



Gasless laparoendoscopic single-site surgery for management of unruptured tubal pregnancy in a woman with moderate COVID-19 pneumonia after administration of remdesivir and casirivimab-imdevimab: A case report

Shotaro Hayashi, Akihiro Takeda *

Department of Obstetrics and Gynecology, Gifu Prefectural Tajimi Hospital, Tajimi, Gifu, Japan

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ABSTRACT

Background: Diagnostic and therapeutic challenges may arise in the management of gynecologic emergencies, such as ectopic pregnancy, for women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Case: A 33-year-old woman (gravida 3, para 2) with a history of SARS-CoV-2 infection 8 months prior experienced sudden onset of fever and cough. Four days later, she consulted her gynecologist because of a positive pregnancy test and was further referred because of suspected ectopic pregnancy at 11 weeks of gestation, as calculated from her last irregular menstrual period. At triage, the patient complained of dyspnea, chest pain, and cough. Real-time reverse transcription-polymerase chain reaction assay detected SARS-CoV-2, which was subsequently identified to be an L452R variant. Chest computerized tomography (CT) showed moderate COVID-19 pneumonia. Transvaginal ultrasonography and pelvic CT showed a right tubal mass without an intrauterine gestational sac, suggesting right tubal pregnancy. Systemic methotrexate (MTX) therapy was chosen for management of the tubal pregnancy because of the patient's unruptured hemodynamically stable status, along with immediate administration of remdesivir and casirivimab-imdevimab to prevent worsening of the pneumonia. After failed MTX therapy, gasless laparoendoscopic single-site right salpingectomy was performed due to concern for tubal rupture. Four days after surgery, the patient was discharged from the hospital without subsequent complications.

Conclusions: Laparoscopic surgery, preceded by anti-viral therapy for COVID-19, is a feasible option for the management of hemodynamically stable tubal pregnancy in a woman with moderate COVID-19 pneumonia.

1. Introduction

Coronavirus disease 2019 (COVID-19) results from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The common clinical symptoms include dyspnea, cough, fever, myalgia, and dyspnea [2]. In the worst-case scenario, COVID-19 can lead to multiple organ failure due to a cytokine storm, which is the leading cause of severe morbidity and mortality [2].

Diagnostic and therapeutic challenges may arise in the management of acute abdominal events, such as ectopic pregnancy, for patients with SARS-CoV-2 infection [3,4,5]. Here, we present a case of unruptured tubal pregnancy in a woman with moderate COVID-19 pneumonia,

which was successfully managed by gasless laparoendoscopic single-site (LESS) surgery [6] after failed methotrexate (MTX) therapy, along with immediate anti-viral therapy [7,8].

2. Case Presentation

A 33-year-old woman (gravida 3, para 2) with a body mass index of 24.9 kg/m² (height: 165 cm; weight: 68 kg) experienced sudden onset of fever exceeding 38 °C. Four days later, she consulted her gynecologist because of a positive pregnancy test and was referred because of suspected ectopic pregnancy at 11 weeks of gestation, as calculated from her last irregular menstrual period. The patient had had SARS-CoV-2

Abbreviations: β-hCG, β-human chorionic gonadotropin; COVID-19, coronavirus disease 2019; CT, computerized tomography; LESS, laparoendoscopic single-site; MTX, methotrexate; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

* Corresponding author at: Department of Obstetrics and Gynecology, Gifu Prefectural Tajimi Hospital, 5-161 Maebata-cho, Tajimi, Gifu 507-8522, Japan.

E-mail address: gyendoscopy@gmail.com (A. Takeda).

