Autopsy Case Reports

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# Pulmonary thromboembolism secondary to pelvic thrombosis related to giant ovarian tumor

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## ABSTRACT

Pulmonary thromboembolism (PTE) is one of the major complications in oncologic patients. The incidence of PTE in these cases is 4 to 7 times higher than in non-oncologic patients. Ovarian tumors, specifically those of large sizes, may impair the blood flow through the pelvic veins as tumor pressure over the pelvic vessels increases the incidence of thrombosis. The authors report the case of the unexpected death of a 74-year-old female due to massive pulmonary thromboembolism, associated with an ovarian tumor almost of 15 kg of weight that filled the abdominal and pelvic cavities. The compressive effect on the walls of the pudendal and periuterine veins somehow facilitated the local thrombosis. According to the histological characterization on post-mortem samples, the mass was identified as an "atypical proliferative (borderline) mucinous tumor." The case emphasizes the important association between pulmonary thromboembolism and ovarian tumors

**Keywords**
Autopsy; Sudden Death; Ovarian Neoplasms; Pulmonary Thromboembolism.

## INTRODUCTION

Deep vein thrombosis (DVT) and pulmonary thromboembolism (TEP) are severe[1] and frequent[2] complications (42%) in women with advanced ovarian neoplasms,[1-4] large uterine fibromas[5] and in patients undergoing chemotherapy.[6] In patients with large solid malignancies, besides the mechanism triggered by the immunologic, inflammatory and the released substances related to the tumor response, the pressing on the large vessels such as the inferior vena cava, pelvic and iliac veins may result in bloodstream stasis, turbulent flow and vessels injury, increasing the probability for thombosis.[7] Among all abdominal and pelvic tumors in women, ovarian neoplasms represent the main cause of pulmonary embolism and thrombophlebitis.[8,9]

The WHO classification of 2014 divides the surface epithelial tumors of the ovary into benign, borderline and malignant and the different histological types into serous, mucinous, endometrioid, clear cells, Brenner and seromucinous.[10] Borderline ovarian tumors are characterized by a smaller aggressiveness when compared with other epithelial forms[11] and

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are currently defined "atypical proliferative epithelial tumors." This type of tumor usually occurs in the third or fourth decade and is unilateral in 80% of cases.[12] According to the tumor biology and behavior, the prognosis is usually favorable, but life-threatening outcomes may be observed by the compression on the surrounding structures when the tumor reaches large dimensions, leading to unexpected death.

In this context, the main goal of this case report is to emphasize the important association between pulmonary thromboembolism and ovarian tumors of such greatness.

## CASE REPORT

A 74-year-old female who lived alone was found dead in her home. The estimated time of death was evaluated to be of 48 hours. According to the relatives' information, she was diagnosed with hypertension and was under a diagnostic workup of an ovarian cyst. The judicial authority required an autopsy, which was performed 2 days after the discovery of the corpse.

### Autopsy Presentation

The external examination revealed an apparent well-preserved corpse with a body mass index of 34.8, without any sign of external injuries. The examination of the head and neck was unremarkable. However, the examination of the lung depicted an extensive bilateral thrombosis of the main pulmonary arteries until their segmental subdivision. The large thrombus entirely occluded the arterial lumen, reproducing the shape of the vessel as a "cast", coated by the intimal surface, characterizing a bilateral massive pulmonary thromboembolism.

According to the morphological characteristics, a thromboembolic nature was macroscopically confirmed (Figures 1 and 2).

At the opening of the abdominal and pelvic cavities, the left uterine adnexa were represented by a smooth cystic tumor, weighing 15 kg (Figure 3) and measuring 33 cm in its longest axis. At the cut surface, the cyst was multiloculated and drained a yellowish mucinous material. No papillary excrescences were seen, but a partly necrotic and solid nodule of 8.5 cm was found adhered to the cystic wall.

