




Fatal pulmonary thromboembolism associated with uterine carcinosarcoma

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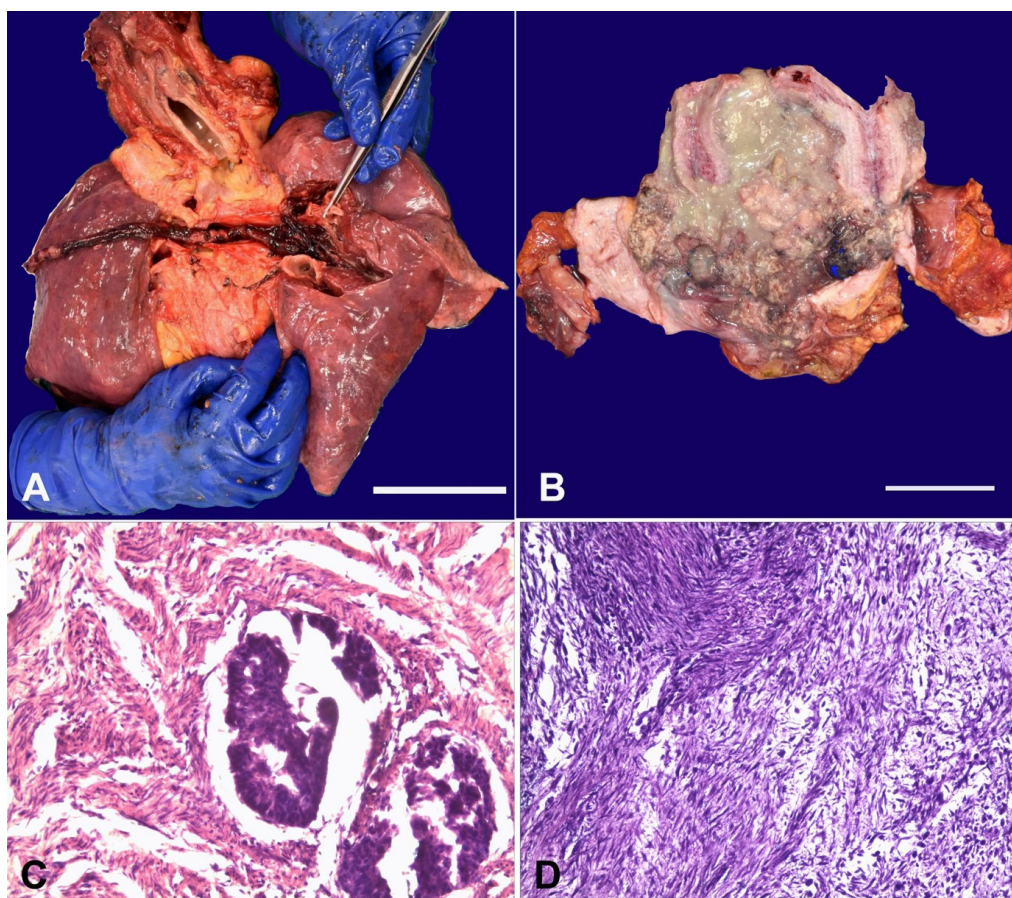


Figure 1. A – Macroscopic view of lungs showing red-brownish clots in the pulmonary artery trunk extending along the intraparenchymal branches (scale bar= 8 cm); **B** – Macroscopic view of the uterus after dissection with a vegetative neof ormation almost occluding its lumen, in association with abundant yellow-green-blackish material of pasty consistency (scale bar= 7 cm); **C** – Photomicrograph of the endometrial tumor with remnants of neoplastic glandular epithelial component and of residual glandular pseudo-lumen with multi-layered epithelium and cellular atypia (H&E, 200x); **D** – Photomicrograph of the endometrial tumor with sarcomatous component partly with fused cellularity, partly in the form of compact bundles with marked nuclear atypia and partly with a myxoid-like structure with foci arranged in bundles associated with a scattered cell neoplastic component (H&E; 100x).

