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THE PROBLEM AND REALITIES OF UTERINE LIPOLEIOMYOMA THROUGH THE PRISM OF A CLINICAL CASE

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Uterine lipoleiomyoma is a rare variant of uterine leiomyoma, which usually develops in perimenopausal women and rarely reaches large sizes. Its sonographic similarity to ovarian teratoma, leiomyoma, or sarcoma creates diagnostic problems in practical gynecology. The relevance of reporting this clinical case is determined by the extreme rarity of uterine lipoleiomyoma in women of reproductive age and the localization of its development from the cervix and uterus simultaneously. The clinical case presented in the article demonstrates an incidental finding of uterine lipoleiomyoma in a woman of reproductive age, which was mistaken for a right ovarian teratoma during ultrasound examination. The large size of the tumor, its external similarity to sarcoma, and its close attachment to the sacrouterine ligaments, parietal peritoneum, sigmoid and rectum, ureters, and iliac vessels created technical and diagnostic problems during surgery. Given the presence of a large neoplasm in the right appendage area, increased pain, positive symptoms of peritoneal irritation, and suspicion of uterine sarcoma, extirpation of the uterus with appendages was performed. The diagnosis of uterine lipoleiomyoma was verified by histological and immunohistochemical studies.

Key words: uterine lipoleiomyoma, uterine leiomyoma, mesenchymoma, uterus, teratoma, uterine sarcoma.

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ПРОБЛЕМИ ТА РЕАЛІЇ ЛІПОЛЕЙОМІОМИ МАТКИ ЧЕРЕЗ ПРИЗМУ КЛІНІЧНОГО ВИПАДКУ

Ліполейоміома матки є рідкісним варіантом лейоміоми матки, яка, зазвичай, розвивається в жінок перименопаузального віку й рідко досягає великих розмірів. Її сонографічна схожість з тератомою яєчника, лейоміомою чи з саркомою створюють діагностичні проблеми в практичній гінекології. Актуальність висвітлення клінічного випадку визначається надзвичайною рідкісністю розвитку ліполейоміоми матки в жінок репродуктивного віку та локалізацією її розвитку з шийки й матки одночасно. Представлений у статті клінічний випадок демонструє випадкову знахідку ліполейоміоми матки в жінки репродуктивного віку, яку під час ультразвукового дослідження помилково сприйняли за тератому правого яєчника. Великі розміри пухлини, її зовнішня схожість з саркомою, щільне прилягання до крижово-маткових зв'язок, парієтальної очеревини, сигмовидної й прямої кишки, до сечоводів і здухвинних судин створили технічні та діагностичні проблеми під час оперативного втручання. Ураховуючи наявність великого новоутворення в ділянці правих додатків, посилення больового синдрому, позитивних симптомів подразнення очеревини, підозри на саркому матки виконано екстирпацію матки з придатками. Діагноз ліполейоміоми матки був верифікований даними гістологічного та імуногістохімічного досліджень.

Ключові слова: ліполейоміома матки, лейоміома матки, мезенхімома, матка, тератома, саркома матки.

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Tumors of the female reproductive system represent numerous and diverse, both in clinical and morphological manifestations of diseases. Among them, mesenchymomas are most often found - uterine tumors that develop from tissues of mesodermal origin or differentiate into them. It is noteworthy that their differentiation can occur both towards the normal components of the uterine body, namely: endometrial stromal cells, smooth muscle cells of the myometrium, and towards heterologous tissues, such as: striated muscle, cartilage, bone, adipose and other tissues. An example of such tumors is uterine leiomyoma (LM) [1, 14].

Uterine leiomyoma is the most common hormone-dependent benign mesenchymal tumor of the uterus, with many variants [14]. One of its least described variants is uterine lipoleiomyoma (LLM) [4], which is histologically distinguished from it by the presence of mature adipocytes [15].

