



# Case report: An Ovarian Inflammatory Mass, Possibly Related to a Recent COVID-19 Infection

**Stefan Timmerman<sup>1</sup>; Anne-Sophie Van Rompuy<sup>2</sup>; Christophe Deroose<sup>3</sup>; Vibeke Vergote<sup>4</sup>; Raphaëla Dresen<sup>5</sup>; Ignace Vergote<sup>1</sup>; Thomas Tousseyn<sup>2</sup>; Els Van Nieuwenhuysen<sup>1</sup>; Jonas Yserbyt<sup>6</sup>; Wouter Froyman<sup>7</sup>; Toon Van Gorp<sup>1</sup>**

<sup>1</sup>Department of Gynaecology and Obstetrics, Division of Gynaecological oncology, Leuven Cancer Institute, University Hospitals Leuven.

<sup>2</sup>Department of Pathology, University Hospitals Leuven, KU Leuven.

<sup>3</sup>Department of Nuclear medicine, University Hospitals Leuven, KU Leuven.

<sup>4</sup>Department of Hematology, University Hospitals Leuven.

<sup>5</sup>Department of Radiology, University Hospitals Leuven.

<sup>6</sup>Department of Respiratory Diseases, University Hospitals Leuven, KU Leuven.

<sup>7</sup>Department of Gynaecology and Obstetrics, University Hospitals Leuven.

## \*Corresponding Author(s): Stefan Timmerman

Department of Gynaecology and Obstetrics, Division of Gynaecological oncology, Leuven Cancer Institute, University Hospitals Leuven.

Tel: +32488482312, Fax: 016344205;

Email: stefan.timmerman@hotmail.com & stefan.timmerman@student.kuleuven.be

## Abstract

Inflammatory ovarian masses may be difficult to distinguish preoperatively from ovarian malignancies. We present a case of a 54-year old woman with an ovarian mass, diagnosed during a COVID 19-infection. She underwent surgery because of pain and a challenging differential diagnosis on imaging. The frozen section was inconclusive and the final pathological examination showed no malignancy but only an inflammatory mass. Further extensive investigations revealed sarcoidosis, associated with a specific inflammatory changes. In view of the COVID-19 infection and the signs of a systemic inflammatory syndrome, an association with SARS-CoV-2 infection is plausible. With this case report we hope to alert clinicians for the possibility of new COVID-19-related extra pulmonary disease manifestations.

Received: Feb 18, 2020

Accepted: Mar 10, 2021

Published Online: Mar 12, 2021

Journal: Annals of Gynecologic Cancer

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

Copyright: © Timmerman S (2021). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

## Case reports

Between the 11th and the 17th of April 2020, this 54-year-old patient was hospitalized due to a severe COVID-19 infection with respiratory symptoms. She was treated with hydroxychloroquine and amoxicillin/clavulanic acid. No mechanical ventilation was required. During this admission, a Computed Tomography (CT)-scan of the chest showed extensive ground glass opacities predominantly at the periphery of the lungs

in the context of a pulmonary COVID-19 infection. In addition, multiple mediastinal lymph nodes were found, atypical for a COVID-19 infection. Due to worsening lower abdominal pain during the hospitalization, an abdominal CT scan was performed. This showed a novel multilocular cystic mass of 7.2 centimeters in the left ovary, suspected to be malignant on the basis of this imaging. Enlarged lymph nodes were present in the



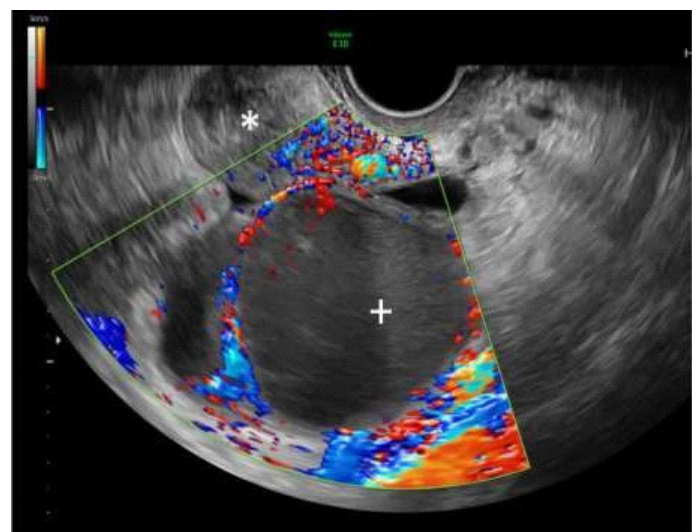
**Cite this article:** Timmerman S, Rompuy ASV, Deroose C, Vergote V, Dresen R, et al. Case report: An Ovarian Inflammatory Mass, Possibly Related to a Recent COVID-19 Infection. *Ann Gynecol Cancer*. 2021; 4(1): 1006.

