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Lesions of the Lower Uterine Segment-A Review

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Word count 2146
Running title: Lesions of the Lower Uterine Segment
Disclosures: none
Precis:

Lesions of the lower uterine segment are reviewed.
Abstract:

Background: The lower uterine segment may become involved by cervical as well as endometrial lesions. In addition, there are lesions unique to the lower uterine segment, and identifying carcinomas in this region may have prognostic significance.

Objectives: This review covers the scope of lesions affecting the lower uterine segment.

Methods: A Medline search was used, using the term lower uterine segment. Reported lesions of the lower uterine segment were reviewed.

Results: Endometrial carcinomas arising from, as well as spreading to this area may have prognostic significance. Adenocarcinomas arising in the lower uterine segment can be associated with Lynch syndrome. Endometrial adenocarcinoma spreading to the lower uterine segment may indicate an increased risk of lymph nodal involvement.

Conclusions: A review of the scope of lower uterine segment lesions is presented to assist in developing a differential diagnosis if a patient with such a lesion is encountered.

Key words: Lower uterine segment, uterine neoplasms, cervical neoplasms
**Introduction:**

The lower uterine segment may become involved by cervical as well as endometrial lesions. In addition, there are lesions unique to the lower uterine segment, and identifying carcinomas in this region may have prognostic significance. This review covers the scope of lesions affecting the lower uterine segment.

**Methods:**

A Medline search was used, using the term lower uterine segment. Reported lesions of the lower uterine segment were reviewed.

**Results:**

In addition to lesions that usually affect the uterine fundus or cervix, there are lesions unique to the lower uterine segment. Endometrial carcinomas arising in the lower uterine segment, as well as those spreading to the lower uterine segment may have unique prognostic implications.

**Discussion:**

**Anatomy & Histology**

The lower uterine segment(LUS), also originally known as the isthmus uteri of Aschoff(1), was the subject of much early debate. The lowermost aspect of the lower uterine segment(LUS) has an easily identifiable gross structure, the anatomic internal os. The histologic internal os, the transition from LUS to endocervical mucosa, lies 6-10 mm below that(1). The uppermost
portion, where the LUS meets the lowermost portion of the uterine fundus, is not so well delineated. In studies utilizing the lowermost aspect of low lying placentas to identify the upper limit of the LUS, Morrison et al(2) estimated that at 20 weeks, the LUS measured 0.5 cm in length, with increasing length during gestation. Much of what has been written about the exact location of the LUS is in relationship to pregnancy and labor. In the nonpregnant patient, the significance of the LUS is different. Normal LUS may be sampled during endometrial sampling, and does not cycle or respond to hormones to the same degree. Thus it does not decidualize or shed with menses to the same degree as the functionalis(3). As such, it may be interpreted as inactive endometrium, if it is not recognized, and the clinician may not be alerted to the fact that the area of interest, the functional endometrium, has not been sampled. LUS mucosa is characterized either by a mix of endocervical and endometrial glands, hybrid glands with mixed features, or inactive endometrial glands. Ciliated epithelium in these glands is a normal finding(4). The stroma is more eosinophilic and less cellular that that of the functionalis, reflecting greater amounts of collagen. The muscle bundles of the LUS wall are arranged somewhat differently and are fewer than that of the corpus proper(1), in a manner to accommodate labor.

Recognition of cytologic features of the LUS have been stressed for cytopathologists, to avoid overinterpretation of LUS sampling after radical trachelectomy as atypical(5).
Benign lesions

Cesarean section scar and associated complications

In a series of hysterectomy specimens, Morris(6) looked for pathologic changes in the region of old Cesarean section scars that might be associated with clinical symptomatology. Findings that might correlate with abnormal uterine bleeding included overhang of congested endometrium above the scar, and the formation of polyps. Pain symptoms such as abdominal pain, dyspareunia, and dysmenorrhea were thought to be potentially correlated with inflammation, fibrosis, and tissue distortion. Other findings of note included residual suture material, dilated capillaries, hemorrhage, endometrial distortion and breakdown, and iatrogenic adenomyosis(6).

Much has been written about the use of ultrasound in evaluation patients for a trial of labor after prior Cesarean section. In one meta-analysis(7), the measurement of lower uterine segment thickness by ultrasound was found to be useful in predicting risk of dehiscence and rupture during trial of labor. Cesarean scars can rupture spontaneously in both the pregnant and nonpregnant uterus, as well as in labor. In one case, neglected ruptured membranes led to sepsis and spontaneous uterine dehiscence of a repeat lower uterine scar at 20 weeks(8). Of note, uterine rupture of the pregnant uterus in the absence of a prior scar is most often in the lower uterine segment as well, most likely related to thinning of the region(9).