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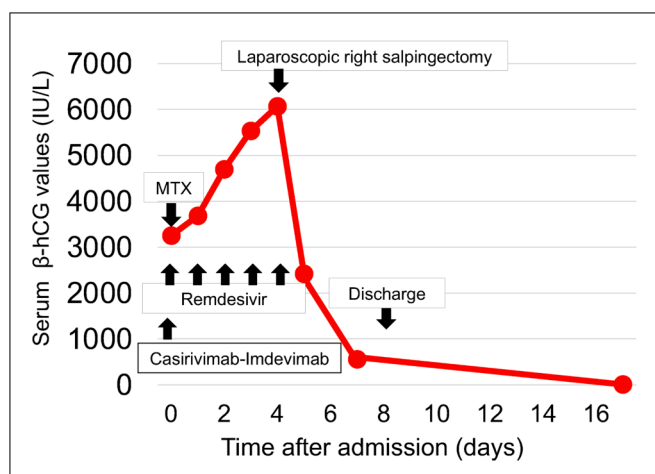


Fig. 1. Clinical course of right tubal pregnancy in a woman with moderate COVID-19 pneumonia. hCG; human chorionic gonadotropin.

infection 8 months prior, and had made an uneventful recovery; she had not been vaccinated against SARS-CoV-2.

At triage, dyspnea, chest pain, and cough were reported. The patient's serum β -human chorionic gonadotropin (hCG) level was 3254 IU/L (Fig. 1). Real-time reverse transcription polymerase chain reaction (RT-PCR) was positive for SARS-CoV-2, which was subsequently shown to be an L452R variant [9]. Chest computerized tomography (CT) showed multilobar and bilateral glassy opacities distributed peripherally under the pleura (Fig. 2A) [10]. Her oxygen saturation was 96%

under room air and her body temperature was 37.8 °C. Thus, moderate COVID-19 pneumonia was diagnosed.

Transvaginal ultrasonography and pelvic CT (Fig. 2B, arrow) revealed a right heterogeneous adnexal mass without an intrauterine gestational sac, suggesting tubal pregnancy. Peritoneal effusion was not evident.

Considering the hemodynamically stable status of the unruptured tubal pregnancy and possible further worsening of COVID-19 pneumonia after emergency surgery under general endotracheal anesthesia, systemic MTX (80 mg/body) was chosen for the management of the tubal pregnancy rather than immediate surgical intervention [3,5].

At the same time, to prevent the progression of moderate COVID-19 pneumonia to severe illness, immediate anti-viral therapy was initiated with remdesivir (Veklury; Gilead Sciences, Foster City, CA, USA) [7] and casirivimab-imdevimab (Ronapreve; Regeneron Pharmaceuticals, Tarrytown, NY, USA) [8]. Remdesivir was given intravenously as a 200-mg loading dose on day 0, followed by a daily 100-mg maintenance dose from days 1 to 4. Casirivimab (600 mg)-imdevimab (600 mg) was administered on day 0 (Fig. 1).

Four days after admission, respiratory symptoms, including cough, had improved. On the other hand, despite MTX treatment, serum β -hCG increased to 6070 IU/L (Fig. 1), suggesting the insufficient cytotoxic effects of MTX.

Because of concern for rupture after failed MTX treatment, laparoscopic exploration was selected rather than continuation of medical therapy. Under endotracheal general anesthesia, gasless laparoendoscopic single-site surgery using an abdominal wall-lift device (Mizuho Co., Tokyo, Japan) was performed through a 2.5-cm umbilical incision attached with an Alexis wound retractor (Applied Medical, Rancho Santa Margarita, CA, USA), similar to that normally performed for acute

