosis. This provisional diagnosis was reviewed in detail with the patient and her husband, with recommendation for an immediate exploratory laparotomy and tissue removal as required.

**Clinical Diagnosis:** Ovarian cystic adenocarcinoma with intra-abdominal metastases.

Primary ovarian cancer was favoured clinically over metastatic ovarian disease because the tumour was unilateral, showed a spread pattern typical of ovarian cancer, and there was no history that suggested any other primary site. The clinical plan was to perform an exploratory laparotomy with tissue removal as required.

**Surgery**

Two weeks prior to oncology consult: The patient underwent an exploratory laparotomy under general anaesthetic. A small amount of ascitic fluid with mucosal consistency was expelled following midline incision of the abdomen. The findings made during the course of the surgery are summarized in Table 3. The omentum was entirely displaced by a tumour measuring 30 cm in diameter x 10-15 cm in depth x 2-3 cm in thickness. This large 'omental cake' involved the entire greater and lesser omentum up to the diaphragm. There were moderate-sized tumour implants on the serosal surfaces of the stomach, spleen and small bowel, and small amounts of tumour studding on the dome of the right liver lobe and the peritoneal aspect of the right diaphragm. A large cystic mass replaced the left ovary, while the right ovary had a normal appearance. A large tumourous plaque was located on the surface of the bladder and the peritoneal cul-de-sac. The peritoneum was observed to have a gravel-like appearance, suggesting multiple small tumour nodules.

A total abdominal hysterectomy with bilateral salpingo-ophorectomy (TAH-BSO) and an omentectomy were performed. The incidental finding of a tumour involving the tip of the appendix prompted the removal of the appendix. Tumour implants on the bladder surface and cul-de-sac were also removed. Approximately 5% of tumour remained as residual disease; unresectable disease was found at the anterior stomach wall, duodenum and transverse colon. The patient tolerated the procedure well and had an uneventful recovery.

**Pathological Discussion**

All sections were submitted for fixation in 10% neutral buffered formalin. Fixed sections were then embedded in paraffin and 5 µm sections were cut, put on glass slides, and stained with hematoxylin and eosin (H&E). Light microscopy of the left ovary revealed extensive areas of tall columnar mucous-secreting epithelium with moderately hyperchromatic nuclei, changes consistent with mucinous adenocarcinoma. Similar tumours were also seen involving the serosal surfaces of the uterus, bladder, omentum and appendix. Examination of samples taken from the right ovary, fallopian tubes and cervix did not reveal the presence of any neoplastic changes.

The mucin associated with the tumour was noted on microscopy to dissect through the stromal tissues. This histological finding, along with the mucinous ascites, is consistent with a rare condition known as pseudomyxoma peritonei. It is known that both the appendix and ovaries may show mucinous tumours when pseudomyxoma peritonei is present. Because the greater bulk of the tumour was in the ovary, it was assumed that the primary site was ovarian. Accordingly, the pathological findings were recorded as a primary malignant mucinous adenocarcinoma of the ovary with metastases to the bladder, myometrium, appendix and omentum.

**Pathological Diagnosis:** Stage IIIC ovarian carcinoma and associated pseudomyxoma peritonei.

---

**Table 3**

**Tumour Findings During Exploratory Laparotomy**

<table>
<thead>
<tr>
<th>Tumour-involved organs</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>entire omentum</td>
<td>large 'omental cake': 30cm x 15cm x 3cm</td>
</tr>
<tr>
<td>stomach, spleen, small bowel, right liver lobe and right half diaphragm, urinary bladder and cul-de-sac</td>
<td>serosal surface tumour implants</td>
</tr>
<tr>
<td>left ovary</td>
<td>large cystic mass</td>
</tr>
<tr>
<td>appendix</td>
<td>small tumour at tip</td>
</tr>
<tr>
<td>peritoneum</td>
<td>gravel-like appearance</td>
</tr>
</tbody>
</table>
Ovarian Cancer

Etiology. Ovarian cancer is a frequently fatal and insidious disease, which predominantly affects post-menopausal women. Although the etiology of this disease is unknown, a number of theories have been proposed. The majority of all ovarian cancers are believed to arise from the single layer of epithelial cells that lines the ovarian surface. Two of the most prominent theories propose that trauma-induced disturbances in the growth of ovarian surface epithelium (OSE) lead to neoplastic transformation. The proposed mechanisms for such growth-disturbing trauma are incessant ovulation and inclusion cyst formation. Recent studies have also proposed a putative role for endometriosis in the etiology of ovarian cancer.4,5

