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# **Endometriosis and Sars-Cov2: Another Comorbidity?**



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#### Abstarct

After identified a novel human coronavirus in Wuhan, China, in December 2019, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it has spread across the globe to reach over 180 countries. This clinical case examined a endometriosis case and its possible comorbid conditions to cause progression of the COVID-19 disease. From what is known at the moment, patients with COVID-19 disease who have comorbidities, such as hypertension and diabetes mellitus are more likely to develop a more severe course and progression of the disease. Factors like age and weight also need to be considered. We describe a postoperative endometriosis case that developed an acute respiratory condition, with progressive dyspnea associated with cough. Laboratory and imaging tests conirmed the diagnosis for Covid, the patient worsened and had to receive intensive care until she died.

Keywords: Endometriosis; SARS-CoV-2; Woman Health; Comorbidity

Abbreviations: SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19: Coronavirus Disease 2019; sp02: Blood Oxygen Saturation Levels; PCR: Polymerase Chain Reaction; O2: Oxygen Levels; NOC: Nasal Oxygen Catheter; CT: Computerized Tomography; ICU: Intensive Care Unit

## Introduction

In view of the in lammatory character of covid-19, the purpose of this case is to propose a possible relation between endometriosis and COVID19. Endometriosis is a benign pathology, but of in lammatory character, as a possible effect of increasing risk, in view of the morbidity that this SARS-COV-2 causes. We know that there are aggravating factors in this clinical report, but there is a need for more detailed discussion regarding endometriosis and its relation to SARS-COV-2.

We described a postoperative endometriosis case in a young woman that developed an acute respiratory condition, with

progressive dyspnea associated with cough. Laboratory and imaging tests confirmed the diagnosis for Covid, the patient worsened and had to receive intensive care until she died. Then, we made a short discussion about the physiopathology related by endometriosis and its possible relation to a bad evolution of Covid-19.

### Result

Patient arrived at the East Regional Hospital-HRL after suffering a fall from the standing height during an episode of lipothymia. She developed severe abdominal pain, nausea and vomiting. Weight: 100 kg. Height: 1,62m (5,31 feet).

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# Journal of Gynecology and Women's Health

Comorbidities: Obesity and Depression. Medications in use: Sertraline. Tomography performed in Base Hospital in the Federal District-HBDF showed luid in the abdominal cavity and pelvis, and also left adnexal cyst measuring 43mm. After medical evaluation at the HRL, she presented physical examination with abdominal pain on deep palpation, being worse in right iliac fossa.

She underwent a surgical procedure that showed: Presence of a lot of chocolate-like blood; "frozen" pelvis. Large amount of adhesions in cavity identified. Upon requesting the presence of a general surgery team that took over the procedure with the gynecology team. Careful debridement of all adhesions bilaterally, between discharge and retro-uterine region. Right ovary with large extension rupture, and contralateral ovary with enlarged dimensions and in lammatory signs; Uterine tubules adhered to sigmoid, posterior uterus, and ovaries. Normal size uterus.

Bilateral adnexectomy was performed with great difficulty, because pedicles adhered, it is difficult to define cleavage points. Visualized, both ureters, without changes; Blood aspiration; Exhaustive washing of the abdominal cavity; Inventory of all intestinal loops (small and large intestine); Review of rigorous hemostasis; Synthesis of the abdominal wall in reverse order to the skin. Patient evolved in good general condition, normotensive and afebrile, without complications. Antibiotics, hydration and blood pressure, glycemic and diuresis control were performed. Good acceptance of the oral diet offered.

On the third postoperative day, she developed an acute respiratory condition, with progressive dyspnea associated with cough. Saturation 74%, and after supplemental oxygen therapy it improved slightly to 85%, and after a nasal catheter at 3 l/ min it became saturated at 94%. At respiratory exam, vesicular murmur abolished in right hemithorax. Left hemithorax vesicular murmur. Respiratory frequence: 30 , sp02 85% without supplemental oxygen therapy. With  $\rm O_2$  in NOC at 3L/ m saturates 94 %. PCR requested for Covid. Further complementary exams were requested and the patient was transferred to the ICU.