For the first time, LLM of the uterus was described by Lobstein in 1816. Since then, according to our data, this problem has not attracted attention for more than a century. Clinical cases of uterine LLM diagnosis have been described since 1978 [2]. Currently, 180 such cases are known [11, 12]. In the majority of cases, LLM developed from the body of the uterus [10, 13]. According to our data, only 31 cases in which this tumor developed from the cervix have been described in the medical literature [4]. At the same time, we have not found any reports of the uterus LLM development from the body and cervix simultaneously.

According to the professional medical literature, the incidence of uterine LLM ranges from 0.03 % to 0.2 % [1, 11, 14]. It is most often diagnosed in perimenopausal women, usually on the background of obesity, diabetes mellitus, hypothyroidism or other diseases accompanied by impaired lipid metabolism [11].

The etiology and pathogenesis of uterine LLM are not fully known. Genetic factors have been reported. There is evidence that LLM arises from genetic and chromosomal changes. It is suggested that the main predictors of the development of mesenchymal tumors are the high mobility group protein A2 gene, chromosomal translocations in 12q15, especially t(12;14), and changes in chromosomes 7, 8, 10, 11, 12, and 14 [3]. The possibility that the development of uterine LLM occurs as a result of direct transformation of immature mesenchymal or smooth muscle cells into adipocytes cannot be ruled out [15]. At the same time, the results of a review of the relevant literature have shown that uterine LLM can also arise as a result of "lipomatous" metaplasia of an already existing uterine LM [2]. Under this condition, localized or diffuse mature adipose tissue can form in the leiomyoma or in the myometrium [1, 4]. The role of the pathological action of exogenous and endogenous factors or iatrogenic factors, which, according to the literature, contribute to the manifestation of LLM development, cannot be excluded [9].

The clinical course of uterine LLM varies from prolonged asymptomatic to the development of pain, hemorrhagic, anemic, compression syndromes, dysmenorrhea, etc. [10].

The nature of clinical manifestations depends significantly on the location of the LLM relative to the uterine cavity (intramural, submucosal or subserosal), the number, size and blood supply of its nodes. [13].

Pelvic ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) with contrast, hysteroscopy and/or diagnostic laparoscopy are commonly used to diagnose uterine LLM [10, 12]. However, the diagnosis is only confirmed by histological and immunohistochemical studies [15].

Uterine lipoleiomyoma is primarily differentiated from dermoid ovarian cyst, non-teratomatous lipomatous ovarian tumor, benign pelvic lipoma, liposarcoma, lymphadenopathy, hemangioma, retroperitoneal cystic hamartoma, adenocarcinoma, and uterine sarcoma [8, 12, 13].

The main methods of asymptomatic uterine LLM treatment are pathogenetic hormone therapy, uterine artery embolization and focused ultrasound ablation under MRI control [7]. Symptomatic uterine LLM is subject to surgical treatment. Indications for surgical treatment are: severe pain, compression, hemorrhagic syndromes, an increase in the size of the uterus up to 12 weeks or more, the presence of a submucosal or subserosal node on the leg, signs of nutritional disorders, infection or its atypical location [2, 5, 6]. The volume of surgical intervention depends on the location and size of the tumor, the presence of external signs of its malignancy, etc.

The purpose of the study: was to analyze the localization, features and clinical course of uterine lipoleiomyoma through the prism of a patient of reproductive age clinical case, to highlight the problems of timely diagnosis verification and to determine the real causes of progressive tumor growth, which led to the extirpation of the uterus with appendages.

Materials and methods. In our study, we used the following methods: general clinical blood and urine tests, biochemical blood tests, blood test for ovarian tumor markers (CA 125, HE4 and ROMA index), electrocardiogram (ECG), pelvic ultrasound and lower-midline laparotomy with extirpation of the uterus and appendages.

The materials of the scientific work comply with generally accepted moral standards, requirements for respecting the rights, interests, and personal dignity of the research participant, generally accepted moral and ethical standards, and requirements of legislative documents of Ukraine (Excerpt from the minutes of the meeting of the Commission on Ethical Issues and Biomedical Ethics of the PSMU No. 232 dated 11/21/2024).