Cesarean scar pregnancy, the implantation of pregnancy in a prior lower segment scar, with thinning of the LUS wall, has a high complication rate, and can result in catastrophic rupture and hemorrhage in the first trimester(10), but has rarely resulted in a live pregnancy. In one study of cases identified by first trimester ultrasound, patients opting for minimally invasive interventions
to terminate the pregnancy markedly reduced the need for hysterectomy. Women with viable pregnancies who continued had a 62.5% liveborn rate, but 37.5% ended up with hysterectomy for accreta(11). Minimally invasive methodology for treatment has included hysteroscopic resection after chemoembolization(12) and robotic-assisted laparoscopic resection(13). Medical therapy with methotrexate as well as surgical resection have also been utilized, as in a case of recurrent scar pregnancy in a patient treated by surgery the first time, and methotrexate the second(10).

In addition to obstetric complications associated with cesarean scar defects, gynecologic complications have been described, including abnormal uterine bleeding, dysmenorrhea, pelvic pain, infertility, and complications during gynecologic procedures. Rare abscesses and fistulas have also occurred. Symptomatic scar defects may be amenable to repair by minimally invasive surgery(14).

**Vascular and hemorrhagic lesions**

Lower uterine segment varicosities can be present, particularly with placenta previa(15), and may pose a dilemma at Cesarean section. It has been suggested that they can be responsible for both antenatal and postpartum bleeding as well(16). Prior classical Cesarean section has also been suggested as a potential underlying etiology(17). Suggested methods of delivery have included clamping the vessels before the lower segment uterine incision(15), and fundal transverse hysterotomy(17).

A case of a patient with Klippel-Trenaunay-Weber syndrome, a syndrome associated with vascular malformations, was documented by Bouchard-Fortier et al(18). The patient, who had a
prior history of severe postpartum hemorrhage, was found to have multiple abnormal vessels in her LUS on ultrasound, which were seen at the time of her classical cesarean section.

Cavernous hemangioma of the LUS may lead to abnormal vaginal bleeding, as well as suspicion for a neoplasm. Imaging modalities such as ultrasound and magnetic resonance imaging can help clarify the presence of a hemangioma.(19)

It has been postulated that lower uterine segment atony in the absence of fundal atony can result in severe postpartum bleeding, with ballooning of the lower uterine segment(20).

**Vesicouterine fistula**

While considerably less frequent than vesicovaginal fistulas, vesicouterine fistulas are highly associated with lower segment Caesarean delivery, and may relate to devitalization of bladder tissue at that time. They may present immediately, or as a delayed presentation after Caesarean(21). Presenting symptoms can include cyclic menouria, vaginal urinary leakage, amenorrhea, infertility, and first trimester pregnancy loss(22). Youseff’s syndrome is cyclic hematuria, amenorrhea, menouria, and urinary continence(23). Cystograms and hysterograms have been used in diagnosis(21). Although conservative management is sometimes attempted, many of these cases come to surgery(22).
**Benign masses:**

Leiomyomata arising in the LUS may obstruct labor, or cause urinary retention(24), and have been associated with greater frequency of Caesarean section and retained placenta(25). In one case, a large LUS leiomyoma was the cause of uterine sacculation, a rare pregnancy complication where an aneurysmal dilatation of the uterine wall occurs, and can be associated with a variety of complications(26).

Rarely, condyloma acuminiatum can involve the endocervix and lower uterine segment. In one such case, the large lesion filled the endocervical canal, and may well have been the cause of the patient’s persistent uterine pain, which resolved after hysterectomy(27).

An unusual case of pyogenic cervical cyst, arising at the site of incision of prior lower uterine segment myomectomy was described(28). In this case, the cyst contained evidence of endometriosis as well as E. coli, and it was postulated that the endometriosis may have been an iatrogenic effect of the myomectomy, that may have become infected, even though 13 years had elapsed since the myomectomy. Intramyometrial abscess may also obstruct labor if arising in the LUS(29).

**Miscellaneous lesions:**

It has been suggested, that while fewer adenomyotic nests are present in the LUS than the fundus, that in patients undergoing hysterectomy for symptomatic adenomyosis, that if a supracervical hysterectomy is undertaken, that care be taken to remove the entire LUS, to
minimize the likelihood of persistent lesional tissue(30). Mass-forming adenomyomas have also occurred in the LUS(31)

Amniotic fluid embolus is thought to arise from entry of amniotic fluid through LUS vessels exposed via tears during labor, or trauma (32).

A case of psammoma body formation in the lower uterine segment endometrium, but not the functionalis, was reported(33). The patient was nulliparous, and had been treated with clomiphene. The authors attributed the psammoma bodies to the altered hormonal milieu, and demonstrated that this finding is not always associated with malignancy.