The incessant ovulation theory was initially proposed in 1971 and suggested that continuous ovulation causes repeated trauma to the ovary that leads to ovarian cancer development.6 This theory was proposed as a means of explaining the protective effect of multiple pregnancies (which interrupt ovulation) on the risk of developing ovarian cancer in later years. It has been suggested that the trauma of incessant ovulation results in increased proliferation of OSE cells which results in a greater frequency of spontaneous mutations.7,8

Surface inclusion cysts are believed to arise from the invagination and trapping of the ovarian surface. The sealing off of small cysts in the ovarian stroma may occur from inflammation caused by carcinogens or chemical irritants. Alternatively, inclusion cysts may arise during remodeling of the ovarian surface following ovulation-induced proliferation or follicular attrition.9,10 These OSE-lined cysts are common and generally benign in women, although they are widely held to be the origin of many epithelial cancers, following early malignant changes.11 While a defined mechanism for the promotion of benign inclusion cysts to a malignant phenotype has yet to be elucidated, various features have recently been proposed to be involved in the onset of inclusion cyst-derived ovarian tumorigenesis. Proposed factors include failure of the cellular apoptotic signalling system, morphologic variation in OSE cells (focal atypia) and increased expression of adhesion molecules such as E-cadherin.12,13

Incidence, Screening and Risk Factors. Ovarian cancer is the leading cause of death among all gynecologic malignancies and the fifth-leading cause of cancer-related death in Canadian women.13 According to the National Cancer Institute of Canada, it was estimated that 2,600 new cases were diagnosed in 1999, and 1,500 deaths will occur from ovarian cancer.13 Approximately 1.4% of North American women will develop ovarian cancer during their lifetime.14

Estimates suggest that the five-year survival rate from ovarian cancer is 93%, provided that the cancer is diagnosed and treated early. Unfortunately, cancer of the ovary is relatively asymptomatic and therefore most ovarian cancers are not recognized early; only 24% of all cases are detected at the localized stage.17

Some patients may complain of vague gastrointestinal disturbances, discomfort, abdominal swelling or abnormal vaginal bleeding (rarely). However, early-stage ovarian cancer is generally without warning signs. (A complete list of possible clinical features is presented in Table 4.) Even with aggressive treatment, patients with advanced-stage ovarian cancer face a dismal prognosis: only 15-25% survive and are disease-free after 5 years.17,18 Therefore, a more realistic five-year survival rate for all stages combined is 47%, nearly half of the survival rate for early-diagnosed tumours.17

<table>
<thead>
<tr>
<th>Table 4 Clinical Features of Ovarian Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ** asymptomatic **</td>
</tr>
<tr>
<td>• abnormal vaginal bleeding</td>
</tr>
<tr>
<td>• abdominal pain, fullness, discomfort</td>
</tr>
<tr>
<td>• gastrointestinal disturbances</td>
</tr>
<tr>
<td>• post-menopausal bleeding</td>
</tr>
<tr>
<td>• urinary frequency</td>
</tr>
<tr>
<td>• dyspareunia</td>
</tr>
<tr>
<td>• abdominal swelling</td>
</tr>
<tr>
<td>• ascites</td>
</tr>
<tr>
<td>• coughing (pleural effusions)</td>
</tr>
</tbody>
</table>

Currently there are no effective screening tests for ovarian cancer. Approximately 5% of ovarian cancers are familial in nature with a discernible pattern of heredity.18 Detailed evaluation of the patient’s clinical and family medical histories and thorough physical examination remain the only techniques dependable for early detection of ovarian cancer. While several screening tools such as ultrasonography, colour flow Doppler, magnetic resonance imaging, serum determination of tumour marker CA-125, PET imaging and pelvic and abdominal computed tomography have become available, none of these tools has demonstrated its effectiveness as a screening modality. Furthermore, there is great variation in their sensitivity and/or specificity for ovarian cancer.18

Several risk factors have been identified as predisposing to ovarian cancer development. Long menstrual intervals (early menarche and late menopause), uninterrupted or hyper-ovulation (due to nulliparity and infertility drugs respectively), high fat diets, the use of asbestos-containing talc, North American or European descent, age, and genetic factors

