Lesions of the Broad Ligament: A Review

Rutgers University has made this article freely available. Please share how this access benefits you. Your story matters. [https://rucore.libraries.rutgers.edu/rutgers-lib/50618/story/]

This work is an ACCEPTED MANUSCRIPT (AM)

This is the author's manuscript for a work that has been accepted for publication. Changes resulting from the publishing process, such as copyediting, final layout, and pagination, may not be reflected in this document. The publisher takes permanent responsibility for the work. Content and layout follow publisher's submission requirements.

Citation for this version and the definitive version are shown below.


Terms of Use: Copyright for scholarly resources published in RUcore is retained by the copyright holder. By virtue of its appearance in this open access medium, you are free to use this resource, with proper attribution, in educational and other non-commercial settings. Other uses, such as reproduction or republication, may require the permission of the copyright holder.

Article begins on next page
Lesions of the Broad Ligament - a review

Debra S. Heller, MD

From the Department of Pathology & Laboratory Medicine, Rutgers-New Jersey Medical School, Newark, NJ

Address Correspondence to:

Debra S. Heller, MD
Dept of Pathology-UH/E158
Rutgers-New Jersey Medical School
185 South Orange Ave
Newark, NJ, 07103
Tel 973-972-0751
Fax 973-972-5724
hellerds@njms.rutgers.edu

Word count: 2123
Running title: Lesions of the Broad ligament
Funding: Departmentally funded
Disclosures: none
Lesions of the broad ligament are reviewed.

Key words: Broad ligament, uterine neoplasms, female genital tract
Abstract:

The differential diagnosis of lesions arising in the broad ligament is quite large. Many of these lesions can be clinically interpreted prior to surgery as adnexal or uterine neoplasms. While some lesions are similar to those arising in other Müllerian sites, there are unique lesions as well. The lesions are uncommon, and may prove challenging to clinicians. The purpose was to review the scope of lesions affecting the broad ligament. A literature review was conducted. A Medline search was used, using the terms broad ligament, mesosalpinx, and mesovarium. A review of the scope of broad ligament lesions is presented to assist in developing a differential diagnosis if a patient with such a lesion is encountered.
Introduction:
The differential diagnosis of lesions arising in the broad ligament is quite large. Many of these lesions can be clinically interpreted prior to surgery as adnexal or uterine neoplasms. While some lesions are similar to those arising in other Müllerian sites, there are unique lesions as well. The lesions are uncommon, and may prove challenging to clinicians. The purpose was to review the scope of lesions affecting the broad ligament. A literature review was conducted. A Medline search was used, using the terms broad ligament, mesosalpinx, and mesovarium. A review of the scope of broad ligament lesions is presented to assist in developing a differential diagnosis if a patient with such a lesion is encountered.

Embryology, Anatomy & Histology
The broad ligament is a fold of peritoneum that drapes over the uterus and Fallopian tubes. It has three components, the mesovarium, the mesosalpinx, and the portion below the adnexa, the mesometrium, which is referred to as the broad ligament in common usage. The broad ligament contains many structures, including vessels, the uterine arteries, the round ligaments, a portion of the ureters, the uteroovarian ligament medially and suspensory ligament of the ovary laterally, cardinal ligaments laterally, and uterosacral ligaments posteriorly.

Embryonic rests are normal components of the broad ligament, and may give rise to some of the neoplasms that can occur there. Mesonephric(Wolffian) duct remnants may be seen in tissue adjacent to the fallopian tube, sometimes invested in muscle(Figure 1). Paramesonephric(Müllerian) remnants may also be present in the broad ligament near the
ovary(Figure 2). In addition, heterotopic hilar cell clusters, as well as adrenal cortical rests(Figure 3) may be incidental findings in the broad ligament, often in a paratubal location(2).

**Broad ligament defects**

Defects in the broad ligament may permit small bowel, colon, adnexa, or ureter to pass through, with subsequent strangulation, although this is uncommon(3,4,5). Defects may be congenital or acquired, and may involve one leaf, both leaves with a through and through defect, or an outpouching of intact peritoneum(5). The Masters Allen (or Allen Masters) syndrome refers to traumatic laceration of the posterior leaf of the broad ligament, often after childbirth, and is associated with an abnormally mobile cervix. It may cause pelvic pain and dyspareunia(6).

