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Research Article

Diaphragmatic Clear Cell, Carcinoma Associated with Endometriosis: Second Case Report and Literature Review

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Abstract

Endometriosis is a chronic, inflammatory gynecological condition that can undergo malignant transformation and was first described in 1925. While endometriotic implants are most commonly located in the pelvis, they can also be found in other locations, with diaphragmatic endometriosis being extremely rare.

We present the case of a 43-year-old patient who was found to have a cystic formation on the right diaphragmatic surface during a cholecystectomy. A biopsy of this formation revealed a clear cell tumor that was immunophenotypically compatible with a gynecological origin. Following the complete removal of the cyst, the pathology confirmed the presence of a clear cell tumor along with foci of endometriosis in the same specimen. To date, only one other case has been published involving a 55-year-old patient with pathological confirmation of a clear cell tumor and endometriosis within the same diaphragmatic cystic formation [1]. Unlike the previous case, our patient had no history of gynecological endometriosis, which was ruled out even after a pathological examination of a hysterectomy and bilateral adnexectomy performed during cytoreductive surgery.

Keywords: Diaphragmatic clear cell carcinoma; Endometriosis

Introduction

Endometriosis is a chronic gynecological condition of unknown etiology, characterized by the presence of functioning endometrial glands and stroma outside the uterine cavity. This condition can induce a chronic inflammatory response, leading to symptoms such as dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility. While endometriotic implants are most commonly found in the pelvis, they can also occur in various other locations throughout the body. Implants have been documented in nearly all tissues, with diaphragmatic endometriosis being particularly rare. Although endometriosis is primarily an inflammatory, non-malignant, estrogen-dependent process, there is a potential for malignant transformation into clear cell carcinoma and endometrioid carcinoma [2,3].

In this report, we present the case of a 43-year-old patient diagnosed with a clear cell tumor located on the diaphragm, accompanied by foci of endometriosis.

Materials and Methods

We present the case of a 43-year-old female patient with a complex medical history, including bronchial asthma, subclinical hypothyroidism, myasthenia gravis, morbid obesity, and right diaphragmatic paralysis lasting two years, which has resulted in segmental atelectasis of the right lower lung lobe. Additionally, she has a history of a herniated disc with an annular fissure at the T11-T12 level, without significant root or spinal cord involvement, as well as cholelithiasis and polycystic ovaries.

The patient underwent laparoscopic cholecystectomy due to cholelithiasis and persistent pain in the right hypochondrium and flank, which had been ongoing for several months. During the surgical procedure, a cystic formation approximately 5 cm in size was discovered on the right hepatic dome. This cyst contained yellowish fluid with septa and fleshy formations. Multiple biopsies and a sample of the cystic fluid were collected for further analysis.

Prior to surgery, imaging studies were conducted, including an MRI, which revealed a multi-cystic perihepatic lesion of uncertain significance. This lesion was described as very hyperintense on the T2-weighted sequence, measuring approximately 4 × 4.5 × 4.1 cm, and hypointense on the T1-weighted sequences. No significant changes were noted on the dual sequence. Additionally, a 19 mm cephalic nodule of lower intensity was observed on the T2 sequence.

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Notably, there was thickening and nodular hyperintensity on the T1 sequence in the right hemidiaphragm, suggestive of endometriosis.

The anatomical-pathological study confirms the diagnosis of clear cell carcinoma, which is immunophenotypically consistent with a gynecological origin. Immunophenotype: The tumor cells exhibit intense expression of CK 7 and PAX-8, along with focal expression of Napsin A. No expression of calretinin, WT-1, CA 125, estrogen receptors, or progesterone receptors was identified. There is weak p53 expression with a patchy pattern. The nuclear expression of MLH1, MSH2, MSH6, and PMS2 in the tumor cells is preserved (normal). The probability of high microsatellite instability (MSI-H) is low.

Comment: It is recommended to evaluate the possibility of an endometriotic origin, despite the review not identifying residual endometrial glands or stroma in the endometrial or ovarian cavity. Additionally, the cytological examination of the cyst contents revealed atypia of uncertain significance.

Based on these findings and the evaluation conducted by the gynecological tumor committee, the patient was referred to gynecology for further investigation. The patient has no history of prior gynecological examinations. The gynecological examination yielded normal results.