The examination of the contralateral ovary and uterus was unremarkable, the latter showing an atrophic endometrium. The bilateral dissection of the deep vessels of the lower limbs failed to show thrombosis, while the exploration of the veins of the pudendal plexus (ovarian and periuterine veins) showed the presence of extensive thrombosis (Figure 4).

No other noteworthy finding was detected. The cause of death was identified as massive pulmonary thromboembolism in a woman with a large ovarian neoplasm. During the autopsy, different organs were sampled (uterus, ovarian neoplasm, pudendal plexuses and thrombotic formations) for histopathologic investigation.

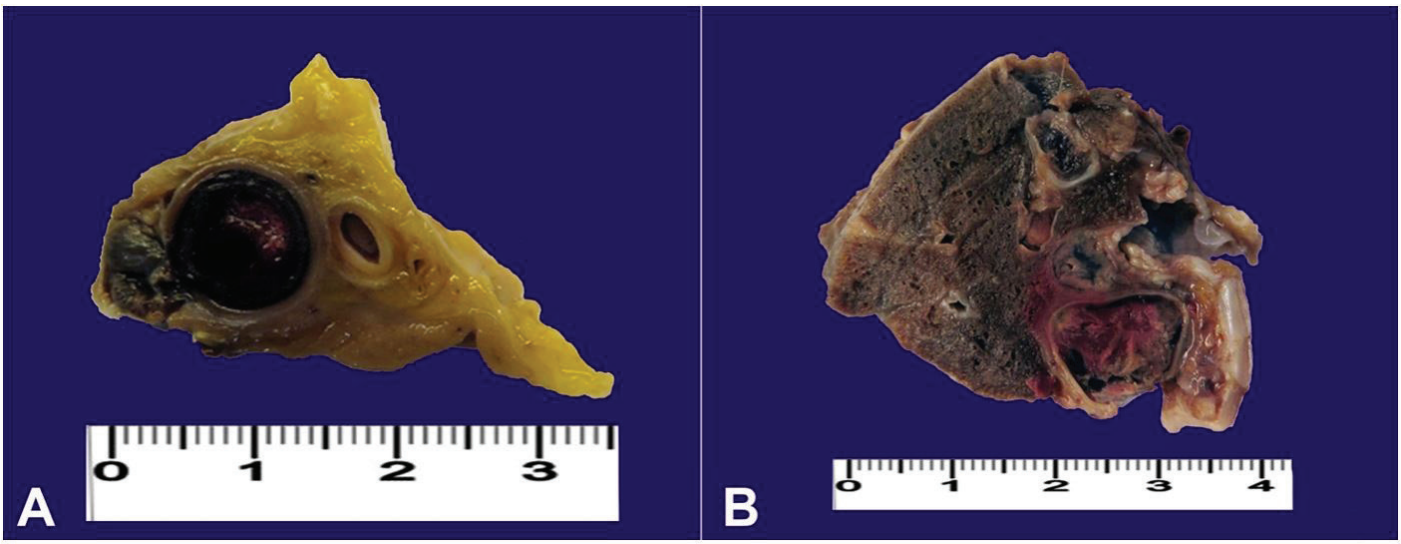


**Figure 1.** Macroscopic view of the thromboembolic events. **A –** Gross view of the thrombus in the pelvic vessels; **B –** Gross view of pulmonary thromboembolism.

Moreover, samples of biological fluids (heart and femoral blood, urine, bile and gastric content) were taken for toxicological analyses. The search for drugs and/or alcohol was performed and results were negative.