Discussion

Ovarian Cancer
(genetic anomalies or positive family history) have all been correlated to greater individual risk of ovarian cancer.\textsuperscript{19-21} Conversely, protective effects against ovarian cancer have been associated with prolonged lactation, tubal ligation, and the use of oral contraceptives.\textsuperscript{21,22}

The incidence of ovarian cancer increases significantly around the perimenopausal period. In fact, the median age for epithelial ovarian cancer is 60-65 years, with only 10-15\% of tumours discovered in pre-menopausal women.\textsuperscript{23} It is believed that gonadotropins which are excessively secreted at the time of menopause, play a significant role in ovarian carcinogenesis.\textsuperscript{24}

Aberrant expression or mutations of tumour suppressor genes and protooncogenes have been implicated in the pathogenesis of many cancers, including those of the ovary. Examples of genes associated with the development of ovarian cancer include, but are not limited to the oncogenes c-erb-B, c-erbB-2, ras, c-myc, c-kit, and BRCA-1 and the tumour-suppressor gene p53.\textsuperscript{25} Due to the regenerative nature of OSE cells that substantially increases the likelihood of significant mutations being passed on to future OSE cell generations, it is not surprising that many altered/absent gene products have been described for ovarian cancer.\textsuperscript{25}

**Classification of Ovarian Tumours.** There are four classification systems used to describe primary ovarian tumours. Firstly, the tumours are classified according to the ovarian structure from which the cancer is derived. Despite composing only a small fraction of the total ovarian mass, the surface epithelium gives rise to nearly 90\% of all ovarian cancers.\textsuperscript{21,22}\textsuperscript{26} Nonepithelial ovarian malignancies are less common and account for the remaining 10\% of all malignancies. The non-epithelial ovarian tumours include those derived from germ cells and tumours of sex cord-stromal origin.\textsuperscript{27}

The second classification system as described by the International Federation of Gynecology and Obstetrics (FIGO) describes the basic stages of disease progression of ovarian tumours (Stages I to IV, refer to Table 5).\textsuperscript{28} Prognosis is good if the growth has remained limited internally to the ovary (Stage IA or IB).

The histological classification of ovarian carcinoma comprises the third classification system. This classification is made on the basis of similarities of the carcinoma to normal tissues (refer to Table 6).\textsuperscript{29}

Finally, ovarian tumours can be further categorized on the basis of their metastatic potential into benign,

### Table 5

**FIGO Staging of Ovarian Cancer**\textsuperscript{28}

<table>
<thead>
<tr>
<th>FIGO STAGE</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| I          | Growth limited to the ovaries  
 IA - one ovary; no ascites; no tumour on external surfaces; capsules intact  
 IB - both ovaries; no ascites  
 IC - tumour either IA or IB but with tumour on surface of one or both ovaries; or with capsule ruptured; or with ascites present containing malignant cells or with positive peritoneal washings and extrusion of malignant cells from ruptured inclusion cyst into peritoneal cavity (ascites) |
| II         | one or both ovaries with pelvic extension of malignant cells  
 IIA - extension to oviducts, uterus  
 IIB - other pelvic tissues  
 IIC - ascites |
| III        | Spread of peritoneal implants within the abdomen outside of the pelvis, with or without surrounding lymph node involvement  
 Cancer cells may extend onto surface of the liver or intestine  
 IIIA - microscopic seeding  
 IIIB - macroscopic nodules > 2 cm in diameter  
 IIIC - macroscopic nodules > 2 cm in diameter; retroperitoneal or inguinal nodes |
| IV         | One or both ovaries with distant metastases |
secondary to either appendiceal or ovarian primary tumours. Recently, however, it has become apparent the primary cancer is always appendiceal and when ovarian involvement is identified, it is almost certainly secondary to the appendiceal primary tumour. Appendiceal tumours can be quite small as was observed in this patient's pathology. Therefore, the pathologist concluded that the appendix was the primary cancer and all other tumour findings, including those in the ovary, were secondary in nature.

Revised Pathological Diagnosis: Malignant appendiceal cancer with associated pseudomyxoma peritonei.