The following complementary tests were performed:

- Gynecological Ultrasound: The uterus is in anteflexion with a normal endometrium. The uterine height measures 95 mm. Two fibroids were identified on the anterior surface, classified as type 4, measuring 3 cm, with a score of 1. The ovaries appear normal, and there is no free fluid present.

- CT scan: A right subdiaphragmatic lesion is noted, which exerts pressure on the hepatic dome. There is a lesion on the anterior margin of the right diaphragm that also contacts the liver surface and pericardial fat. Additionally, there is a laminar increase in soft tissue at the periphery of hepatic segment VIII/V, with nodular extension towards the lateroconal fascia. An umbilical lesion requires further evaluation through histological study. There is also a questionable lesion in the distal portion of the cecal appendix.

PET Scan: Right subphrenic lesion exhibiting irregular peripheral hypermetabolism, corresponding to the biopsied neoplasm. Multiple hypermetabolic areas are noted in the diaphragmatic and perihepatic regions, as well as in the peritoneum (laterocoronal and anterior renal fascia, and in relation to the wall of the small intestine loops), consistent with an active inflammatory process (possibly of endometriotic origin), although other etiologies cannot be ruled out in this context.

- Tumor Markers: CEA, Ca 19.9, and Ca 125 are negative.

The patient has been proposed for cytoreductive surgery followed by HIPEC (at 42˚C for 90 minutes, with 28 mg of doxorubicin and 95 mg of cisplatin.

Results

Intraoperative Findings: The intraoperative findings were as follows: In the right dome of the diaphragm, there was a nodule suggestive of a 5 cm to 6 cm endometriosis plaque, featuring a raised central portion of approximately 2 cm that appeared tumorous. Adjacent to the suprahepatic veins, another nodule with a firm consistency measuring about 3 cm was palpable, both exhibiting extensive and firm adhesion to the liver surface. There was a 1 cm endometriotic implant in the terminal ileum, with retraction and involvement of the ileocecal valve, as well as possible microimplants in the ascending colon. An implant was also noted at the parietal peritoneum level, in the right and left parietocolic regions, measuring 1.5 cm. Additionally, two millimetric implants were found in the uterus and sacrum, along with a nodule in the umbilicus. The uterus and adnexa appeared normal. There were foci of mild endometriosis at the confluence of both uterosacral ligaments, located in the posterior part of the cervico-isthmic junction. The remainder of the cavity showed no pathological findings. An endometriotic-appearing implant was observed in the wall of the rectum and sigmoid colon, with Meckel's diverticulum located approximately 25 cm from the ileocecal junction.

Pathological Anatomy: In the pathological anatomy, endometriotic foci were described in the dermis of the umbilicus. There was evidence of extensive endometriotic foci at the tip of the cecal appendix, in a thickened area of the terminal ileum, a sigmoid nodule, and in the right and left colonic regions. The omentum was negative for malignancy. A patch on the right diaphragm revealed the presence of extensive foci of endometriosis, as highlighted in the histological study, which shows a transition between benign glands, atypical endometriosis, and clear cell carcinoma (Figures 1-6). The uterus exhibited foci of adenomyosis. Following the histological study of hysterectomy and bilateral salpingo-oophorectomy, no foci of endometriosis were found in the internal genital organs.

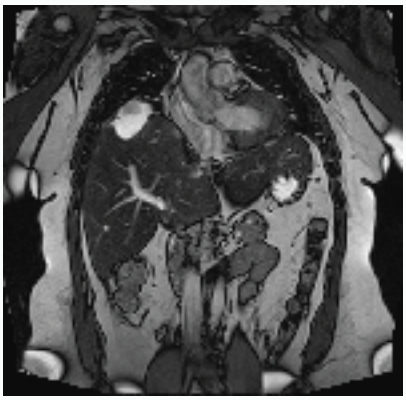

Figure 1: T2 sequence (HASTE) in coronal plane showing a cystic-appearing lesion approximately 40 mm in size, located extra-hepatic/diaphragmatic, multilobulated, with a solid cephalic pole measuring 19 mm, of lower intensity on the T2 sequence.