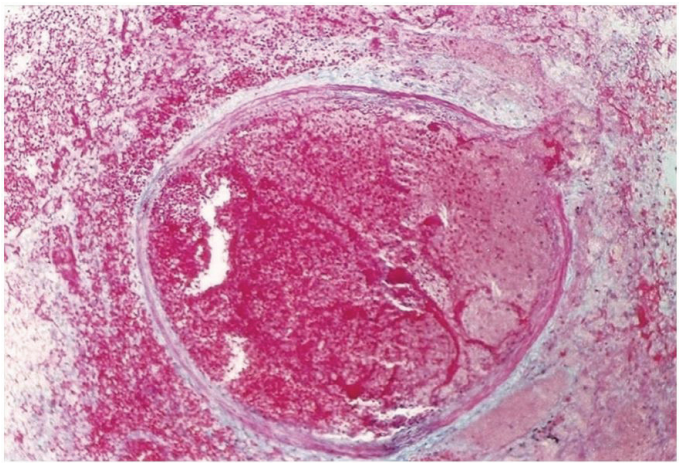

**Figure 2.** Photomicrograph of thrombosis of a pelvic vein (Masson's trichrome staining: 200 X).

Microscopically, the massive ovarian neoplasm was assessed as "atypical proliferating mucinous tumor (borderline)" (Figure 5) and the thrombotic nature of the occluding material in the periuterine veins was confirmed, with secondary thromboembolism in the pulmonary arteries.[13]

Therefore, the cause of death was identified as pulmonary thromboembolism due to pelvic thrombosis, concomitant with a giant ovarian neoplasm. According to the evidence provided by the autopsy and the histological findings, the compression effect of the mass on the pudendal venous plexus enabled the formation of intravascular thrombi, whose detachment led to pulmonary embolism and death.