In one case, Masters Allen syndrome presented with signs suggestive of acute peritonitis(6). It has been suggested that this peritoneal tear may permit development of deep infiltrating endometriosis(7). It has also been argued that underlying endometriosis rather than pregnancy is the etiology of the acquired defect(8)

**Hemorrhagic lesions of the broad ligament**

Pregnancy is a time of increased risk for the broad ligament. Hemoperitoneum has been reported after rupture of a broad ligament varix(9), as well as with rupture of broad ligament and uterine vessels(10). A spontaneous broad ligament hematoma has also been reported in the absence of pregnancy, where it was attributed to venous injury associated with the combination of large uterine fibroids and the exertion of mowing a lawn(11)
Benign Tumors and Tumor-like Lesions

Intraligamentous pregnancy

Ectopic pregnancy arising in the broad ligament is rare, and usually associated with pregnancy loss and maternal hemorrhage, although a rare viable pregnancy has been reported(12). The authors postulated that the pregnancy was originally a tubal ectopic that had ruptured and re-implanted in the broad ligament. A case in a woman who underwent IVF after two prior ectopics had resulted in bilateral salpingectomies was postulated to have arisen either by rupture of the uterus during the IVF procedure, or recanalization of the fallopian tube stump(13).

Rare cases of uterine rupture with expulsion of the fetus into the broad ligament have been reported, as in Dhont’s case where a second trimester termination utilizing prostaglandins was complicated by this occurrence(14).

Broad ligament cysts

Cysts of the broad ligament may be of mesonephric or paramesonephric origin, with epithelium similar to that described for the corresponding remnants, or of mesothelial origin. Most of these cysts are paramesonephric(Müllerian)(15). Paratubal/Paraovarian broad ligament cysts represent about 10% of adnexal masses(16). The distinction between paratubal and paraovarian is sometimes arbitrary, with interchangeable usage, and these cysts are present in the broad ligament between the tube and ovary. In terms of distinguishing cysts from rests, which
can be dilated, cysts have been described as grossly visible lesions(1). Most of these cysts are incidental findings, but they may torsse with accompanying tube or ovary, rupture, or undergo hemorrhage(16). In addition, epithelial neoplasms may arise in paramesonephric cysts, with the same multipotentiality of Müllerian epithelium elsewhere, giving rise to benign, borderline, and malignant epithelial neoplasms that usually arise in the ovary.

**Leiomyoma of Broad Ligament**

The most common broad ligament neoplasm is a leiomyoma(17), with similar presentation to the uterine counterpart. Rarely, pseudo-Meig’s syndrome has occurred(18). A variant, leiomyomatosis, with over 400 small smooth muscle nodules confined to the broad ligament has also been reported(19). Angioleiomyomas, a benign tumor of smooth muscle and vessels, may be a variant, or may be similar to the soft tissue neoplasms arising elsewhere, and these have occasionally occurred in the broad ligament as well(20).

Mimics of leiomyoma that can arise in the broad ligament include extra-gastrointestinal stromal tumors(e-GIST) and perivascular epithelioid tumors(PEComas). Both of these are tumors of uncertain malignant potential, which can histologically mimic leiomyomas but are positive for C-kit and Dog-1 for e-GIST (21), and HMB45 for PEComas (22). These immunostains help distinguish these lesions from the much more common leiomyoma, which would be negative for these stains, but stain for smooth muscle markers.

Adenomyomas may also occur, and should not be mistaken for adenosarcomas due to overinterpretation of malignancy of the endometrial stroma surrounding glands(17). An extremely rare mimic of a parasitic leiomyoma in endemic areas is a calcified guinea worm(23)
Other rare benign tumor-like lesions and neoplasms

The broad ligament is a common site for endometriotic implants, however rarely, endometriosis may actually form a tumor mass in the broad ligament(24).