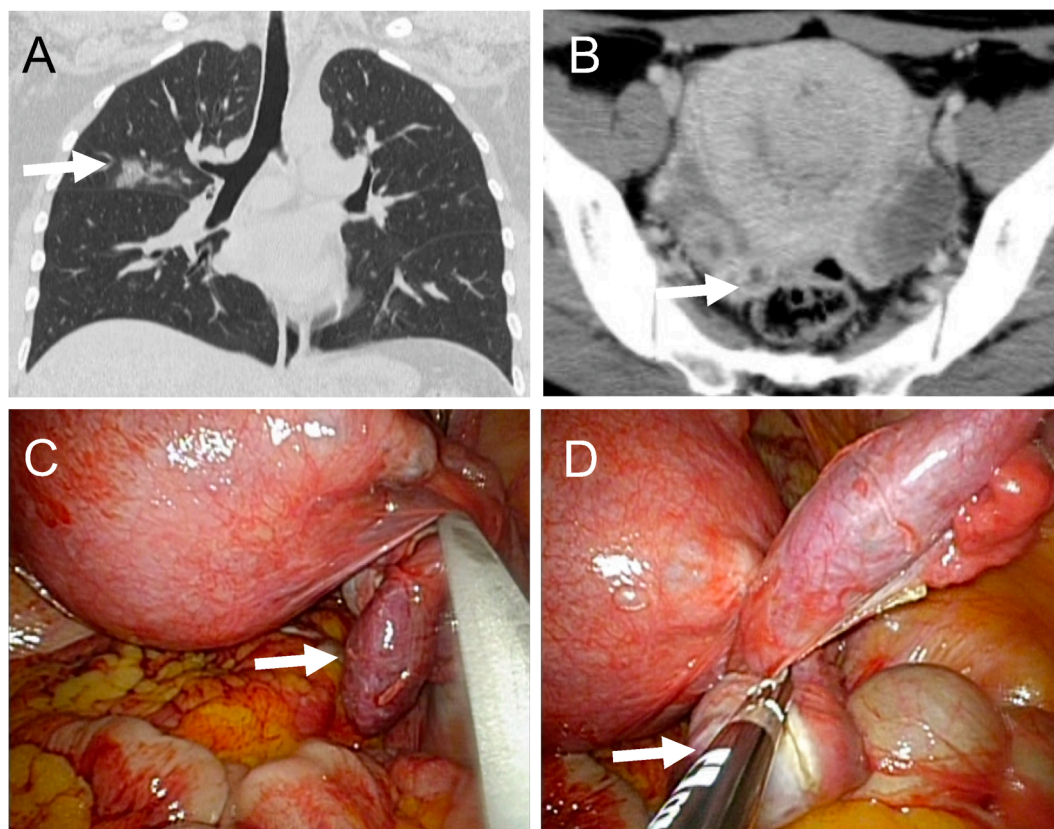


Fig. 2. (A) Computerized tomography scan of the chest showing multilobar and bilateral ground-glass opacities (arrow). (B) Pelvic computerized tomography scan showing a right tubal mass (arrow) suggesting tubal pregnancy, along with a right corpus luteum and a left functional ovarian mass. Peritoneal bleeding was not evident. (C) Laparoscopic observation showing an unruptured right tubal pregnancy (arrow) with pelvic adhesion. (D) Excision of right tube using the Ligasure Maryland (Covidien Japan, Tokyo, Japan) (arrow). Apparent peritoneal bleeding was not noted.

Table 1
Literature review on ectopic pregnancy complicated with severe acute respiratory syndrome coronavirus 2 infections

Case	Author, year of publication	Age (years)	Body mass index	Serum β-hCG value at triage (IU/L)	Estimated gestational weeks	Severity of COVID-19 pneumonia	Signs and symptoms of COVID-19	Comorbidities	Treatment for ectopic pregnancy	Treatment for COVID-19	Complications	Outcomes
1	Hansen and Stovall, 2020 [3]	37	42	6500	NA	Normal pulmonary examination	Asymptomatic	Type 2 diabetes mellitus	Laparoscopic surgery	NA	NA	NA
2	Millan et al., 2021 [5]	36	55	3838	6	Severe	Worsening dyspnea and chest pain	Asthma, chronic hypertension, morbid obesity	Systemic methotrexate (50 mg/body) administration, twice	Low-flow nasal canula oxygen therapy, dexamethasone, albuterol as needed	Mild transaminitis	Uneventful
3	Current case	33	24.9	3254	11	Moderate	Fever, dyspnea, chest pain and cough	None	Laparoscopic salpingectomy after single methotrexate (80 mg/body) administration	Remdesivir and Casirivimab-Imdevimab	None	Uneventful

hCG, human chorionic gonadotropin; NA, not available.

gynecologic emergencies in this department [6].