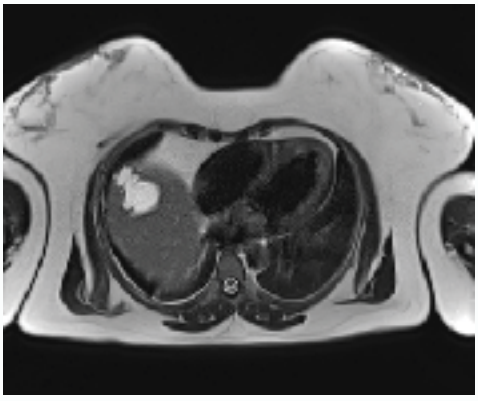

Figure 2: T2 sequence (HASTE) in the axial plane showing the same lesion.

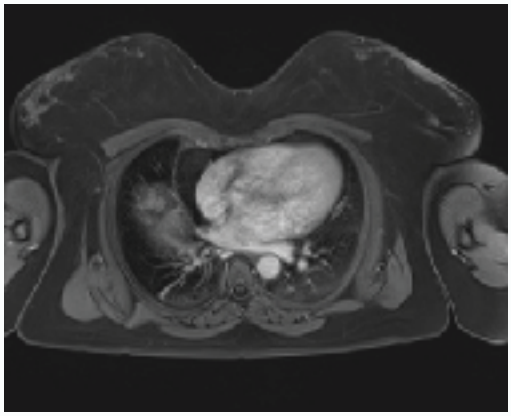

Figure 3: T1 fat-sat axial sequence with gadolinium: after contrast, there is peripheral enhancement of the cystic nodule, with moderate enhancement of the described solid cephalic pole.

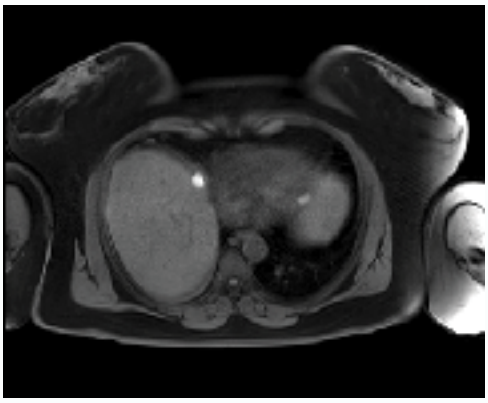

Figure 4: T1 fat-sat axial sequence without contrast showing two lesions measuring 16 and 11 mm, markedly hyperintense due to hematologic components, with additional hyperintense foci observed in the left diaphragm and right parietal peritoneum (not shown in the image). After contrast, all the described foci show mild enhancement. Findings consistent with extrapelvic endometriosis.

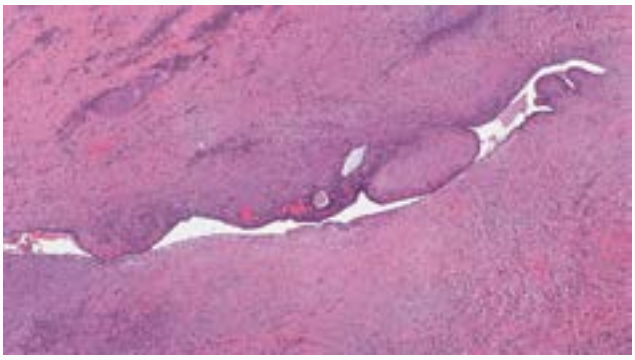

Figure 5: Transition between endometriosis and carcinoma: Endometriotic cyst.

Discussions and Conclusion

Endometriosis is a chronic, inflammatory gynecological pathology in which malignant transformation is possible and was first described in 1925. Most of the time endometriotic implants are located in the pelvis. The finding of endometriosis in the diaphragm is

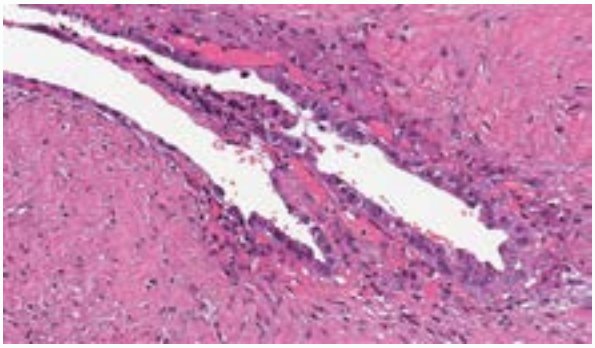

Figure 6: Transition between endometriosis and carcinoma: Atypical endometriosis.

rare and typically occurs in the right hemidiaphragm, suggesting that its occurrence is linked to the theory of retrograde menstruation, in combination with the direction of peritoneal fluid circulation (Figures 7-10).