We give an example of an accidental large uterine LLM finding in a patient of reproductive age who had not undergone preventive examination for 10 years. She sought medical help only when pain syndrome appeared. The patient gave written consent to the publication of her clinical case.

Results of the study and their discussion. Clinical case: patient V., 41 years old, was in the gynecological department of the municipal enterprise "City Maternity Hospital of the Poltava City Council" in April 2023. The main complaints during hospitalization were unbearable pain in the lower abdomen, mainly on the right, which intensified when walking and changing body position.

From the anamnesis: considers herself sick for 6 days. Examined at the place of residence. According to the ultrasound of the pelvic organs: ultrasound signs of dermoid cyst of the right ovary. O-RADS 2. The level of ovarian tumor markers CA 125, HE4 and ROMA index are not elevated (33,6 U/ml; 49,2 pmol/l and 7.53 %, respectively).

As a result of the research, signs of non-specific inflammation were found in the general blood test. No other pathological changes were detected in laboratory parameters and on the ECG. During physical examination: body temperature is 36.8 ^{o}C, BMI 29.9 kg/m^2. Somatically healthy.

During the gynecological examination: a large nodular formation of elastic consistency and an enlarged (15 cm in diameter) right ovary, painful on palpation, were found in the posterior vaginal vault. Banki and Prontov symptoms were sharply positive.

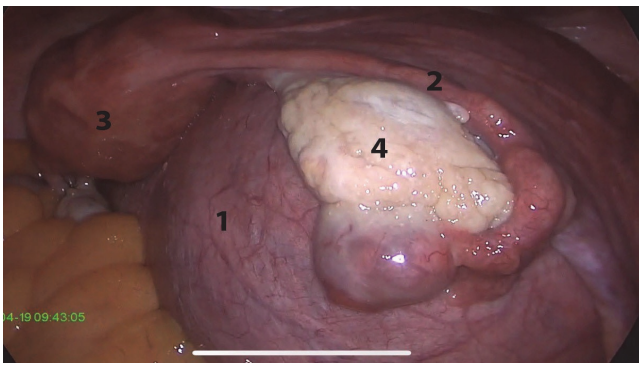

Fig. 1 Dimensions and localization of the tumor detected in patient V. during laparoscopy. 1 – tumor-like formation that extends from the uterus into the abdominal cavity; 2 – right fallopian tube; 3 – uterus; 4 – right ovary

Given the presence of symptoms of "acute abdomen" in the patient, a preliminary diagnosis was made: "Right ovarian cyst, nutritional disorders?" It was decided to perform a laparoscopic surgical intervention. Under the control of a television camera, an abdominal cavity inspection (ABI) was performed, gradually examining and assessing the condition of the uterus and tumor-like formation, determining its size, localization, condition of the fallopian tubes, ovaries and other abdominal organs that were within the visibility of the laparoscope. A large tumor-like formation of a purple-cyanotic color was detected, on which the right fallopian tube was flattened (Fig. 1).

On Fig. 2, it can be seen that this tumor-like formation comes from the cervix in the area of its isthmus with a wide base (Fig. 2).

Given the large size of the tumor and its localization, it was decided to continue surgical treatment by lower-midline laparotomy. During the operation, it was found that this large tumor-like formation was located outside the uterus and began its growth from the body and cervix with a wide base, occupying the entire Douglas space, the area of the sacrouterine ligaments and the parietal peritoneum. In addition, this tumor was intimately adjacent to the sigmoid and rectum, to the ureters and iliac vessels. Therefore, a surgeon and an oncologist were called to the operating room. The diagnosis was made: "Nodular uterine leiomyoma with subserosal location of the node (type 7). Malignancy?". The tumor, 30x25x20 cm in size, was removed and the uterus and appendages were extirpated.