para-aortic region. Prior to the COVID-19 infection the patient was in good health. She had a medical history of two diagnostic laparoscopies in the context of subfertility, a cystectomy for a benign ovarian cyst and two vaginal deliveries. There was no family history of cancer. After her hospitalization, the patient made a slow recovery, with persisting exertional shortness of breath and tiredness.

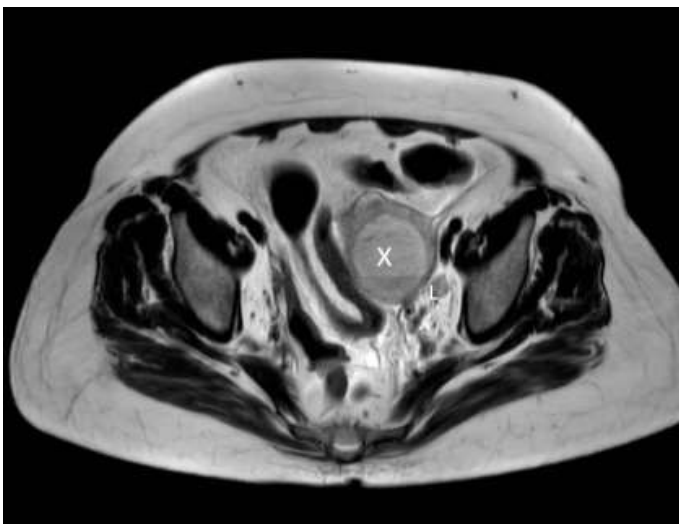
When she presented at our gynaecological oncology unit in May 2020, clinical examination showed a mass of 8 cm in the left ovarian fossa, tender on palpation. Ultrasound assessment revealed a large bilocular cystic mass with strong vascularization in the septum and cyst wall and with mixed echogenicity (with a fluid-fluid level) (Figure 1). The mass was fixed in the cul-de-sac and subjective assessment was suggestive for an infectious process. Whole-body diffusion weighted magnetic resonance imaging (WB-DWI/MRI) confirmed the presence of the cyst, however, without pathological contrast enhancement or restricted diffusion, most likely being post-torsion or post-infection, with the presence of multiple enlarged lymph nodes (in the obturator, para-aortic, liver hilum, mesenteric, mediastinal, axillary, and cervical areas)(Figure 2). The serum marker CA 125 was mildly elevated to 65 kU/L (normal range: <35). On the other hand, a strong elevation in CRP (242.7 mg/L; normal range: <5) was observed, together with liver function tests (gamma-glutamyltransferase (202 U/L; normal range: <40) and alkaline phosphatase (199 U/L; normal range: 35-105)) suggestive of bile duct or gallbladder problems. Bilirubine was within normal range. Surgical evaluation (laparotomy) with bilateral salpingo-oophorectomy with frozen section was performed. The left ovary was cystic and there were adhesions to the pelvic wall. No other aberrant findings were noted intra-abdominally. Malignancy could not be excluded on frozen section. Therefore, a total hysterectomy with appendectomy, omentectomy, sampling of the enlarged obturator and para-aortic lymph nodes was performed. She had an uneventful recovery and could be discharged from the hospital after a few days. On final pathological examination no malignancy was found. The ovarian cyst was lined with a thick fibrous wall, containing a heterogeneous inflammatory infiltrate, rich in eosinophils admixed with a reactive mesothelial proliferation and partly covered by prominent granulation tissue. The fallopian tube also showed fibrous changes and an eosinophilic infiltrate. In the contralateral adnexa, an extensive salpingitis, partly granulomatous, was noted (Figure 3). The uterus, appendix and the omentum showed no significant changes. No micro-organisms were detected using periodic acid-Schiff staining after  $\alpha$ -amylase. Additional immunohistochemical staining with CD3 and CD20 confirmed a reactive inflammatory infiltrate. CD 68 confirmed the presence of granulomas in the right adnexa. CD 138 was negative in the endometrium, excluding chronic endometritis, an indication for ascending infections. The lymph nodes of the obturator and para-aortic region showed hyperplasia of the marginal zone. Clonality analysis by PCR of the IGH- and IGK-loci was polyclonal, excluding a lymphoma. No granulomatous changes were observed. Reactive hyperplasia of the marginal zone was the preferential diagnosis. Due to the presence of the enlarged lymph nodes, it was decided to perform an additional positron emission tomography with  $^{18}\text{F}$ -fluorodeoxyglucose combined with CT ( $^{18}\text{F}$  FDG-PET/CT). This PET-CT showed bilateral supraclavicular, mediastinal, paratracheal and hilar moderate to intense hypermetabolic nodes (Figure 4). The pattern showed a typical "lambda sign", compatible with sarcoidosis or other types of chronic inflammation, although a lymphoma could