Under laparoscopic view, right tubal swelling with pelvic and fimbrial adhesion was noted (Fig. 2C, arrow). Peritoneal bleeding was not evident. Under diagnosis of unruptured right tubal pregnancy, right salpingectomy was performed by sealing and cutting the mesosalpinx using the Ligasure Maryland (Covidien Japan, Tokyo, Japan) (Fig. 2D, arrow). The excised tubal tissue was placed into a retrieval bag and taken out of the body through the umbilical incision. Surgery lasted 36 min, and intraoperative blood loss was 5 mL. During the procedure, intensive use was made of a suction device to minimize the potential aerosol and airborne transmission of SARS-CoV-2 virus [11].

After the surgical procedure, extubation was possible without respiratory distress. The patient was admitted to the isolation room in the intensive care unit and managed overnight. She made an uneventful recovery. The medical staff involved in the treatment of this patient complied with the tertiary protection regulations, and full personal protective equipment was worn throughout [11]. Four days after surgery, the patient was discharged from the hospital without subsequent complications.

3. Discussion

COVID-19 is a global health concern in the 21st century because of its rapid spread [1,2]. Over 80% of patients infected with SARS-CoV-2 experience mild to moderate symptoms, whereas 14% and 5% present severe and critical illness, respectively. Mostly due to multiple organ failure induced by a cytokine storm, the overall case-fatality rate is 2.3% among those with confirmed illness [1]. Older age and comorbidities, including obesity, hypertension, and diabetes mellitus, are potential risk factors for progression to severe illness [1].

Whether ectopic pregnancy is a risk factor for the progression of COVID-19 pneumonia is not known. However, a cytokine storm, which is thought to play an essential role in the development of the severe comorbidities of COVID-19, could be blunted during pregnancy because of the physiological silencing of the pro-inflammatory response. As a result, SARS-CoV-2 infection in pregnant women present with a more benign clinical course than anticipated [12].

For the management of patients suffering from COVID-19 pneumonia, a number of therapeutic options, including novel anti-viral drugs and substances that modify the immune response or other intrinsic pathways, and combined regimens are developed to continuously improve outcomes [7,8].

The most essential aspect in the management of COVID-19 pneumonia is to determine the procedure according to the severity of morbidity. For patients with moderate illness as in the current case, antiviral therapy utilizing remdesivir [7], an inhibitor of the viral RNA-dependent RNA polymerase, and/or casirivimab-imdevimab [8], an antibody cocktail composed of two recombinant human monoclonal antibodies that bind to non-overlapping epitopes of the spike protein receptor-binding domain of SARS-CoV-2, are recommended to prevent progression to severe or critical illness.

The immediate administration of remdesivir and casirivimab-imdevimab in the current patient resulted in the early relief of symptoms associated with moderate COVID-19 pneumonia, and allowed urgent surgery for unruptured ectopic pregnancy after failed MTX therapy.

When ectopic pregnancy is indicated in patients with positive RT-PCR for SARS-CoV-2 [3] (Table 1), triage to examine the severity of the underlying intra-abdominal condition, as well as the degree of COVID-19 pneumonia, is fundamental [13,14]. If COVID-19 pneumonia is not apparent despite a positive finding for SARS-CoV-2 [3] (Table 1), surgical intervention for ectopic pregnancy could be a safe and feasible option. On the other hand, when active COVID-19 pneumonia occurs concurrently in a patient with ectopic pregnancy, the health care team may encounter difficult decision-making [5] because different therapeutic options, including expectant management, medical cytotoxic therapy by MTX, and surgical intervention, should be explored.