Macroscopic preparations were sent for histological, macro- and microscopic examination.

Macroscopically: a tumor-like formation, 30x25x20 cm in size, pink in color and soft in consistency, on section it had a dirty-brown color and a spongy, finely lobulated structure (Fig. 3).

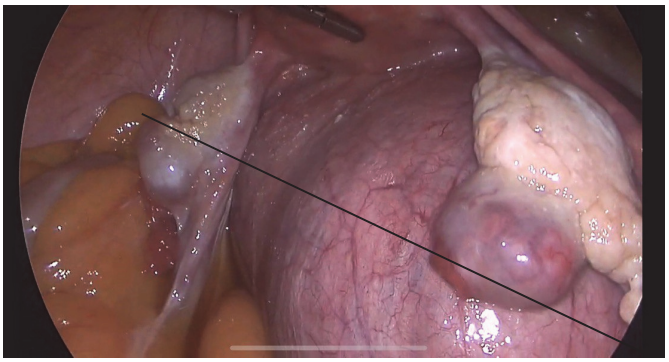

Fig. 2. Place of tumor attachment to the body and cervix of patient V. (pointed by an arrow)

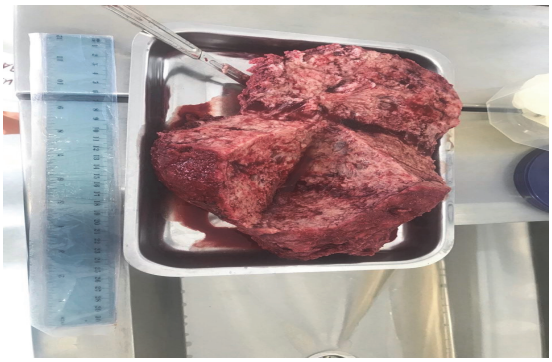

Fig. 3. View of uterine lipolemyoma on section. Macroscopic specimen.

Pathomorphological conclusion: ovaries: serous cysts, hemorrhages into the corpus luteum; fallopian tubes of normal histological structure; simple hyperplasia of the endometrium; uterine LM; cervix with cysts; neoplasm, which has a mesenchymal structure with a predominance of the vascular component.

Microscopic description: the formation of myometrium, which is represented by bundles of short spindle-shaped cells located around vessels with hyalinized walls, is found in tumor preparations. Between the bundles of these cells, clusters of fat cells of normal histological structure are found. Signs of cytological atypia and mitosis are not detected.

Immunohistochemical study showed: total cytokeratins (DAKO, clone AE 1/AE3) – negative reaction, S.100 (DAKO, polyclonal) – negative reaction in tumor cells, positive reaction in fat cells; desmin (DAKO, clone D33) – positive reaction in tumor cells; caldesmon (high molecular weight) (DAKO, clone h-CD) – positive reaction in tumor cells; smooth muscle actin alpha (DAKO, clone 1A4) – positive reaction in tumor cells; melan A (DAKO, clone A103) – negative reaction; immature melanosomes (DAKO, clone HMV-45) – negative reaction: STAT6 (Cell Marque, clone EP325) – negative reaction; Ki-67 (DAKO, clone MIV-1) – positive reaction (in approximately 1 % of tumor cells).

Uterine lipoleiomyoma is a rare variant of uterine LM, which histologically consists of smooth muscle cells, which most often have a spindle-shaped shape with an admixture of varying amounts of mature adipose tissue without signs of cytoatypia [3].

According to the literature, uterine LLM most often develops in the body (90.7 %) [5, 7, 9, 10, 11] or in the cervix (6.5 %) [6, 12]. However, our clinical case shows the possibility of its development from the body and cervix simultaneously. To our knowledge, such data have not been reported in the literature so far. Therefore, this fact should complement the global indicators of the development of LLM of the uterus with this localization of the tumor.

Most uterine LLMs are characterized by extremely slow growth, so these neoplasms may not manifest themselves clinically for a long time [5, 7, 8, 12, 13], which is confirmed by our clinical case.