not be excluded. As the patient was asymptomatic and infra-diaphragmatic lymph node sampling showed no lymphoma, no histological analysis of the thoracic nodes was performed. After two months, the patient was re-assessed at the department of respiratory diseases. After the initial conservative management, a CT-scan of the thorax showed progressive enlargement of the thoracic lymph nodes. The lung function had markedly improved compared with the lung function during the COVID-19 pneumonia. However, the exercise tolerance remained poor. An excision biopsy of a hypermetabolic cervical lymph node showed a non-necrotizing granulomatous lymphadenitis, with sarcoid-type granulomas. Additional repeat of the PCR of the IGH- and IGK-loci and the molecular analysis showed again no arguments for a lymphoma. Standard cultures and auramine cultures for mycobacteria remained negative. Immunohistochemical evaluation with antibodies against SARS-CoV-2 was negative in this node.

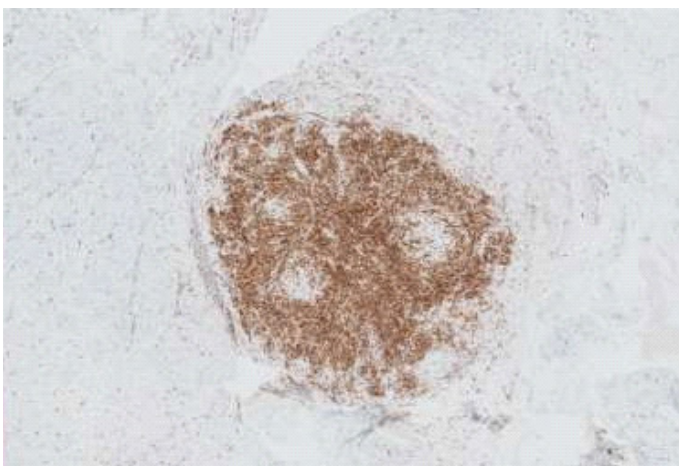
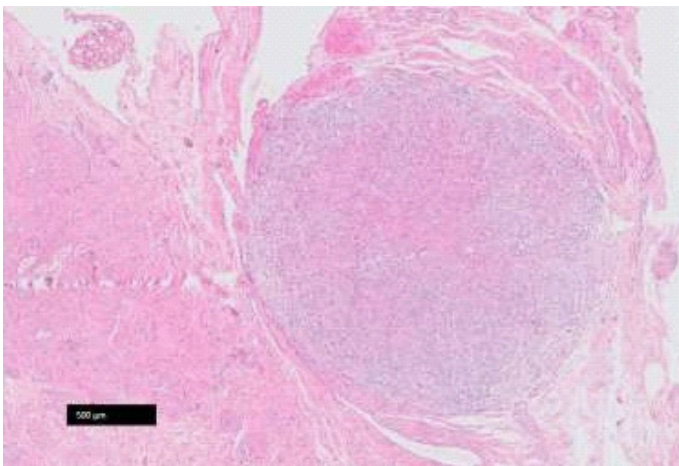
Based on these results, together with an elevated kininase on blood results (Kininase II: 142 U/L; normal range: 8-52), the tentative diagnosis of sarcoidosis was made. A further complete immunological blood test showed no evidence for other disorders. Antinuclear antibody test was positive with 1/160 titer. The presence of antineutrophil cytoplasmic antibodies was dubious. Arguments against the diagnosis of sarcoidosis were the absence of systemic inflammation at this point and no clinical signs. An additional ultrasound of the liver could not find an alternative cause for the elevated liver enzymes. They were presumed to be secondary to sarcoidosis. Empirical treatment with ursodeoxycholic acid was initiated. At follow-up after 3 months, the patient had no residual symptoms. However, a CT-scan showed progressive enlarging of the hilar and mediastinal lymph nodes, as well as subpleural micronoduli with perilymphatic distribution, suggestive for evolutive sarcoidosis. The liver function tests were still equally elevated and a liver elastography showed no fibrosis, although an image more suggestive for evolutive steatosis. In accordance between the pneumologists and hepatologists, an additional treatment with Methylprednisolone (Medrol 8 mg) was initiated for its inflammatory effect.