Early administration of MTX could be a feasible option when the serum β -hCG level is <5000 IU/L, and hemodynamic stability is maintained with minimal symptoms [3], as in the current case. However, when initiating MTX therapy, negative effects should also be considered [15]. These include MTX-induced lung injury, which may lead to a worsening of the COVID-19 pneumonia. Furthermore, because MTX may exacerbate COVID-19 infection by immunosuppression, the COVID-19 pneumonia could be prolonged or worsened. These side-effects are more likely due to increased MTX dose and treatment duration [15]. Therefore, as in the current case, if any ineffective cytotoxic effects are apparent, surgical intervention should be definitively considered.

Once surgical treatment is decided, the route of approach by either laparotomy or laparoscopy should be determined [13] (Table 1), along with the evaluation of the potential risk of general anesthesia. Laparoscopy is a minimally invasive approach and has the potential advantage of the reduced need for analgesia and early recovery, as well as a cosmetic benefit [6] over laparotomy. However, a concern about airborne transmission of SARS-CoV-2 during laparoscopic surgery with pneumoperitoneum remains [16]. To reduce this potential risk of viral transmission [3], leakage of blood spray and rapid venting from the working port should be avoided. Furthermore, smoke production can be minimized by using lower-power instruments and a shorter duration of energy application.

Laparoscopy performed under a lower-pressure pneumoperitoneum could be an option [3]. However, an adequate view may not be obtained due to insufficient expansion of the peritoneal cavity, and the surgical procedure may be prolonged, contrary to the original aim. On such occasion, if available, gasless laparoscopy without need of carbon dioxide gas insufflation could be a feasible option [17], as described in the current report.

In conclusion, despite the lack of apparent evidence and established guidelines, laparoscopic surgery, at most preceded by medical therapy for COVID-19, is an option for the management of hemodynamically stable tubal pregnancy in a woman with moderate COVID-19 pneumonia.

Contributors

Shotaro Hayashi contributed to patient management.
Akihiro Takeda was involved in drafting the manuscript.
Both authors read and approved the final manuscript.