According to the literature, lipid metabolism disorders lead to abnormalities in intracellular lipid storage and contribute to “lipomatous” metaplasia of the already existing uterine LM [8]. Therefore, it can be assumed that the patient’s excess body weight could have provoked this consequence. In addition, the histological examination data showed that the patient also had uterine LM, endometrial hyperplasia, and a cervical cyst in addition to LLM. This is consistent with the literature that LLM of the uterus can develop against the background of existing typical LM, uterine hemangiomas, vertebromas, pelvic lipomas, ovarian cysts, teratomas, and other benign or malignant gynecological tumors [4]. This fact also indicated the patient’s predisposition to proliferative processes and cyst formation.

It has been reported that uterine LLM can be detected during ultrasound of the uterine cavity, however, it can be mistaken for uterine fibroids or ovarian teratoma [2, 7, 9]. This is confirmed by our clinical case, where ultrasound of the uterine cavity mistakenly detected a dermoid cyst of the right ovary. This created diagnostic problems, as there was no time to perform CT or MRI of the uterine cavity. The urgency of the clinical situation required urgent surgical intervention, which was decided to be performed laparoscopically, which is consistent with the literature [2].

The volume and method of surgical intervention in the future depended on many reasons, namely: a large tumor with a pronounced pain syndrome, the presence of a subserosal node on the leg with an atypical location (in this case, the tumor began its growth from the body and cervix) and external signs of malignancy, as was described in the clinical case. Taking into account the above indications, it was decided to perform extirpation of the uterus and appendages with tumor removal, as recommended in professional medical literature [5, 11].

The removed tumor had a purplish-bluish color with a pronounced vascular component on the outside, and a dirty-brown color and spongy structure on the section, which distinguished it from a typical LLM. According to the literature, it usually has a yellow or yellow-white cut surface and a soft-elastic consistency [8]. Taking into account the typical macroscopic picture for uterine LM, the diagnosis was made: “Nodular uterine leiomyoma with subserosal location of the node (type 7). However, as a result of histopathological and immunohistochemical studies, this tumor was found to be uterine LLM. According to the data known in the literature, its histological structure consists of bundles of smooth muscle cells located in different directions, between which a different number of mature adipocytes is determined. This indicates that they have a pathogenetic origin similar to typical uterine LM [3]. Based on the identified histological changes typical for LLM, the diagnosis of "uterine lipoleiomyoma" was established, which was also verified by immunohistochemical studies. The positive reaction of tumor cells to the proliferation marker K-67, desmin, caldesmon (high molecular weight), smooth muscle actin alpha and negative – to total cytokeratins S-100, Melan A STAT6, HMB-45 confirmed this diagnosis [1].

Conclusions

1. This clinical case can complement the global statistical indicators of the development of uterine lipoleiomyoma from the body and cervix simultaneously.

2. Excess body weight in women of reproductive age can provoke the development of uterine lipoleiomyoma, due to the anomaly of intracellular lipid storage, leading to “lipomatous” metaplasia of the already existing uterine leiomyoma.

3. Uterine lipoleiomyoma can hide under the “mask” of an ovarian dermoid cyst, uterine leiomyoma, sarcoma, creating diagnostic problems.

4. Macroscopically, uterine lipoleiomyoma can have a soft consistency, pink color on the outside and a spongy, finely lobulated structure and dirty-brown color on the cut.

5. For routine verification of the diagnosis of uterine lipoleiomyoma, preference should be given to non-invasive diagnostic methods, such as: magnetic resonance and computed tomography with contrast.

6. Final verification of the diagnosis is carried out on the basis of histological and immunohistochemical studies.

7. Late diagnosis of female genital organs neoplasms can lead to unnecessary surgical complications.

The prospects for further research are to find a combination of optimal methods of examination and treatment of patients with tumorous formations of the female genital organs in order to reduce the frequency and volume of surgical interventions.

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