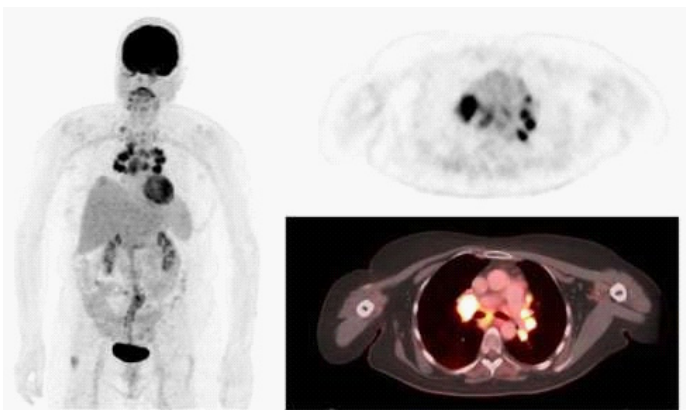
**Figure 1:** Ultrasound imaging of the ovarian cyst at initial presentation, showing a large bilocular cystic mass with strong vascularization in the septum and cyst wall and with mixed echogenicity with a fluid-fluid level (+). Anterior of the cyst we note a normal uterus (\*).



**Figure 2:** T2-weighted magnetic resonance imaging showing the cyst(X), without pathological contrast enhancement or restricted diffusion, most likely being post-torsion or post-infection. On this axial plane we note an enlarged iliac lymph node (L).



**Figure 3:** Histopathological slides of granulomatous changes in the right adnex, using Haematoxylin and Eosin on the top slide and a CD68 immunohistochemical stain on the bottom.



**Figure 4:** [18F] FDG-PET/CT imaging, showing bilateral hypermetabolic supradiaphragmatic lymph nodes, suggestive for sarcoidosis. This imaging was performed after the staging laparotomy.

**Discussion**

We describe the case of a patient with recent symptomatic COVID-19 infection presenting with an inflammatory ovarian mass, associated with an eosinophil-rich infiltrate, the presence of histologically proven reactive infra-diaphragmatic lymph nodes and an elevated serum CA125. Concomitantly enlarged thoracic lymph nodes were noted, which turned out to have typical characteristics of sarcoidosis at pathological examination. The pathological finding of the ovary showed a granulomatous inflammation which could be related to the sarcoidosis. This is a very rare finding, with only a limited number of case reports describing the presence of ovarian sarcoidosis [1,2]. A recent case report describes a sarcoid reaction in the skin after COVID-19 infection. No other articles have described a triggering of sarcoidosis by COVID-19 infection [10].

Due to the overt presence of leukocytes and the enlarged lymph nodes, a lymphoproliferative disease with ovarian localization was one of the considered diagnoses [3,4]. However, the ovarian mass was examined thoroughly, using histopathology, molecular analysis and PCR for clonal expansion, and no arguments were found for a malignancy, including a lymphoproliferative disease. Another possible cause for inflammatory lesions of the ovary, is genital tuberculosis. However, this will often present with necrotizing granulomatous lesions [5]. Microscopic examination and cultures of the cervical lymph node excluded the presence of Mycobacteria. A final option to consider is a viral-induced inflammatory response. The lesions on the ovary and the abdominal lymph nodes became symptomatic during an active COVID-19 infection and could be part of a systemic inflammatory syndrome. The COVID-19 virus invades the target cells by binding to Angiotensin-Converting Enzyme (ACE) 2. It has been suggested that the expression of ACE 2 receptors on the ovaries, could make these tissues susceptible to infection [6]. Different pathological studies have shown the direct influence of COVID-19 infections on other extra-pulmonary organs such as the heart, kidney and liver [7-9].