Clinical Discussion

Management of ovarian cancer versus appendiceal cancer

Ovarian Cancer. Treatment for ovarian cancer is generally prescribed according to stage. The cancer must be surgically staged prior to treatment onset (usually during exploratory laparotomy). The treatment plan for Stage IIIC ovarian carcinoma typically involves TAH-BSO, peritoneal washings, and surgical debulking plus adjuvant chemotherapy for 3-6 months. This patient was managed according to these established guidelines.

Appendiceal Cancer. Appendiceal cancers are rare but important. These neoplasia make up less than 0.5% of all intestinal tumours. The majority are incidental findings on pathological examination of appendectomies, but symptomatic patients present with features of appendicitis. It is difficult to diagnose appendiceal cancers pre-operatively, and some may even be missed during surgery. However, it is important to diagnose and treat these rare neoplasia, since recurrent malignancy will occur in 15-20% of cases, either concurrent with, or subsequent to the initial tumour. Malignant lesions represent 60% of appendiceal tumours, the most common being the carcinoid (85%) and benign tumours represent 40% of neoplastic lesions of the appendix and include polyps and adenomas.

Appendiceal polyps are classified similarly to colonic polyps. These lesions include the Peutz-Jeghers, hamartomatous, metaplastic, and juvenile hamartomatous types. Polyps and adenomas differ in that nuclear atypia is seen in adenomas. An adenoma that produces a large amount of mucus can develop into a sausage-shaped cystic mass known as a "cystadenoma." If the mucus invades the appendiceal wall this will result in a “mucocele.” Sometimes the cystadenoma or mucocele ruptures into the peritoneal cavity causing a gelatinous type of ascites known as “jelly belly,” or “pseudomyxoma peritonei.” Cystadenoma and mucoceles may present as appendicitis, a RLQ palpable mass, torsion, or as ureteral obstruction and/or hematuria. Appendectomy will cure

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Histological Classification of Ovarian Tumours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histological subtype</td>
<td>Normal Structure Derivation</td>
</tr>
<tr>
<td>serous (50%)</td>
<td>fallopian tube</td>
</tr>
<tr>
<td>mucinous (10%)</td>
<td>endocervix</td>
</tr>
<tr>
<td>endometrioid (10%)</td>
<td>endometrium</td>
</tr>
<tr>
<td>clear cell (5%)</td>
<td>mesonephric</td>
</tr>
<tr>
<td>transitional</td>
<td>urothelial</td>
</tr>
<tr>
<td>mixed epithelial</td>
<td>—</td>
</tr>
<tr>
<td>undifferentiated</td>
<td>—</td>
</tr>
<tr>
<td>unclassified</td>
<td>—</td>
</tr>
</tbody>
</table>
patients with these conditions, as long as the resection limit
at the base of the appendix is tumour free. Localized PMP
is treated by appendectomy and excision of any local mucin
deposits.32

These ‘benign’ tumours associated with PMP underscore a
problem with nomenclature and classification. PMP is a
manifestation of metastatic disease; therefore, the append-
decal tumours while histologically benign, have malignant
behaviour.

Malignant appendiceal tumours. Primary malignancies of
the appendix include carcinoid tumours (85%), mucinous
cystadenocarcinomas (8%), colonic adenocarcinomas (4%),
and adenocarcinoid tumours (2%).32 This section will elab-
orate further on the two most prevalent subtypes of append-
decal malignancies.

Carcinoid tumours. These tumours are derived from
subepithelial neuroendocrine cells and represent the majori-
ty of malignant lesions of the appendix. Most carcinoid
tumours are benign but all have the potential for invasion
and metatases. Eighty percent are an incidental finding dur-
ing surgery especially in women undergoing appendectomies
concurrent with hysterectomy or cholecystectomy. Carcinoid
tumours can occur at all ages, although this subtype is more commonly seen in adults. In adults, the mean
age at presentation is 32 years with a predilection for
women over men of 4:1.33

Unless found incidentally, most cases will present with
symptoms that are indistinguishable from acute appendici-
tis. Rarely, liver metastases occur. The size of the tumour
helps determine the type of surgery. Measurements should
be taken (in vivo) because size determinations can be under-
estimated due to shrinkage artifacts. The treatment of
appendiceal carcinoids is controversial, since incidental dis-
covey of the lesion by the pathologist may result in a sec-
ond, unexpected operation.33 However, several large stud-
ies recommend appendectomies for tumours less than 2.0
and without involvement of the mesoappendix or lym-
phatics.33-35 A right hemicolectomy is recommended if: (1)
the lesion is larger than 2.0 cm; (2) it is located at the base
of the appendix; (3) there is invasion of the serosa, lym-
phatics, or mesoappendix; (4) there is mucin production;
and (5) there is cellular pleomorphism with a high mitotic
rate.33 The prognosis with treatment is good with a 5-year
survival rate greater than 90%.