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Uterine carcinosarcoma (USC), also known as malignant mixed Müllerian tumor, is a rare and high-grade endometrial cancer composed of epithelial and mesenchymal elements.¹ UCS accounts for 4.3% of all uterine corpus cancer, with a worldwide annual incidence of 0.5-3.3 cases per 100.000 women.¹ Common risk factors include obesity, nulliparity, chronic endogenous or exogenous hyperestrogenism exposure, older age (with a median age of 70 years), African-American ethnicity, genetic predisposition, tamoxifen therapy, and prior pelvic irradiation.²

Typical UCS-related symptoms, unfortunately, associated with an already advanced stage of the disease, are large masses occupying the abdominal cavity, postmenopausal metrorrhagia, and abdominal pain. One of the most important complications of endometrial tumors, especially in UCS, is venous thromboembolism (VTE), with an incidence of 8.1%.³⁻⁴ It may also involve pulmonary arteries and is usually associated with aggressive tumor characteristics and poor patient health.³⁻⁴

While Trans-Vaginal Sonography (TVS) is the first-line method for the assessment of UCS, as it can detect neoformations of the myometrium, diagnosis can usually be made by the histopathological examination of targeted endometrial biopsies, possibly associated with hysteroscopy.⁵⁻⁶ Magnetic resonance imaging (MRI) is the best imaging modality for staging. Furthermore, it shows a typical high enhancement with a "spotty" distribution, which may suggest bleeding and is a distinct hallmark of carcinosarcoma.⁶⁻⁷

Depending on the histopathologic assessment of the tumor (depth of invasion and presence or absence of metastases) and clinical presentation,⁸ the management of UCS requires a multimodality treatment comprised of surgery, systemic therapy, and radiotherapy. The estimated 5-year survival rate ranges from 33 to 39%, but the recurrence rate remains high.^{2,8}

Figure 1 refers to a 61-year-old woman found dead in her flat, dressed in a sanitary napkin and a nightgown. Because the woman lived alone and had no family members, no health information could be achieved. An autopsy was performed to determine the cause of death. The body was in a good state of preservation; it weighed 85 kg and was 158 cm long (BMI = 34 Kg/m² – Class I obesity). The sanitary napkin was smeared with a yellow-green-blackish creamy material upon external examination. At dissection, both

branches of the pulmonary artery trunk were occupied by red-brownish clots with multiple whitish streaks extending along the intraparenchymal course of the dividing branches of the pulmonary arteries (Figure 1A). They appeared to adhere tenaciously to the intimal surface, replicating the shape of the vascular lumen as a mold. All these characteristics were confirmed upon slicing, and a friable consistency was noted. On the abdominal incision, abundant yellow-green-blackish material of pasty consistency and purulent appearance was noted near the pelvic notch and between some intestinal loops. The uterus (longitudinal diameter = 18 cm, transversal = 11 cm, anteroposterior = 5 cm) appeared to be increased in volume, and the wall had a wall thickness of 1.5 cm. Inside the uterine cavity, a vegetative neoformation was detected (longitudinal diameter = 6 cm, transversal = 5 cm, anteroposterior = 4 cm), almost occluding the lumen. It was associated with abundant material resembling in color and consistency that was found in the abdomen. This neoformation adhered to the lateral walls and fundus of the uterus, extending almost to the cervix (Figure 1B). The ovaries were unscathed.

Histopathologic examination of the mass revealed features of carcinosarcoma consisting almost entirely of a sarcomatous component and small foci of endometrioid-type adenocarcinoma, with neoplastic embolization of the intraparietal venous vessels. An inflammatory infiltrate associated with marked tumor necrosis was also noted (Figures 1C and 1D). With this background, the abdominal findings were interpreted as purulent discharge and necrosis following the adjoining uterine cancer.

At the end of all investigations, the cause of death was identified as massive pulmonary arterial thrombosis in a subject with uterine carcinosarcoma.

For completeness, we also considered peritonitis and sepsis as possible co-participation in the cause of death. However, we considered this hypothesis unlikely based on the macroscopic and microscopic findings. Specifically, the peritoneum, abdominal viscera, and serosa were shiny, without fibrinous deposits, and of normal consistency. The purulent-looking material appeared free and not adherent to the abdominal wall and intestinal loops, as would be the case with recent extravasation, and was not organized. The histologic findings confirmed these considerations, which revealed no evidence of septic

embolism. Overall, there were no postmortem findings suggestive of peritonitis and sepsis. Had the massive and acutely fatal pulmonary arterial thrombosis not occurred, local or systemic septic complications most likely could have developed.