Two cases of diaphragmatic clear cell cancer had previously been published, but in which coexistence with endometriosis was not demonstrated [4,5]. Only one case has been published of a 55-year-old patient with pathological confirmation of clear cell tumor and endometriosis in the same diaphragmatic cystic formation with radiological-pathological correlation [1].

Unlike our patient, this patient had a history of hysterectomy plus double adnexectomy for high-grade cervical dysplasia, uterine myoma, and bilateral endometriosis.

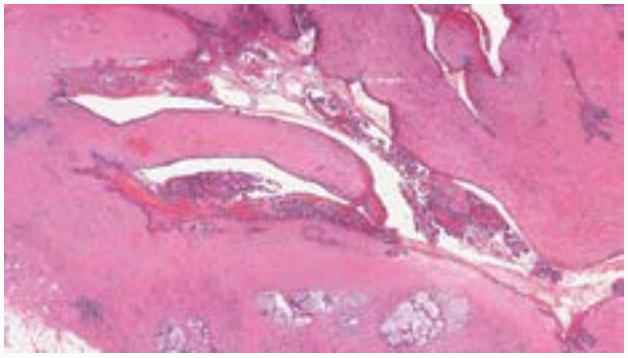

Figure 7: Transition between endometriosis and carcinoma: clear cell ca. arises on atypical endometriosis.

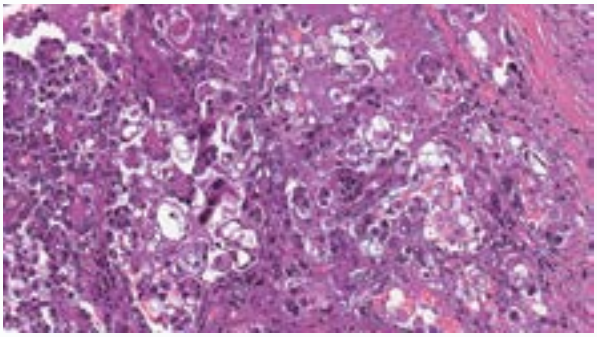

Figure 8: High-power magnification image of the solid pattern of clear cell carcinoma, showing evident atypia.

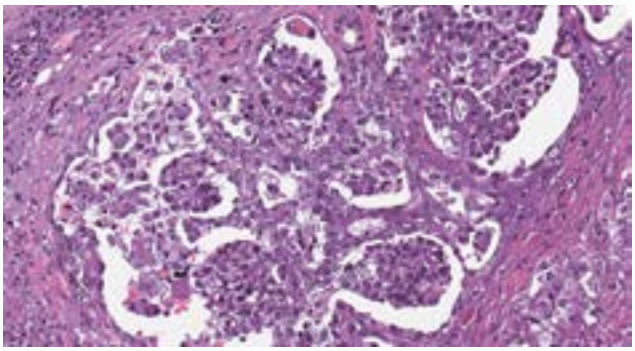

Figure 9: Glomeruloid pattern of clear cell carcinoma.

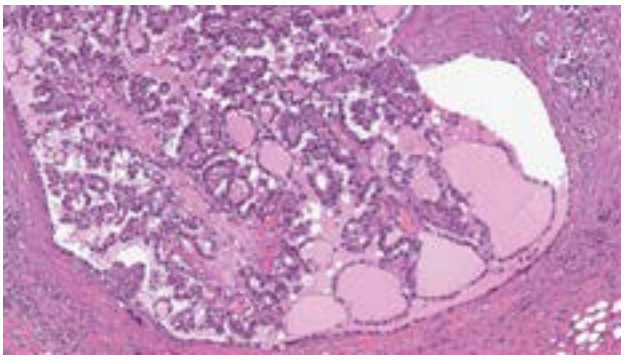

Figure 10: Tubulocystic pattern of clear cell carcinoma. All of these patterns were identified in this case.

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