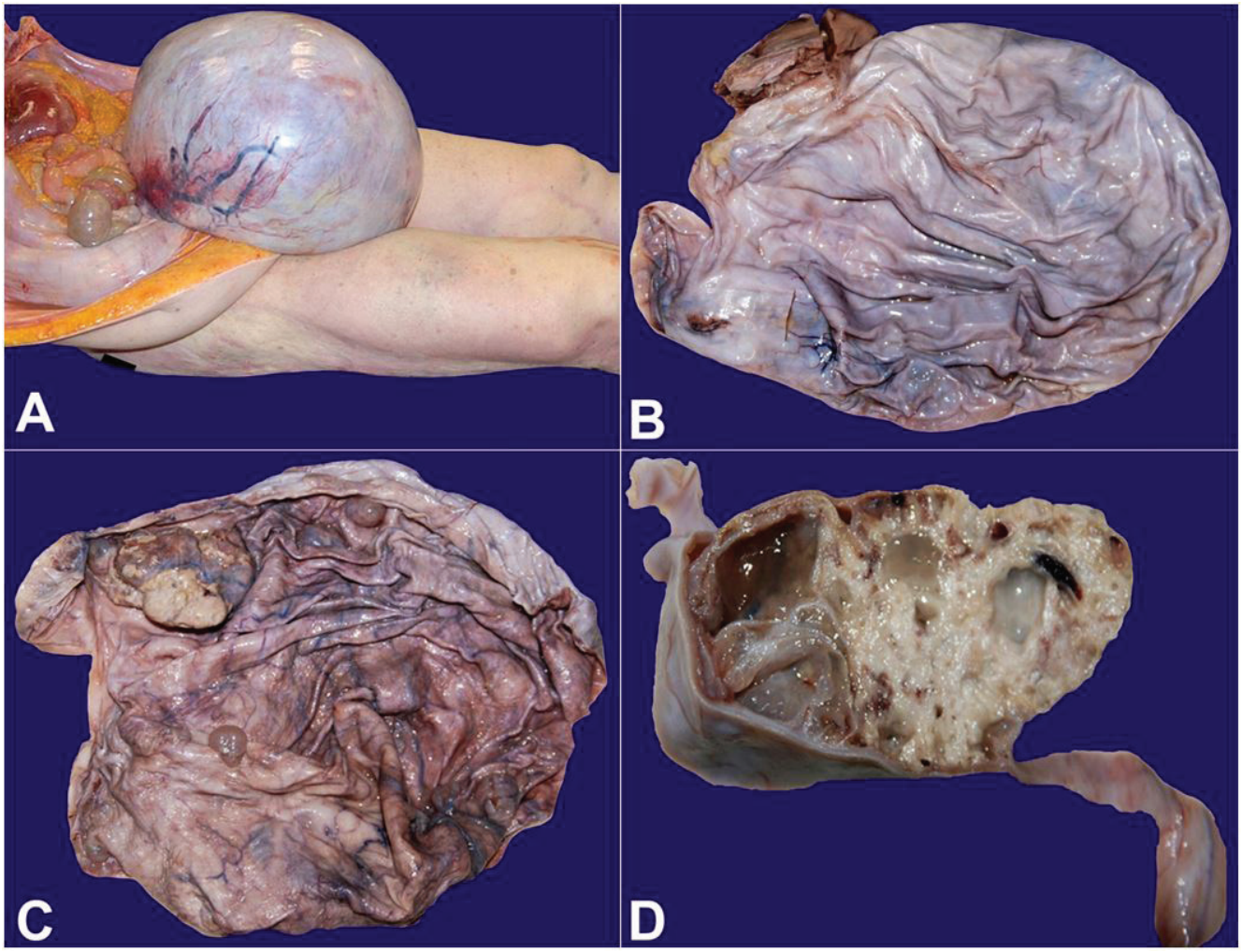


**Figure 3.** Macroscopic examination of the ovarian tumor. **A –** Gross view of the tumor, after the abdominal cavity overture; **B –** Macroscopic view of the tumor external wall; **C –** Inner surface view with the multiple cystic formations of varying sizes; **D –** Cut surface of the solid nodule adhered to the cystic wall.

## DISCUSSION

In 1865, Trousseau[14] described the correlation between tumors and venous thrombosis, and since then, neoplasms have been recognized as a risk factor for venous thromboembolism (VTE) and, consequently, pulmonary embolism (PE).[15] The Virchow classic triad of endothelial damage, hypercoagulability and venous stasis is considered to be the mechanism responsible for the pathogenic onset.[16] The Trousseau syndrome (tumor-associated thrombosis) is the second cause of death in oncologic patients after the progression of the disease itself.[17] The risk of pulmonary embolism in this group of patients is 4 to 7 times higher if compared to non-neoplastic patients.[4,17]

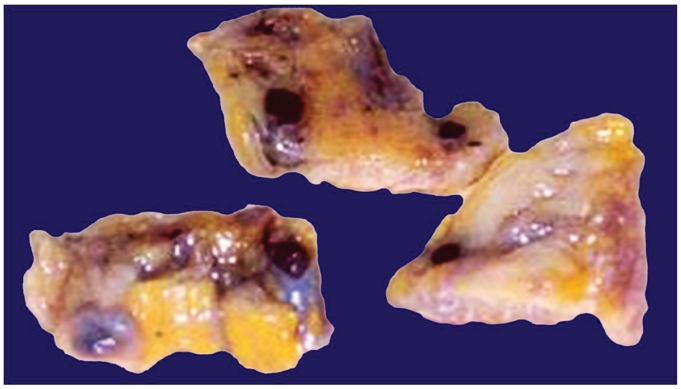

**Figure 4.** Macroscopic examination of the thrombosis of the pudendal plexus sample in three different regions of the plexus.

Previous studies[18] report thrombotic events in 20% of patients with malignancy[18] and up to 20% of these patients will present embolic events.[19] Some neoplasms, especially pancreatic and gastrointestinal,[20] are associated with higher rates of thrombosis.[15,21] Other neoplasms of the peritoneal and pelvic cavities (i.e., endometrial or bladder tumors) and, in particular, ovarian and extrahepatic biliary ducts are usually linked to high incidence of pulmonary embolism.[22,23] In particular, the highest prevalence of pulmonary embolism and thrombophlebitis has been witnessed in neoplastic ovarian patients,[8] especially among germinal types.[24] This is due to the combination of the pelvic blood flow obstruction by the mass,[7] the effect of estrogen hormone treatment[25] and the overexpression of the tissue factor associated with high D-dimer levels, which is considered to be an important factor in hypercoagulability.[26] The coagulation cascade activation and the embolic events occur in association with neoplasms because of the tissue factor (TF) and cancer procoagulant (CP).[27] Moreover, a crucial role may be played by inflammatory cytokines and the relationship between neoplastic cells, monocytes, macrophages, platelets and endothelial cells. Inaddition, thrombosis may be favored by chemotherapy, hormone therapy or radiotherapy. Other mechanisms that also may take part in thrombus formation are related to the relationship between the host and the tumor (i.e., acute phase inflammation,