On the fourth postoperative day, she didn't use supplemental O2. Chest CT was requested and evidenced sparse and bilateral pulmonary opacities in ground glass. Consider the possibility of viral pneumonia of the covid type. Patient was transferred. On the sixth postoperative day, dropped the hemoglobin levels. Has evolved again with respiratory failure. As her respiratory condition worsened, she was intubated. Paciente has evolved with worsening of his respiratory condition, having received all the routine support for intensive care, but after twenty four days the surgical procedure, she evolved to death.

### **Discussion**

SARS-CoV-2 has infected humans in all age groups, of

all nationalities, both adults and children. It is believed that COVID-19, in those with underlying health conditions or comorbidities, has an increasingly rapid and severe progression, often leading to death. Endometriosis is defined as presence of endometrial glands and stroma outside the uterine cavity. It can occurs in pelvis and multiple sites. Affects women during their pre-menarche, reproductive and post-menopausal hormonal stages, evidencing the relation with estrogen. Has an in lammatory and benign character. The symptoms arise due to in lammatory response by the increased production of in lammatory and pain mediators. As systemic chronic in lammation another outcomes can be present. For example, the presence of oxidative stress could elevate risk of atherosclerosis and coronary heart disease [1,2].

SARS-CoV-2 is a new and understudied disease. It was observed that the comorbidities with in lammatory character, such as hypertension, diabetes mellitus, obesity increase morbidity and mortality associated with COVID-19. The main diseases considered comorbidities are cardiovascular disease, diabetes mellitus, hypertension, chronic lung disease, cancer and chronic kidney disease. And why endometriosis cold be between these diseases?

Factors linked endometriosis pathophysiology to include: increased oxidative and nitrosative stress (O&NS), chronic immune in lammation, increased immune tolerance, autoimmunity, t helper (Th)17 cells and interleukin (IL)-17, as well as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) associated activation of the aryl hydrocarbon receptor (AhR) [3]. Estrogen at the estrogen receptor-alpha (ERα) can exacerbate symptoms, with estrogen also having regulatory, and symptomatic, effects via the ERB. As both of these estrogen receptors can be mitochondria-located, there can be significant changes in mitochondria functioning in endometriosis. Raised O&NS in endometrial tissue is overly compensated by an ERβ-mediated increase in mitochondria superoxide dismutase (SOD)2, leading to mitochondria with heightened levels of oxidative phosphorylation and ATP production. Within mitochondria cytochrome P450 (CYP)1B1 is increased [4], as often occurs in many cancers. Increased brain-derived neurotrophic factor (BDNF) [5] and the activation of its receptor, TrkB, are also associated with endometriosis [6]. As such, endometriosis shows alterations in mitochondrial functioning, oxidative stress regulation and increased trophic factors, linking endometriosis with tumor-associated pathophysiology [7].

A growing body of research has found multiple links between endometriosis and systemic in lammation, immunologic dysfunction, and metabolic changes. In addition, recent studies have identified several comorbidities that are associated with endometriosis, including autoimmune disease, allergy, cancers, and cardiovascular disease [8-10]. While the mechanism behind these associations remains unknown, it has been postulated that the systemic effects induced by endometriosis have a

# Journal of Gynecology and Women's Health

causal role in the development of these comorbidities. Recent observational studies have demonstrated that endometriosis lesions excrete aberrant levels of cytokines, growth factors, microRNAs (miRNAs), and excreted endometrial cells [11-13]. Recently, controlled experiments utilizing endometriosis animal models demonstrate that the presence of ectopic endometrium can alter the eutopic endometrial gene expression and cell migration, and can impact hepatic metabolism and body mass index (BMI) [11,14-16]. Our aim is to review the known clinical comorbidities associated with endometriosis, and present emerging data supporting endometriosis as a cause of systemic immune, in lammatory, metabolic, and stem cell dysfunction.

Although in the clinical case described the patient has two important risk factors, obesity and postoperative status, it is possible that the endometriosis was determinant in the death of a young woman. She was 26 years old, attended at the correct time and by a team of specialists. All of these factors can be considered to a clinical worsening and more studies need to be made to elucidate this theme.

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