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**Clinical history:** A 44-year-old woman with the past history of gravida 3, para 3 (all with normal spontaneous delivery) had the chief complaint of prolonged, excessive uterine bleeding during menstrual phase for one year. She had postpartum hemorrhage in the second pregnancy. The cycle length lasted for more than 10 days, and the interval was irregular. She also had severe pain which was refractory to medical treatment. Noted were associated with symptoms and signs including alternative temporal headache, nausea, and dizziness for 1-2 years, and spontaneously skin ecchymosis for 6 months. The preoperative diagnosis of adenomyosis was suggested by characteristic clinical manifestations including menometrorrhagia, dysmenorrheal, and the sonographic findings showing a uniformly enlarged uterus. She underwent surgical resection of uterus. Her further recovery was uneventful after 6 months of follow-up.

**Gross finding:** The specimen received in formalin is the whole uterus measuring 9.0 * 5.5 * 4.0 cm in size, and 90 gm in weight. The serosa over the uterus is smooth and glistening. The outer one-fourth to one-third part of myometrium and cervix shows some diffusely dilated spaces with adjacent brownish-color changes. The myometrium measures 2.0 cm in thickness. No obvious mass-like lesion or focal myometrial thickness is seen. The endometrial cavity measures 4.0 * 2.5 cm in dimension. The endometrium measures 0.1 cm in thickness. The endocervical canal measures 2.5 cm in length.

**Microscopic finding:** Microscopically, the subserosal region of the myometrium shows a picture of irregular shaped cavernous vascular spaces infiltrating between the myometrial fascicles located predominantly in the outer portion of the myometrium. The large vascular spaces are walled by flat, CD31-positive flat endothelial cells and distended by blood. No centrally placed larger vessels or cell atypia is seen.

**Differential Diagnosis:**
1. Cavernous angiomatosis
2. Cavernous hemangioma

3. Capillary hemangioma
4. Adenomatoid tumor
5. Arteriovenous malformation
6. Lymphangioma

**Immunostains:**
The endothelium cells are immunoreactive for Von Willebrand factor, CD31, CD34, and negative for calretinin and cytokeratin.

**Diagnosis:**
Cavernous angiomatosis

**Discussion:**

The first case of diffuse uterine hemangiomas was described in 1897 and was an incidental discovery from an autopsy after a young woman developed anemia and dyspnea and died 24 hours after delivering twins (1). The exact incidence is still unclear due to rare case reports in the past century. This year, a survey of the current literature identified fewer than 50 cases of hemangioma of the uterus (5). However, our hospital found 3 similar cases within the recent half year. Whether the incidence is really so rare or is possibly underestimated by mistakenly regarding as normal variant is unknown. We list the cases we've reviewed in table 1 in below.

The uterine hemangiomas are classified into congenital and acquired. The former is believed to be associated with some hereditary disease, including tuberous sclerosis and hemorrhagic telangiectasia (1). The cell of origin possibly represents pluripotential, embryogenic, mesodermal rests within the uterus (1). The later one is associated with previous pelvic surgery, endometrial curettage, trophoblastic disease, endometrial carcinoma, and maternal ingestion of diethylstilbestrol (1).

The hemangiomas of the uterus can be found in any age groups without predominance in any decades. The youngest patient described in literature was a 14-year-old girl who had to undergo hysterectomy for the life-threatening bleeding (6). Among all these cases, pregnant women are most commonly reported due to the complication like postpartum hemorrhage or disseminated intravascular coagulation (DIC). The hypothesis is that the hormone alternation during pregnancy or the physical changes (increased blood volume, etc) of the uterine structure during pregnancy or delivery may affect pre-existing lesions and trigger DIC (7). The pathophysiology of DIC is generally presumed to be platelet trapped by abnormally proliferating endothelium within the hemangioma (7). Some believe that this vascular lesion may also theoretically originate from angiomatous proliferation in a polypoid

endometrial lesion that persists for a prolonged period. It has been proposed that increased blood flow provided by the endometrial hemangioma may prohibit normal cyclic shedding associated with the usual hormonal flux (1).

Both localized and diffuse cases have been reported. It is possible that the lesion grew gradually during the past many years and gradually involved the whole uterus (6). The most common involving part is the myometrium of uterine corpus, and these are often diffuse (1). The cervix, serosa, endometrium, placenta, vulva, vagina, and ovary have been reported as well (4, 5, 7). We chose the term angiomatosis instead of hemangioma because of the diffuse pattern of the lesion.

