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Lesions of the Pouch of Douglas-A Review

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Precis:
Lesions of the Pouch of Douglas are reviewed.

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Abstract:

Background:

The pouch of Douglas may become involved by a variety of mass-like lesions, which may be challenging to providers who treat women. They may initially be thought to be arising from the uterus or adnexa. A literature review was conducted. A Medline search was used, using the terms Douglas’ Pouch, Pouch of Douglas, cul-de-sac, and rectouterine pouch. A review of the scope of Pouch of Douglas lesions is presented to assist in developing a differential diagnosis if a patient with such a lesion is encountered.
Introduction:
A wide variety of lesions may involve or arise from the Pouch of Douglas (cul-de-sac, POD).
They may initially be thought to be arising from the uterus or adnexa. This paper reviews lesions of the area, in order to provide assistance in developing a differential diagnosis, if such a patient is encountered.

Anatomy & Histology
“The cul-de-sac is the rich domain of the gynecologist” (1). Speert goes on to state that the cul-de-sac allows palpation of the pelvic organs, appreciation of tenderness and masses, is a location for culdoscopy and aspiration of pelvic abscesses and blood from ectopic pregnancies, as well as a source of tissue to approximate in enterocele repair (1). The rectouterine space, cul-de-sac, or Pouch of Douglas (POD), is named after the Scottish anatomist, James Douglas (2), who in a time where medicine consisted mainly of laxatives and emetics, described many aspects of human anatomy, including the rectouterine pouch and fold in 1730. Douglas’ other claim to fame, the debunking of a woman who claimed to give birth to rabbits (1), has not gained quite the same notoriety. The POD is the space between the posterior uterus and the anterior rectum. It is bordered laterally by the rectouterine folds, peritoneal folds that extend from the rectum to the posterior broad ligament at the cervix. This region is further subdivided into the pararectal and ovarian fossae (3) (Fig 1). The rectouterine folds contain the rectouterine muscle. The POD may be appreciated on pelvic examination, particularly rectovaginal examination. The POD is lined by peritoneum, which is comprised of mesothelial cells, similar to the Müllerian lining of the rest of the pelvic genital organs. Because of the common embryology, the female peritoneum can
develop lesions that mimic normal or neoplastic Müllerian structures, hence the peritoneum has been termed the secondary Müllerian system(4). These lesions include benign lesions such as endosalpingiosis, endocervicosis, Müllerianosis, endometriosis, and malignancies such as endometriosis-associated carcinoma, and primary peritoneal carcinoma(5)(Fig 2). In addition, the peritoneum(mesothelium), is also vulnerable to lesions that may affect mesothelium elsewhere, such as mesothelial hyperplasia, or the rare malignant mesothelioma. While this review focuses specifically on the POD, a review of selected peritoneal lesions is available to interested readers(6). Due to its dependent position in the body, as well as peristalsis(7), the POD is a common site for metastatic deposits of peritoneal neoplasia, most often ovarian in women, and gastrointestinal in men(3) as well as abscess formation with peritonitis(3). The POD has also shown utility as a source of tissue for vaginoplasty in cases of vaginal agenesis(8).

**Evaluation of the POD**

The first step in evaluation of the POD is a good physical examination, including a rectovaginal assessment. A variety of imaging modalities may have utility in evaluating diseases of the POD. While transvaginal ultrasound is a first line modality for suspicion of ectopic pregnancy, computerized tomography(CT) imaging has been shown to be useful for detecting POD tumor implants(9), and magnetic resonance imaging(MRI) has been lauded in diagnosis of deep infiltrating endometriosis(10).
Benign lesions

Fluid in the POD

A small amount of fluid may occasionally be present physiologically in the POD, and transvaginal ultrasound has been shown to be extremely sensitive to its detection, in one study able to detect 0.8 ml of fluid(11). In one study of 89 pregnant women, 6 had a small amount of fluid, to a maximum depth of 4 mm. The authors suggested that greater than 2-4 mm depth of fluid may not be physiologic(12). Fluid in the POD probably accumulates due to this being a dependent location. POD fluid can be visualized on ultrasound, but is a nonspecific finding, and may represent a variety of things, including ascites, as well as pus from pelvic inflammatory disease, fluid in peritoneal tuberculosis(13), blood from a ruptured ectopic pregnancy, or fluid from a ruptured ovarian cyst(3). An extremely rare cause of blood in the POD is rupture of a POD vessel in the absence of vaginal trauma, after consensual vaginal intercourse(14).

Culdocentesis, while used less than in the past, occasionally has a place in a gynecologic patient. Culdocentesis has been utilized in the workup of possible ectopic pregnancy, with non-clotting blood obtained supportive of that diagnosis, although both false positives and false negatives occur, with a hematocrit of >15% frequently seen in ectopic pregnancies(15). Retrieval of purulent material may reflect pelvic inflammatory disease. Puncture of the cul-de-sac is also utilized in ovum retrieval for in vitro fertilization. Ascites may be sampled through the cul-de-sac, and cytologic evaluation performed for malignancy, however the risk of seeding tumor has limited the utility of this. A review of the technique with safeguards for this procedure is available(16).
Hernia & genital prolapse

A few rare cases of hernia through the POD have been described(17,18), defined as a peritoneal internal hernia caused by a defect in the POD peritoneum. The rest of the POD is undescended in these cases(17,18). This type of hernia may present as small bowel obstruction(18). Even with radiologic studies, the exact location of a pelvic hernia may be difficult to localize, and this case was confirmed and repaired laparoscopically.