Mucinous cystadenocarcinomas. These slowly progress-
ing tumours are distinct from other appendiceal malignan-
cies in that they can be diagnosed pre-operatively; more
than 70% of patients present with signs resembling acute
appendicitis. The remainder present with signs of an
abdominal mass and can be confused with Crohn's disease,
intussusception, hydronephrosis or bladder carcinoma. The
mean age at presentation is 50 years with men more com-
monly affected than women.36 Half of all patients have
intraabdominal metastases or PMP. Patients with PMP may
also present with ascites, but will not show shifting dullness.
Pathologically, cystadenocarcinomas produce large amounts
of extracellular mucin and are well differentiated.
Treatment is determined by the extent of tumour invasion.
If there is any indication that the lesion has invaded beyond
the mucosa, a right hemicolectomy will result in a 70% sur-
vival rate at five years. If the lesion is confined to the
mucosa, then an appendectomy offers the same survival
advantage as a right hemicolectomy.36 Agressive debulking,
omentectomy, and oophorectomy can result in 5-year sur-
vival rates of 50% for those patients with intraabdominal
metastases or PMP.

Since all appendiceal cancers have a 15-20% risk of recur-
rent malignancy or a second concurrent malignancy, all
patients should undergo exploratory surgery at the time of
appendectomy or hemicolectomy. They are not always easy
to diagnose preoperatively or even during surgery, but
frozen samples should be taken for intraoperative patholog-
ical examination to rule out microscopic abnormalities.31

In summary, appendiceal cancer is not as responsive to
chemotherapy as ovarian cancer and therefore requires as
extensive a surgical excision as possible. Accordingly, the
change in this patient's diagnosis lead to significant alter-
ations in her therapeutic management plan.

Pseudomyxoma Peritonei

PMP is a rare condition characterized by mucinous ascites
("jelly belly") and multifocal mucinous tumours on the peri-
toneal surfaces and omenta.37 It is twice as common in
females than in males and is found in 2/10,000 laparo-
tomies.38 Women with PMP frequently present with simulta-
aneous tumours on both the appendix and ovaries. There
has been considerable debate on the true origin of these
tumours. The origin could be a primary appendiceal malig-
nancy with metastases to the ovary, an ovarian primary
malignancy with metastases to the appendix, or there could
be two independent primary disease processes. This has
considerable significance in the management of the disease.

Pathology. In the past, it was accepted that any mucinous
ovarian tumour present in a female represented the origin
of the disease.39 However, incidental findings of mucoele-
es, adenomas, or carcinomas of the appendix were found
in many of these cases. The ovary was believed to be the
primary site because the ovarian lesions were identical to
some primary ovarian tumours, particularly mucinous
tumours. In addition, the apparent absence of appendiceal
neoplasia in some patients with PMP and mucinous ovarian tumours, favoured either a primary ovarian malignancy or two independent primary malignancies.40 Other investigators argue that the origin of PMP is a primary appendiceal malignancy because: (1) the histological similarity of the mucinous tumours in both the appendix and the ovary; (2) the unusually high frequency of bilaterality of ovarian tumours, as compared with unilateral primary mucinous ovarian tumours; (3) the predominance of rightsided ovarian involvement when the tumours are unilateral; and (4) the usual presence of mucinous epithelium with dissecting mucin on the ovarian surfaces.41,42 The seemingly low malignance potential of the ovary in PMP is explained by some researchers by the fact that the mucus epithelium of primary appendiceal mucinous cystadenocarcinoma is extremely well differentiated to begin with.43