Endosalpingiosis, a lesion usually seen on peritoneal surfaces and lymph nodes, and rarely presenting as a mass, have occasionally produced mass-like lesions, and a few cases have involved the LUS and cervix. In those cases, distinction from an adenoma malignum was stressed(34).

Pathologic uterine rings(Bandl’s ring) are obstructive rings at the junction between the LUS and upper uterus. They are most commonly found in obstructed labor, and are much less rarely seen with the institution of liberal Caesarean section. Bandl’s rings have been reported to rarely cause traumatic brain injury and cerebral palsy by compressive injury to the fetal head(35).

Inflammatory myofibroblastic tumor is a rare mesenchymal lesion that usually occurs in the lungs, mesentery, omentum, or retroperitoneum, but has been reported to occur in the uterus(36). In the largest reported series of 6 cases, 3 arose from the LUS. The tumor behaves in a benign fashion, or is locally recurrent, but needs to be distinguished from more aggressive more common uterine mesenchymal lesions. The presence of ALK positivity, negative or weak
muscle markers, a lymphoplasmacytic infiltrate in the spindle cells, and a myxoid background are helpful features(36).

A case of an intermediate trophoblastic lesion histologically similar to the benign placental site plaque/nodule but coating the lower uterine segment, upper endocervix, and bilateral fistulous tracts to the parametria was attributed to prior Caesarean sections(37).

Neoplasms of Uncertain Malignant Potential

Atypical Polypoid Adenomyoma

Atypical polypoid adenomyoma is a lesion most often arising from the lower uterine segment. It is composed of atypical endometrial glands, sometimes worrisome histologically, embedded in a benign neoplastic smooth muscle stroma. The lesions tend to be well circumscribed and polypoid. LUS lesions may protrude through the cervical os(38) Squamous metaplasia is common. The lesion tends to occur in reproductive aged to premenopausal women, mean age 39.7 in Young’s series(39), raising issues of preservation of fertility. While most cases have been treated with hysterectomy, curettage has occasionally been successful, although the lesion may persist. Cases have undergone malignant degeneration, although most behave in a benign fashion(39,40).
Epithelioid Trophoblastic Tumor (ETT)

This neoplasm is a more recently described tumor that falls under lesions of intermediate trophoblast, along with the better known placental site trophoblastic tumor. ETT is similar in behavior as well, and of uncertain malignant potential. It most commonly arises in the LUS and endocervix, which can make its distinction from cervical squamous cell carcinoma a challenge, particularly as both are positive for p63 and cytokeratins, however ETT stains for Inhibin as well as some trophoblastic markers(41).

Malignant Neoplasms:

Adenocarcinoma of the Lower Uterine Segment

While it is possible at times to determine if adenocarcinomas arising in the LUS are of endometrial or endocervical origin, this is not always possible. Tumors that arise from the lower uterine segment represent about 3-6% of endometrial cancers(42), have been shown to be deeper and more aggressive than corpus tumors(43,44), and have increased risk of being associated with Lynch Syndrome(44). Lynch syndrome is known to be associated with endometrial but not endocervical tumors(45). Testing for mismatch repair protein mutations has been suggested, particularly if the origin of a LUS cancer can’t be determined(45), as well as when the tumor is of endometrial origin. Distinction is aided by molecular testing and immunohistochemistry, with ER and vimentin favoring endometrial origin, and P16 and HPV DNA positivity favoring cervical origin(42).
Endometrial carcinoma involving the LUS in addition to the fundus does not upstage the tumor without cervical involvement, however in some studies LUS involvement has been shown to worsen prognosis. In one series, LUS spread of lower stage cancers decreased both survival and disease-free survival(46). Stage I high grade endometrial adenocarcinoma, defined as grade 3 endometrioid, serous, clear cell, carcinosarcoma, or mixed histology, spreading to the LUS was shown to be associated with pelvic and paraaortic nodal disease in one study(47), and this held true in another study for endometrioid histology as a predictor of nodal histology as well, although nodal group was not specified(48). However, the same group(49) found that in cases of surgically staged endometrial cancer, if the nodes were negative, LUS involvement did not worsen prognosis.

**Rare malignancies:**

A patient treated for diffuse large B-cell lymphoma of the LUS and cervix subsequently had delivery of a full-term pregnancy(50). A rare alveolar soft part sarcoma of the LUS was reported(51). A primitive neuroectodermal tumor(PNET) arising in the LUS was discovered at the time of Caesarean section(52).

**Conclusions:**

A review of the scope of lower uterine segment lesions is presented. Carcinomas arising in the lower uterine segment can be associated with Lynch syndrome. Endometrial carcinoma spreading to the lower uterine segment may indicate an increased risk of lymph nodal involvement.
Acknowledgements: none

Disclosures: none
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