Enterocoele, more common than the hernia described above, is descent of the entire POD peritoneum itself, due to pelvic floor weakness, into the rectovaginal septum. It often contains small bowel. The cutoff point of an enterocoele, as opposed to a deep POD, is unclear. It has been shown that examination of the patient in the standing position, with an empty bladder, maximizes appreciation of pelvic organ prolapse(19). Culdoplasty, in some form, has been utilized with vaginal hysterectomy, to prevent development of enterocoele(20). It has been suggested(21) that obliteration of the POD by approximation of the uterosacral ligaments improved the outcomes of Burch colposuspension.

Foreign Bodies

The POD is also the rare repository of ingested foreign objects that perforate the gastrointestinal tract, such as the case of a nail ingested by a child(22). In adults, more commonly migrated foreign bodies such as IUDs(23) and less common ones, such as spilled gallstones(24), gossypiboma(25), and a pacemaker(26) have also been described in the POD. In one case, a levonorgestrel containing IUD was found in the POD of a woman with an intrauterine first trimester pregnancy, who decided to continue the pregnancy, and subsequently delivered a viable infant and laparoscopic removal of the IUD(27). The authors suggest
individualization of therapy in such a case, with risks of pain, perforation of internal organs, adhesions, and theoretical risk of masculization of a female infant due to the higher hormonal levels in the mother’s bloodstream in the ectopic location(27). A POD foreign body may present as pain or a pelvic mass. It has been stressed that spilled gallstones may produce occasional severe complications, including infection, adhesions, bowel obstruction or fistulas(28). Foreign body retrieval may be amenable to laparoscopic procedures(23). Clusters of gallstones seen in the cul de sac at laparoscopy have been given the quaint name of “blueberry sign”, for obvious reasons(28).

**Trauma**

The POD may be ruptured with intercourse, particularly in nonconsensual sex, and prolapse of loops of bowel into the vagina is possible(29)

**Infections and inflammation of the POD**

Abscesses in the POD may be secondary to pelvic inflammatory disease, appendicitis, or ruptured diverticulitis. Postoperatively, blood accumulating in the POD may become infected, including after excision of deeply infiltrating endometriosis(30)

A rare abscess of the POD was described secondary to incarceration and necrosis of the appendix after uterine perforation during pregnancy termination(31). Mucormycosis, an infection of immunosuppressed individuals, was described in the POD of a diabetic woman(32). A case of xanthogranulomatous endometritis formed a POD mass in one fatal case(33).

Xanthogranulomatous inflammation is a histologic diagnosis associated with many foamy and hemosiderin laden macrophages, with multinucleated giant cells. In this case(33), the patient had
pyometra, xanthogranulomatous inflammation, and culture proven enterococcus sp. and Peptostreptococcus magnus.

Oil based contrast medium used for hysterosalpingography may cause granulomatous inflammation that can suggest POD endometriosis at laparoscopy(34). Parasitic infections may cause POD masses, including pinworm(35), and echinococcal hydatid cysts, which may obstruct labor(36)

**Endometriosis**

The POD is a common site for endometriosis, and endometriosis in this and the rectovaginal septum may be associated with significant symptomatology. It has been suggested that the Masters Allen syndrome may predispose to and/or indicate deep infiltrating endometriosis in this region (37). Endometriosis may obliterate the POD. On histopathology, the presence of endometrial glandular epithelium and stroma are required to confirm endometriosis(fig2b), however many cases are diagnosed clinically at the time of laparoscopy.

**Pregnancy complications involving the POD**

Ectopic pregnancies can implant in the POD, and this has been described after in vitro fertilization(38). POD pregnancy may occur after tubal abortion, or rupture of a tubal ectopic pregnancy with secondary implantation in the POD(39). One case was described where the POD ectopic was managed by a combination of systemic and transvaginal inraamniotic methotrexate(40). Exceptionally rare is a case of complete hydatidiform mole in an ectopic pregnancy implanted in the POD(41). Because ectopic pregnancies tend to be diagnosed early, when there is more florid proliferation of implantational trophoblast, hydatidiform mole tends to
be over diagnosed in ectopic pregnancies. Ota et al stress that immunohistochemistry with p57 can be useful in some of these cases, as it can confirm a complete mole(41).

Intrauterine pregnancies may also involve the POD, as in a case of a uterine perforation sustained at the time of an 11 week pregnancy termination, with relocation of the fetus to the POD, identified on ultrasound when the patient developed pain five hours after the procedure(42). About 15% of uteri are retroverted, and a very rare pregnancy complication is incarceration of the uterine fundus in the POD in a retroverted uterus. Early diagnosis is important to mitigate complications. A few such cases have been reduced utilizing the assistance of colonoscopy(43). Leiomyomas may also become trapped in the POD during pregnancy(44).