Changing understanding of PMP primaries. The argument for an appendiceal origin for these tumours was further strengthened by molecular genetic and immunohistochemical studies. If there were a single primary neoplasm, then deposits in other sites would show clonality. Recent molecular evidence supports that mucinous tumours involving the appendix and ovaries in women with PMP are derived from a single site, most likely the appendix.37 Specifically, mutations in k-ras were identical between cases of PMP and appendiceal cancers not associated with PMP, but different when compared to ovarian cancers not associated with PMP. It is unlikely that two independent mucinous tumours acquired the same mutation by chance. In addition, Szych et al. suggested that the loss of heterozygosity seen in chromosomes common in ovarian epithelial tumours (6q), but not seen in chromosomes common in appendiceal tumours (18q, 5q, 17p) can be interpreted to mean that most PMP cases showing allelic loss are due to tumour metastases to a secondary site.37 Immunohistochemical studies show that the pattern of cytokeratin expression in mucinous tumours associated with PMP is similar to that of appendiceal mucinous cystadenocarcinomas in the absence of PMP (CK 20+ and usually CK 7-) and different from that of primary ovarian mucinous tumours of low malignant potential (CK 20+ and CK 7+).44

The histological diagnosis of PMP can be made by noting mucin dissection through the stroma, often with sparse strands of neoplastic epithelial cells.41 With ovarian involvement the same mucin deposition is seen in the ovarian stroma and is called ‘pseudomyxoma ovarii’ (PO). PO is a rare finding in primary mucinous ovarian tumours and is therefore useful as the histologic feature that allows one to distinguish primary from secondary.41

PMP is considered to be a clinical entity and is defined by gelatinous ascites. The diagnosis is difficult to make because the gross intraoperative appearance of the appendix harboring the neoplasm may be unremarkable. Some appendices may be distended as a mucocele, while others may be slightly enlarged, or even “normal” if not examined carefully for evidence of a tumour and removed accordingly.

Clinical Presentation. Commonly reported symptoms include abdominal pain, distension or a mass in the abdomen. Less frequent symptoms include nausea, vomiting, fatigue, and urinary symptoms.42 The preoperative diagnosis is usually incorrectly made as appendicitis or an ovarian tumour. Most cases of PMP are unexpected diagnoses found upon laparotomy.45

Common findings during the surgery have been mucinous ascites, and tumour deposits that typically involve the right hemidiaphragm, right retrohepatic space, left paracolic gutter and ligament of Treitz. An abnormal appendix and involvement of one or both the ovaries may also be seen.42

Investigations. Since PMP is a rare condition, the sensitivity and specificity of various imaging modalities have been difficult to quantify using studies based upon only a handful of case reports. However, computed tomography is commonly used to establish the diagnosis and extent of tumour progression. The mucinous material will appear like fat and be heterogeneous in nature.46 Ultrasound will show non-mobile echogenic ascites, with ‘scalloping’ of the hepatic and splenic margins due to extrinsic pressure from adjacent peritoneal implants. Anecdotal data show that the levels of CEA and CA 19-9 may be raised in patients with PMP and may be an indicator of recurrent disease. However the reliability of such measurements is limited due to small sample sizes in the studies examined.47

Management. Radical surgical debulking is the currently accepted mainstay of treatment for patients with PMP of appendiceal origin.41,42,43 This approach should involve systematic removal of all gross disease, and a complete appendectomy if not done previously. A right hemicolectomy is also frequently recommended. Due to the rarity of this condition, there have been no formal trials to provide guidelines for optimum treatment, and the role of adjuvant intraperitoneal chemotherapy (with or without diathermy) or radiotherapy is controversial. While some investigators have described improved outcome if adjuvant intraperitoneal chemotherapy is provided in conjunction with complete surgical cytoreduction, other studies have demonstrated that mortality and morbidity in adjuvant chemotherapy-treated patients are not statistically different from those of non-adjuvant treated patients.45 There is no currently recognized role for adjuvant chemotherapy in PMP.45 The use of mucolytic agents to loosen mucinous deposits and phototheraphy-mediated dissection at laparotomy have not been
would not respond to any adjuvant therapy, radical debulking surgery was felt to be the best course of management. As she was still recovering from her extensive operation, it was recommended that she defer radical debulking for at least 3 months. Given her revised diagnosis, it is not recommended that she undergo chemotherapy at this time. When she is both physically and psychologically stronger she will be reevaluated by CT scan and her suitability for peritoneectomy, distal gastrectomy and splenectomy will be discussed.

Acknowledgements
This interesting case was provided by Dr. William Chapman, Departments of Laboratory Medicine and Pathobiology and Obstetrics and Gynecology, University of Toronto. The authors wish to thank Dr. Chapman for his invaluable contribution.

References