The clinical symptoms varies from asymptomatic to abdominal pain, excessive vaginal bleeding either spontaneous or associated with menstruation, termination of pregnancy, and infertility to maternal (1, 8, 9). However, most of the pregnant course is uneventful no matter the delivery is via vaginal or caesarean section (5). This indicates two possibilities: (1) the lesion grew after the second cesarean section; and (2) the lesion was present and was localized away from the incision site (6). Severe post-partum vaginal bleeding, which might have been due to rupture of congested vessels or an inability of the dilated, thin walled vessels to contract sufficiently (6, 9). Hypervascularity and angiomegaly, with a consequent increase in the vascular cross-sectional area, may lead to amniotic fluid embolism (9). Vaginal delivery is to be preferred. However, if cesarean section is required, a vertical incision should be performed (9).We supposed that the symptoms might become worse if the hemangioma lesions located in the inner part of the myometrium or the endometrium during vaginal delivery or the procedure of dilation and curettage curettage, when the thin endometrial tissue covering the hemangiomas was removed and the blood vessels were exposed (1).

The definite diagnosis relies on the final histological examination. Usually vaginal examination, uterine curettings, ultrasound and hysterogram are non-informative but rarely the uterus may be felt or appear pulsatile on examination, on ultrasound or on fluoroscopy (8). A pelvic angiogram and computerized tomography can confirm the vascular nature of the lesion if there is a clinical suspicion of this abnormality in cases who are refractory to hormonal therapy and curettage (8). Magnetic resonance imaging (MRI) has also been used as an additional imaging modality for diagnosis (6). The sono-guided biopsy might be helpful for diagnosis and can avoid unnecessary total hystecrectomy, especially for reproductive-aged women.

The best treatment for hemangiomas remains unclear. The few cases in the literature describe conservative treatments, such as carbon dioxide laser excision, knife excision, cryotherapy, radiotherapy, electrocauterization, internal artery ligation,

uterine artery embolization, local excision, conization, or by laser ablation having been tried (3, 5, 6). In cases where people are refractory to conservative treatments, hysterectomy might be considered. Non-surgical modalities such as radiotherapy would probably cure the lesions but in the process they would destroy ovarian function (5).

The importance for a pathologist to be aware of the diagnosis of uterine hemangiomas is not only because of the possible life-threatening complication, but also because of the associated syndromes like the Klippel–Trenaunay syndrome or Osler-Weber-Rendu syndrome. The Klippel–Trenaunay syndrome is characterized by a triad of cutaneous port-wine capillary malformations, varicose veins and hemihypertrophy of soft tissues and bone (10). The Osler-Weber-Rendu syndrome, also known as hereditary hemorrhagic telangiectasia (HHT), is diagnosed by the "Curaçao criteria". There are four criteria about testing HHT: (1) spontaneous recurrent epistaxis; (2) multiple telangiectasias in typical locations; (3) proven visceral AVM (lung, liver, brain, spine); and (4) first-degree family member with HHT (11). If three or four of them are met, a patient has "definite HHT". If two of them are met, a patient has "possible HHT". Our patient, though had severe headache and spontaneously skin ecchymosis, didn't meet any of these criteria. After surveying the electroencephalography, brain MRI for suspected vascular or mass-like lesions, auto-immune and other lab data, the results all showed no abnormality.

It's important for a pathologist to identify the cavernous hemangioma or cavernous angiomatosis and remind the clinical physician of these syndromes for early diagnosis and corrective surgery to avoid further disastrous complications (3).

TABLE 1. Hemangiomas of the uterus

| Case | Age | Race | Location | Symptoms/Signs | Diagnosis | Treatment |
|---|---|---|---|---|---|---|
| 1 | 27 | Malay | Diffuse, myometrium of the cervix and uterus | Menorrhagia | Cavernous hemangioma | Hysterectomy |
| 2 | 14 | (India hospital) | Localized, endometrium and superficial myometrium of fundus | Menorrhagia and hemodynamic unstable | Cavernous hemangioma | Hysterectomy |
| 3 | 39 | Hispanic | Nodule, endometrium | Menorrhagia | Capillary hemangioma | Hysterectomy |

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|---|---|---|---|---|---|---|
| 4 | 21 | (USA hospital) | Diffuse, endometrium and myometrium | Heavy bleeding after caesarean section | Diffuse cavernous hemangioma | Hysterectomy |
| 5 | 26 | Caucasian | Diffuse, whole corpus | Atonic bleeding and amniotic fluid embolism after caesarean section | Diffuse cavernous hemangioma | Blood transfusion, PG F2α , Oxytocin |
| 6 | 14 | (Pakistan hospital) | Poly, endometrium | Menorrhagia with passage of clots | Capillary hemangioma | Oral contraceptive pills and low dose steroids |
| 7 | 33 | (Belgrade hospital) | Diffuse, left leg, vulva, uterus, and placenta | Increased D-dimer and low grade DIC at 26 weeks of gestation, fetal demise | Diffuse cavernous hemangioma | LMWH, emergency caesarean section and hysterectomy |
| 8 | 20 | (Italy hospital) | Diffuse, uterus | Swelling in inguinal and vulvar area together with syncope, vaginal, inguinal and vulvar varicosities during pregnancy | Diffuse cavernous hemangioma | Prophylaxis for thrmbotic complications with medical therapy. Caesarean section due to worsening syncope |

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