Several cases of papillary serous cystadenoma, highly but not always associated with von Hippel-Lindau(VHL) disease have been reported(25), and may be the first indication of the condition(17). In addition to the association with VHL, it is important to be aware that the histology of papillary serous cystadenoma can be confused with clear cell renal cell carcinoma. An immunohistochemical panel will help distinguish the two, with clear cell papillary cystadenomas more likely to stain for CK 7 and be negative for renal cell carcinoma antigen RCC and CD10, while the opposite is true for renal cell carcinomas(26). However, immunohistochemical as well as phenotypic overlap has been shown with papillary cystadenoma and clear cell papillary renal cell carcinoma, which is a different variant of renal cell carcinoma than clear cell carcinoma(27). Benign cystic teratoma has occurred in the broad ligament, and in one case herniated through the greater sciatic foramen, presenting as a gluteal mass(28). A variety of other unusual lesions such as Brenner tumor and fibrothecoma have been reported in the broad ligament (29,30). Osseous metaplasia has been reported to be able to form nodules in the mesosalpinx(31). Placental site nodule, usually seen in the endometrium, has also been reported in the broad ligament near the fallopian tube, where it may be a marker for a subinvoluted and unsuspected prior ectopic pregnancy(32).
A rare case of an oncocytic adrenal cortical adenoma arising in an adrenal rest of the broad ligament was reported(33). Pheochromocytoma, a usually benign neoplasm generally arising in the adrenal, has also occurred in the broad ligament, presenting with abnormal urinary catecholamines and hypertension(34).

A uterus-like mass, composed of smooth muscle with an endometrial-lined cavity is a rare occurrence in the ovary, but has also been reported in the broad ligament(35). The lesion presents with pelvic or abdominal pain, which may be cyclic. Histogenesis is unclear, but theories have included congenital anomaly of the Müllerian ducts, metaplasia or heterotopia(35).

Hydatid disease has been reported in the broad ligament and ovary of a child(36), as well as an adult(37), and echinococcosis is something to consider in the differential of patients from endemic areas.

Müllerianosis, the presence of mixed endometrioid, serous(tubal) and/or endocervical benign glands of the Müllerian system, have been reported in a variety of locations. Müllerianosis has been reported in the mesosalpinx(38), comprised mainly of endocervical glands with some tubal epithelium. The lesion occurred, as it not infrequently does, in association with borderline ovarian neoplasms, and the authors stress the importance of not interpreting the finding as metastatic.
**Malignant Neoplasms:**

Primary malignancies of the broad ligament are defined as tumors in the broad ligament completely separate from the uterus, ipsilateral tube and ovary(39).

**Female adnexal tumor of probably Wolffian origin (FATWO)**

This neoplasm is uncommon, but usually arises in the broad ligament. FATWO occurs over a wide age range, and presents as solid and cystic masses that can be small, but some have been up to 25 cm(40). They have a variety of histologic patterns, but the most recognizable is sieve-like (figure 4). A helpful finding is the staining with c-kit (CD117). Although most of these lesions do not metastasize, they are capable of aggressive behavior. A potential rare mimic that can arise in the broad ligament is a granulosa cell tumor. While inhibin is a significant marker for granulosa cell tumor, there can be overlap of this and other markers in FATWO, and the finding of nuclear grooves would favor a granulosa cell tumor(41).

**Epithelial Malignancies**

Müllerian-derived malignancies, including mucinous, serous, clear cell and endometrioid carcinoma, borderline tumors, as well as endometrial stromal sarcoma have arisen in the broad ligament, sometimes in association with endometriosis(40, 42, 43), although some authors postulate that these neoplasms can arise in Müllerian remnants(44). Malignant mixed Müllerian tumor has also been reported(45). Theories reviewed by Aslani et al(43) for the derivation of a serous borderline tumor in this location included invaginated fallopian tube epithelium,
Müllerian remnant, or mesothelial origin. A paratubal transitional cell carcinoma was speculated to have arisen from a Walthard’s rest, paratubal cyst, or tubal serosa(46).

Other rare malignancies and tumors of uncertain potential:

Sex cord stromal tumors have occurred in the broad ligament, including granulosa cell tumor(41), as well as steroid cell tumor. A case of steroid cell tumor, a sex cord stromal tumor of low malignant potential was reported in the broad ligament of an 11 year old female, who had associated virulization(47), and one in an adult, also masculinized, had evidence histologically of arising in an accessory ovary in the broad ligament(48). Carcinoid has been reported(49). A few cases of extraspinal ependymoma have arisen in the broad ligament(50). In the CNS, ependymoma is considered a low grade malignancy with recurrence and rare metastatic potential, but the number of broad ligament cases is too rare to prognosticate. In the literature review of Matsuyama et al, they found 3 cases with initial dissemination, although they were tumor free up to 27 months after surgery, one case that developed spread many years after initial surgery, and two with no documented spread(50). Solitary fibrous tumor has arisen in the broad ligament(51). Ewing’s sarcoma has occurred in the broad ligament(52). As this raises the large differential of small round blue cell tumors, cytogenetics as well as immunohistochemistry is important in making the diagnosis. It is important for clinicians to be aware that unusual tumors may need to be submitted to their Pathology department fresh, so that cytogenetics can be performed, although PCR and FISH modalities may have utility in some tumors, and can be performed after fixation.
Another example of the utility of genetic analysis was a case of choriocarcinoma in the fallopian tube and broad ligament of a young adult patient with a recent pregnancy. While it was initially felt that the choriocarcinoma was gestational, DNA genotyping matching normal patient tissue proved that the lesion was nongestational choriocarcinoma of germ cell origin, which has therapeutic and prognostic significance\(^{(53)}\). Gestational choriocarcinoma has also occurred in the broad ligament, presumably from an ectopic pregnancy in that location\(^{(54)}\). More unusual forms of GTD have also occurred in the broad ligament. A case of epithelioid trophoblastic tumor in the broad ligament of a 41 year old woman who had been treated ten years earlier for gestational trophoblastic disease was reported\(^{(55)}\).

Other rare malignancies have included undifferentiated pleomorphic sarcoma\(^{(56)}\), malignant fibrous histiocytoma\(^{(57)}\) and leiomyosarcoma\(^{(58)}\). In one case, broad ligament leiomyosarcoma metastasized to the pancreas\(^{(59)}\). It has been suggested that the criteria for malignancy in a broad ligament leiomyosarcoma is that of soft tissue, not uterus\(^{(17)}\). Uterine leiomyosarcoma has also spread to the vessels of the broad ligament in a pattern that mimics intravenous leiomyomatosis, and the authors termed this condition intravenous leiomyosarcomatosis\(^{(60)}\).

Conclusions:

The broad ligament can show a wide range of pathology. Preoperatively, these lesions may be thought to arise in the adnexa or uterus. At laparoscopy, as many of the lesions arise between the leaves of the broad ligament, they may be similar in appearance\(^{(5)}\), although preoperative imaging may be helpful in establishing a differential diagnosis. Broad ligament masses may be amenable to laparoscopic excision. In one case of broad ligament leiomyoma, the broad
ligament was opened, and the leiomyoma was morcellated(1). Knowledge of the potential for
the range of lesions of the region will be helpful if such a patient is encountered, and may allow
for planning minimally invasive surgical interventions.

Acknowledgments: None

Disclosures: None
References:


342 43-Aslani M, Ahn G, Scully RE. Serous papillary cystadenoma of borderline malignancy of

344 44-Handa Y, Kato H, Kaneuchi M, Saitoh Y, Yamashita K. High-grade broad ligament cancer of
Müllerian origin: immunohistochemical analysis of a case and review of the literature. Int J
Gynecol Cancer 2007;17:705-34.

347 45-Arora P, Rao S, Khurana N, Talwar D, Tanwar R. Malignant mixed Müllerian tumor of broad
ligament with synchronous ovarian and endometrial carcinoma: a rare association. J Cancer Res
Ther 2011;7:88-91.


352 47-Smith D, Crotty TB, Murphy JF et al. A steroid cell tumor outside the ovary is a rare cause of

354 48-Roth LM, Davis MM, Sutton GP. Steroid cell tumor of the broad ligament arising in an


358 50-Matsuyama A, Hisaoka M, Yamamoto I, Toyoshima S, Hashimoto H. Extraspinal


Legends:

Figure 1 - Mesonephric (Wolffian) remnant showing cuboidal epithelium with eosinophilic secretions

Figure 2 - Paramesonephric (Müllerian) remnant showing a lining similar to Fallopian tube

Figure 3 - Adrenal cortical rest shows cells with vacuolated cytoplasm in a well circumscribed nodule.

Figure 4 - FATWO, showing characteristic sieve-like pattern.

Figure 5 - Leiomyoma of the broad ligament seen at laparoscopy. Reprinted from J Minim Invasive Gynecol 12(6), Theodoridis TD, Zepiridis L, Grimbizis G, Bontis J. Laparoscopic management of broad ligament leiomyoma. p469, 2005, with permission from Elsevier.