A rare case of a tear in the POD following a successful VBAC has been described and the authors stressed the importance of awareness of unusual pain and bleeding associated with VBAC(45).

Rare pregnancy-associated malignancies in the POD have included a malignant placental site trophoblastic tumor in association with a lithopedion, indicating a prior abdominal pregnancy(46), and unrelated metastatic disease to the POD during pregnancy, such as a case of primary osseous adamantinoma, originally from the tibia(47).
Miscellaneous lesions

The peritoneum of the POD is prone to the same reactive changes as elsewhere in the peritoneal cavity, and mesothelial hyperplasia may be seen microscopically in association with a wide variety of lesions, benign and malignant. This may raise concern for an epithelial neoplasm, but can be shown to be mesothelial by utilization of mesothelial immunostains such as calretinin.

Benign neoplasms

The most commonly reported neoplasm in the POD is benign cystic teratoma. This can be a dermoid arising from the ovary that has fallen into the POD due to the increased weight associated with the contents, or an autoamputated ovarian dermoid(48). It can also arise de novo, where it is thought to occur due to trapping of germ cells during the fetal migration of germ cells, and can occur in men(49) as well as women(50).

Leiomyomas may be found in the POD. They may be pedunculated uterine fibroids, a leiomyoma arising from small bowel(51), or parasitic, including from iatrogenic spread after morcellation(52). An interesting case of an extraovarian fibrothecoma in the POD mimicked a leiomyoma clinically(53). The authors postulated that the lesion arose in a supernumerary ovary, although this was not demonstrable histologically.

Benign multicystic mesothelioma, a benign multicystic lesion with a high recurrence rate, may be found in the cul de sac, where it may be free floating, as well as attached, and may be amenable to laparoscopic resection(54). In one case, it was associated with high serum CA19.9, which decreased after laparoscopic resection(55). Multicystic mesothelioma may be confused
with multilocular peritoneal inclusion cysts, which usually occur after prior surgery, and in fact may represent the same entity(56).

An adenomatoid tumor, a benign mesothelial lesion, has also been reported in the POD(57).

Malignant lesions

Primary malignancies may rarely arise in the POD, of Müllerian origin, and the mechanism is potentially malignant transformation of endometriosis, although this cannot always be demonstrated, as the tumor may have overgrown an endometriotic focus. Malignant transformation of Müllerian remnants is another possibility(58). Müllerian tumors that have arisen in the POD include adenosarcoma(59,60), carcinosarcoma(58), and clear cell carcinoma(61). Rarer primary tumors of the POD include malignant placental site trophoblastic tumor(46), malignant mesothelioma(62), and extragastrointestinal stromal tumor(63), which has a high local recurrence rate(64).

Perhaps because of the dependent location and peristalsis, seeding of tumors within the peritoneum tends to go to the POD(7), particularly ovarian carcinomas(fig2c), as well as colon carcinoma(65). Other ovarian neoplasms such as carcinoid have been reported as well(66). Endometrial carcinoma cells have been documented in the POD after curettage(67), but it is not clear whether or not that increases the risk of implantation of these cells.

Rarely, evaluation of POD fluid may confirm a non-ovarian malignancy, and the modes of tumor transport may be unusual as well. Some neoplasms, such as pseudomyxoma peritonei in
association with an appendiceal primary, may be present in the POD, but culdocentesis may be
difficult and yield little, due to the thick mucinous fluid, scant cellularity in the mucus, and
loculation. Culdocentesis, however, has fallen by the wayside as a diagnostic tool for
malignancy, as there may be risk of seeding a malignant tumor. In one case(68), peritoneal
keratin granulomas were present in the cul de sac, from transtubal spread of an endometrial
adenocarcinoma with squamous differentiation. This finding is more likely associated with
leakage of a benign cystic teratoma(68). Transtubal spread of tubal carcinoma has occurred(69).
Pineal tumors have been transported via ventriculoperitoneal shunts and implanted in the
POD(70). Intestinal lymphoma has presented with effusion in the POD, unusual for a non-
effusion lymphoma, where this is usually a late, not initial finding(71).

**Conclusions:**
The Pouch of Douglas may be involved in a wide variety of lesions. A knowledge of specific
lesions of the region will be helpful in developing a differential diagnosis, if such a patient is
encountered.
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Figure 1 - Pelvic exenteration for cervical carcinoma, extending anteriorly to the bladder. The POD is free of tumor(arrow).

Figure 2 - Patient with endometriosis who developed mixed clear cell and endometrioid carcinoma of the ovary. Biopsy of the POD showed endosalpingiosis(2a), with a tubal-type lining and no surrounding stroma, endometriosis(2b), showing endometrial type stroma between glands(arrow), and endometrioid carcinoma(2c), showing more atypical glands. Lymphvascular space involvement was present(inset), and the endothelial lining of the lymphovascular space(arrow) is confirmatory that the space is a lymphovascular space.