**Conclusion**

Ovarian masses of inflammatory origin in patients with a recent COVID-19 infection pose a difficult diagnostic challenge, prone to avoidable medical interventions. In our case, the patient was referred to our center, based on the suspicion of ovarian cancer center on CT scan. Ultrasound and MRI resulted in a benign preoperative diagnosis. Because of the presence of enlarged lymph nodes and abdominal pain, the patient underwent surgical exploration. The results from frozen section were



not inconclusive and his has led to a more extensive surgical approach. Further extensive investigations revealed sarcoidosis, associated with aspecific inflammatory changes. In view of the COVID-19 infection and the signs of a systemic inflammatory syndrome, an association with SARS-CoV-2 infection is plausible. With this case report we hope to alert clinicians for the possibility of new COVID-19-related extrapulmonary disease manifestations.

#### Author contributions

ST wrote the main manuscript body, with revisions from all authors. IV, EVN, TVG, JY were clinically involved in the patient's care. AVR and TT were responsible for histopathologic examination. RD examined the MRI images and CDR the nuclear imaging. WF re-evaluated the ultrasound images. All the authors have read and approved the final manuscript.

#### Informed consent statement

The patient, described in the report, gave written informed consent for publication of her case.

#### References

1. Karmaniolas K, Liatis S, Dalamaga M, Mourouti G, Digeni A, et al. A case of ovarian sarcoidosis mimicking malignancy. *Eur J Gynaecol Oncol.* 2005; 26: 231-232.
2. Wuntakal R, Bharathan R, Rockall A, Jeyarajah A. Interesting case of ovarian sarcoidosis: The value of multi disciplinary team working. *World J Surg Oncol.* 2007; 5: 38.
3. Vang R, Medeiros LJ, Warnke RA, Higgins JP, Deavers MT. Ovarian non-Hodgkin's lymphoma: A clinicopathologic study of eight primary cases. *Mod Pathol.* 2001; 14: 1093-1099.
4. Stepniak A, Czuczwar P, Szkodziak P, Wozniakowska E, Wozniak S, et al. Primary ovarian Burkitt's lymphoma: A rare oncological problem in gynaecology: a review of literature. *Arch 133 Gynecol Obstet.* 2017; 296: 653-660.
5. Grace GA, Devaleenal DB, Natrajan M. Genital tuberculosis in females. *Indian J Med Res.* 135 2017; 145: 425-436.
6. Jing Y, Run-Qian L, Hao-Ran W, Hao-Ran C, Ya-Bin L, et al. Potential influence of COVID-19/ACE2 on the female reproductive system. *Mol Hum Reprod.* 2020; 26: 367-373.
7. Beigmohammadi MT, Jahanbin B, Safaei M, Amoozadeh L, Khoshavi M, et al. Pathological Findings of Postmortem Biopsies From Lung, Heart, and Liver of 7 Deceased COVID-19 140 Patients. *Int J Surg Pathol.* 2020: 1066896920935195.
8. Santoriello D, Khairallah P, Bomback AS, Xu K, Kudose S, et al. Postmortem Kidney Pathology Findings in Patients with COVID-19. *J Am Soc Nephrol.* 2020; 31: 2158-2167.
9. Martines RB, Ritter JM, Matkovic E, Gary J, Bollweg BC, et al. Pathology and Pathogenesis of SARS-CoV-2 Associated with Fatal Coronavirus Disease, United States. *Emerg Infect Dis.* 2020; 26: 2005-2015.
10. Behbahani S, Baltz JO, Droms R, Deng AC, Amano SU, et al. Sarcoid-like reaction in a patient recovering from coronavirus disease 19 pneumonia. *JAAD Case Rep.* 2020; 6: 915-917.