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Patient consent

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Provenance and peer review

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

References

- [1] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention, *JAMA*. 323 (2020) 1239–1242, <https://doi.org/10.1001/jama.2020.2648>.
- [2] J.J. Zhang, X. Dong, Y.Y. Cao, Y.D. Yuan, Y.B. Yang, Y.Q. Yan, C.A. Akdis, Y. D. Gao, Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China, *Allergy*. 75 (7) (2020) 1730–1741, <https://doi.org/10.1111/all.14238>.
- [3] K.A. Hansen, D.W. Stovall, Ectopic pregnancy during coronavirus disease 2019 (COVID-19): to operate, or not to operate, *Obstet. Gynecol.* 136 (2) (2020) 288–290, <https://doi.org/10.1097/AOG.0000000000003995>.
- [4] H.V. Toma, T. C. Bank, M.K. Hoffman, Care for women with ectopic pregnancies during the coronavirus disease 2019 (COVID-19) pandemic, *Obstet. Gynecol.* 137 (6) (2021) 1041–1042, <https://doi.org/10.1097/AOG.0000000000004392>.
- [5] N.M. Millan, J. Morano, L. Florez, J. Carugno, C.A. Medina, Management of tubal ectopic pregnancy with methotrexate in the setting of symptomatic Coronavirus disease 2019 (COVID-19): a case report, *Facts Views Vis Obgyn* 13 (3) (2021) 277–281, <https://doi.org/10.52054/FVVO.13.3.030>.
- [6] A. Takeda, S. Imoto, M. Mori, T. Nakano, H. Nakamura, Early experience with isobaric laparoendoscopic single-site surgery using a wound retractor for the management of ectopic pregnancy, *Eur. J. Obstet. Gynecol. Reprod. Biol.* 154 (2) (2011) 209–214, <https://doi.org/10.1016/j.ejogrb.2010.10.006>.
- [7] J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, Remdesivir for the treatment of Covid-19 - final report, *N. Engl. J. Med.* 383 (19) (2020) 1813–1826, <https://doi.org/10.1056/NEJMoa2007764>.
- [8] R.A. Siemieniuk, J.J. Bartoszko, J.P.D. Martinez, E. Kum, A. Qasim, D. Zeraatkar, A. Izcovich, S. Mangala, L. Ge, M.A. Han, T. Agoritsas, D. Arnold, C. Ávila, D. K. Chu, R. Couban, E. Cusano, A.J. Darzi, T. Devji, F. Foroutan, M. Ghadimi, A. Khamis, F. Lamontagne, M. Loeb, A. Miroshnychenko, S. Motaghi, S. Murthy, R. A. Mustafa, G. Rada, B. Rochwerf, C. Switzer, P.O. Vandvik, R.W. Vernooij, Y. Wang, L. Yao, G.H. Guyatt, R. Brignardello-Petersen, Antibody and cellular therapies for treatment of covid-19: a living systematic review and network meta-analysis, *BMJ* 374 (2021), <https://doi.org/10.1136/bmj.n2231>.
- [9] J. Chen, R. Wang, M. Wang, G.W. Wei, Mutations strengthened SARS-CoV-2 infectivity, *J. Mol. Biol.* 432 (19) (2020) 5212–5226, <https://doi.org/10.1016/j.jmb.2020.07.009>.
- [10] F. Fu, J. Lou, D. Xi, Y. Bai, G. Ma, B. Zhao, D. Liu, G. Bao, Z. Lei, M. Wang, Chest computed tomography findings of coronavirus disease 2019 (COVID-19) pneumonia, *Eur. Radiol.* 30 (10) (2020) 5489–5498, <https://doi.org/10.1007/s00330-020-06920-8>.
- [11] Y. Gao, H. Xi, L. Chen, Emergency surgery in suspected COVID-19 patients with acute abdomen: case series and perspectives, *Ann. Surg.* (2020 Apr 13), <https://doi.org/10.1097/SLA.0000000000003961>. Published online 2020 Apr 23.
- [12] T. Ghi, E. di Pasquo, A. Mekinian, L. Calza, T. Frusca, Sars-CoV-2 in pregnancy: why is it better than expected? *Eur. J. Obstet. Gynecol. Reprod. Biol.* 252 (2020) 476–478, <https://doi.org/10.1016/j.ejogrb.2020.07.025>.
- [13] B. De Simone, E. Chouillard, S. Di Saverio, L. Pagani, M. Sartelli, W.L. Biffi, F. Coccolini, A. Pieri, M. Khan, G. Borzellino, F.C. Campanile, L. Ansaloni, F. Catena, Emergency surgery during the COVID-19 pandemic: what you need to know for practice, *Ann. R. Coll. Surg. Engl.* 102 (2020) 323–332, <https://doi.org/10.1308/rcsann.2020.0097>.
- [14] COVIDSurg Collaborative, Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study, *Lancet* 396 (10243) (2020) 27–38, [https://doi.org/10.1016/S0140-6736\(20\)31182-X](https://doi.org/10.1016/S0140-6736(20)31182-X).
- [15] American College of Obstetricians and Gynecologists' (ACOG) Committee on practice, ACOG practice bulletin no. 193: tubal ectopic pregnancy, *Obstet. Gynecol.* 131 (2018) 91–103, <https://doi.org/10.1097/AOG.0000000000002560>.
- [16] K.K. Roy, R. Rai, R. Zangmo, A. Kumari, N. Noor, D. Garg, Laparoscopic gynecological surgery in COVID-19 pandemic, *Obstet. Gynecol. Sci.* 64 (3) (2021) 322–326, <https://doi.org/10.5468/ogs.20312>.
- [17] A.A. Abdelbaset, A.K. Saxena, Gasless laparoscopy revisited in the SARS-CoV-2 pandemic, *J. Pediatr. Endosc. Surg.* 2 (2020) 91–93, <https://doi.org/10.1007/s42804-020-00062-w>.