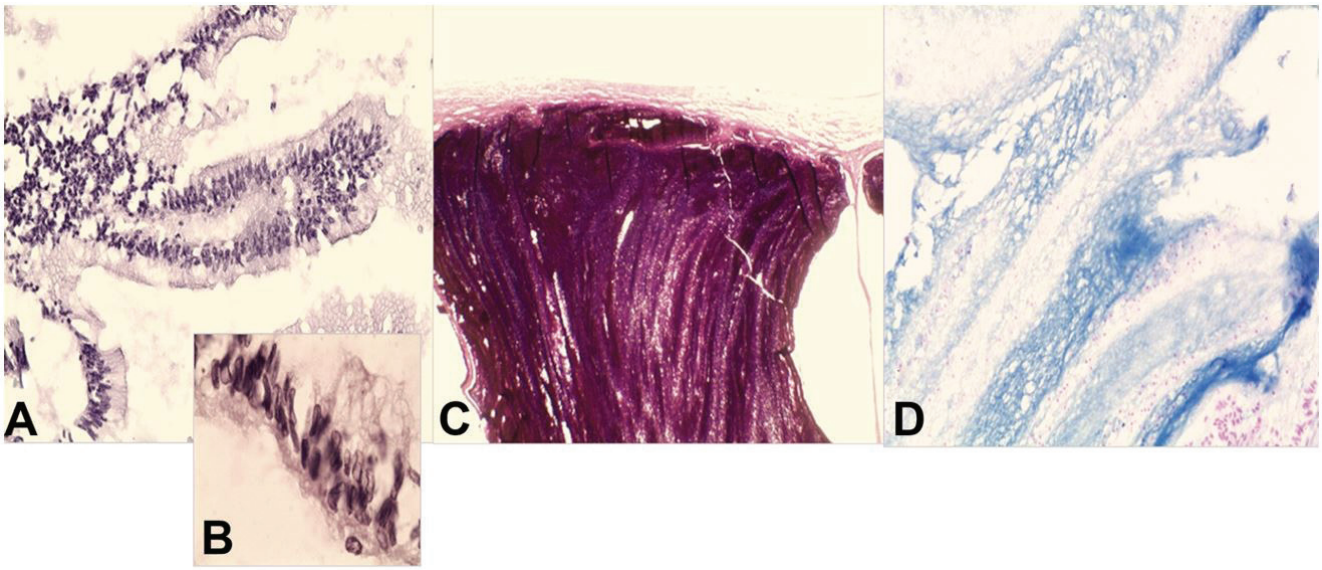


**Figure 5.** In **A**, residual papillary structure of epithelium with multilayer cores (EE: 200X, in **B** higher magnification EE: 1000X), with evidence of moderate nuclear atypia. In **C** (periodic acid-Schiff stain, 32X) and **D** (Alcian blue pH 2.5,100X), high amount of mucus tightly fixed to the internal surface of neoformation.

angiogenesis), decreased inhibitors of coagulation and impaired fibrinolysis.[28,29]

It is evident that the development of the neoplasm highlights the importance of therapeutic choices, even in the case of benign neoplasms, along with the analysis and characterization of the social and cultural conditions of the patient. This case confirms what is reported in the literature[30,31] about the association between pulmonary embolism and epithelial neoplasms.

## CONCLUSION

The presented case is peculiar because a sudden death occurred from complications related to ovarian neoplasm, with increased predisposition to deep venous thrombosis.

According to Italian Law, all the material sampled during a Judicial Autopsy does not require any authorization by the family members of the deceased to be studied and published, except with the precaution of maintaining the anonymity of the patient.

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