The case was considered of interest because of the rare neoplasm, its size, and the very advanced stage of the disease. Another peculiarity was that one of the most lethal direct complications of this neoplasm, pulmonary arterial thrombosis, was observed. Unfortunately, the absence of family members and health information does not allow further clinical considerations, but the severity of the disease found is glaringly the result of neglected and untreated disease. This case demonstrates that such scenarios are still possible today, despite the increased importance of prevention campaigns. In this context, the observed anatomopathological findings are crucial as they enrich the knowledge of uterine carcinosarcoma, and their images may help forensic pathologists who have not previously encountered this rare disease.

REFERENCES

1. Cantrell LA, Blank SV, Duska LR. Uterine carcinosarcoma: a review of the literature. *Gynecol Oncol*. 2015;137(3):581-8. <http://dx.doi.org/10.1016/j.ygyno.2015.03.041>. PMID:25805398.
2. Kim SI, Kim JH, Lee C, Ha J, Jung KW, Lim MC. Incidence and survival rates of primary uterine carcinosarcoma in Korea: a National Cancer Registry study. *J Gynecol Oncol*. 2023;34(1):e9. <http://dx.doi.org/10.3802/jgo.2023.34.e9>. PMID:36366811.
3. Matsuo K, Ross MS, Im DD, et al. Significance of venous thromboembolism in women with uterine carcinosarcoma. *Gynecol Oncol*. 2018;148(2):267-74. <http://dx.doi.org/10.1016/j.ygyno.2017.11.036>. PMID:29248197.
4. Rauh-Hain JA, Hariton E, Clemmer J, et al. Incidence and effects on mortality of venous thromboembolism in elderly women with endometrial cancer. *Obstet Gynecol*. 2015;125(6):1362-70. <http://dx.doi.org/10.1097/AOG.0000000000000866>. PMID:26000507.
5. Savelli L, Ceccarini M, Ludovisi E, et al. Preoperative local staging of endometrial cancer: transvaginal sonography vs. magnetic resonance imaging. *Ultrasound Obstet Gynecol*. 2008;31(5):560-6. <http://dx.doi.org/10.1002/uog.5295>. PMID:18398926.
6. Epstein E, Van Holsbeke C, Mascilini F, et al. Gray-scale and color Doppler ultrasound characteristics of endometrial cancer in relation to stage, grade and tumor size. *Ultrasound Obstet Gynecol*. 2011;38(5):586-93. <http://dx.doi.org/10.1002/uog.9038>. PMID:21547974.
7. Tuan HX, Duc NM, Tri CM, Quyen HD, Dung PX. Carcinosarcoma of uterus. *Radiol Case Rep*. 2023;18(3):1297-301. <http://dx.doi.org/10.1016/j.radcr.2022.12.070>. PMID:36684637.
8. Abu-Rustum N, Yashar C, Arend R, et al. Uterine Neoplasms, Version 1.2023, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2023;21(2):181-209. <http://dx.doi.org/10.6004/jnccn.2023.0006>. PMID:36791750.

This study was carried out at the Institute of Forensic Medicine of Milan, Milan, Italy.

Authors' contributions: Lodetti G and Tambuzzi S equally contributed to this work. They devised the project and the main conceptual idea of the article, collected data, drafted the manuscript and performed literature research. Andreola S and Guendalina G contributed to methodological approach, literature research and editing of the manuscript. Zoja R guarantor of the project and directed the study, devised the main conceptual idea of the article.

Ethics statement: The subject in this study underwent a judicial autopsy at the Institute of Legal Medicine of Milan to identify the cause of death. The inquiring magistrate authorized data collecting, sampling and subsequent analysis. Consequently, by the Italian law, ethical approval is not required in these cases. Publication of data is allowed when the case has been closed, but the anonymity of the subject must be guaranteed.

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