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Pneumoperitoneum and COVID-19. A causal association?

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Dear Editor,

We read with great interest the letter from Pérez Naranjo et al. (1) regarding the case we recently published in this journal (2). We believe that the case presented by the authors is undoubtedly useful as it contributes to the scarce existing casuistry on the relationship between COVID-19 and the development of pneumatosis/pneumoperitoneum.

We would like to emphasize the difficulty of determining the causality of this association due to the frequent co-occurrence of other causes that could justify the presence of pneumatosis/pneumoperitoneum. For instance, in the case reported by Pérez Naranjo et al. (2) the patient was undergoing immunotherapy treatment, and it is known that drugs such as bevacizumab can cause gastrointestinal perforation (3). In COVID-19 patients, the effect of mechanical ventilation must also be considered as another possible etiology, since its association with pneumoperitoneum has been known for decades (4). On the other hand, it should be noted that this association may be underestimated in patients with few symptoms in whom imaging examinations are

not performed or techniques of limited sensitivity (e.g. plain radiography) are used.

Regarding the topic of correspondence, we have performed a review of the computed tomography (CT) scans performed in COVID-19 patients in our institution since the beginning of the pandemic. We found two other cases of pneumoperitoneum of uncertain etiology (**table 1**) in patients admitted to the ICU due to COVID-19 pneumonia. They had been under long-term intubation, thus pneumoperitoneum could be explained by the effects of mechanical ventilation, although there was no associated pneumothorax. In the second patient, spontaneous perforation of the cecum was observed. Although its etiology could not be determined, similar cases attributing spontaneous intestinal perforation to intercurrent thromboembolic and septic phenomena have been reported (5).

In conclusion, clinical cases such as the ones presented (1,2) reinforce the interest in investigating the pathophysiology of abdominal involvement by COVID-19 despite the existence of potential confounding factors.

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Table 1. Patients with pneumoperitoneum detected by computed tomography (CT) during the pandemic in our institution. Both patients had bilateral COVID-19 pneumonia which had required orotracheal intubation at the time of diagnosis.

Age	Sex	Symptoms	Radiological findings	Management	Follow-up
33	Male	Signs of subcutaneous emphysema	Extensive pneumomediastinum and pneumoperitoneum. No pneumothorax	Conservative treatment	Favourable course. Hospital discharge
48	Male	Abdominal distension	Marked pneumoperitoneum with suspicion of perforated hollow viscus (not identified in CT)	Emergent surgery: right hemicolectomy and terminal ileostomy	Bad course. Long-term stay in the ICU to present (>90 days)