Bowel Perforation in Covid-19
Case Series

Donato Sciano*, Raffaele D'Ambrosio**, Antonello Maresca**, Silvio Buonincontro**,
Francesco Mariano**, A. Lenta**, Albertlesandra D'Agostino***

AORN Sant'Anna and San Sebastiano
*Director of Trauma Center
**Division Aorn Sant'Anna and San Sebastiano
***Director of Emergency Division AORN

Bowel Perforation in Covid-19: Case Series

OBJECTIVE: *To describe the clinical characteristics and outcomes of patients with coronavirus disease 2019(COVID-19) who developed bowel perforation.*
MATERIALS AND METHODS: *This case series was conducted in Emergency Department of AORN Sant'Anna and S. Sebastiano located in Caserta. All patients resulted positive to SARS-Cov-2 in nasopharyngeal swabs whith a positive laboratory test for SARS-CoV-2 from real time reverse transcription polymerase chain reaction(RT-PCR) as well as bowel perforation which was identified by abdominal CT, from September 2020 to December 2020.*
RESULTS: *A total of five patients were identified with Bowel perforation occurred despite all patients being on anticoagulation. All patients were Italian, predominantly male(four patients) with an average age of 60 years and the most common comorbidity was hypertension, diabetes and obesity.*
DISCUSSION: *Bowel perforation in COVID-19 is clinically significant with high morbidity and mortality. In our series 40% of patients who were diagnosed of bowel perforation died. Average time to death after bowel perforation diagnosis was 6 days.*
CONCLUSION: *We describe a case series of COVID-19 patients who developed bowel perforation.*

KEY WORDS: Covid-19, Bowel perforation

Introduction

As September 2020 the number of confirmed coronavirus disease (COVID-19) case have exceeded 29 million worldwide, resulting in almost one million deaths. The novel coronavirus disease caused by the severe acute respiratory syndrome but a proportion of patient may present other cpncurrent clinical features and among them with gastrointestinal symptomps [1]. We report case series and describe their clinical characteristics and outcomes.

Materials and Methods

Since September 2020, five patients werw admitted to the Emergency department for hight grade fever, cough dyspnea and severe abdominal pain. All patients resulted positive to SARS-Cov-2 in nasopharyngeal swabs whith a positive laboratory test for SARS-CoV-2 from real time reverse transcription polymerase chain reaction(RT-PCR). Bowel intestinal perforation was identified by abdominal CT.

Results

A total of five patients were included in our case series. All patients were Italian, predominantly male(four patients) with an average age of 60 years. The most common comorbidity was hypertension (three patients), diabetes(two patients), obesity (1 patient), while all patients
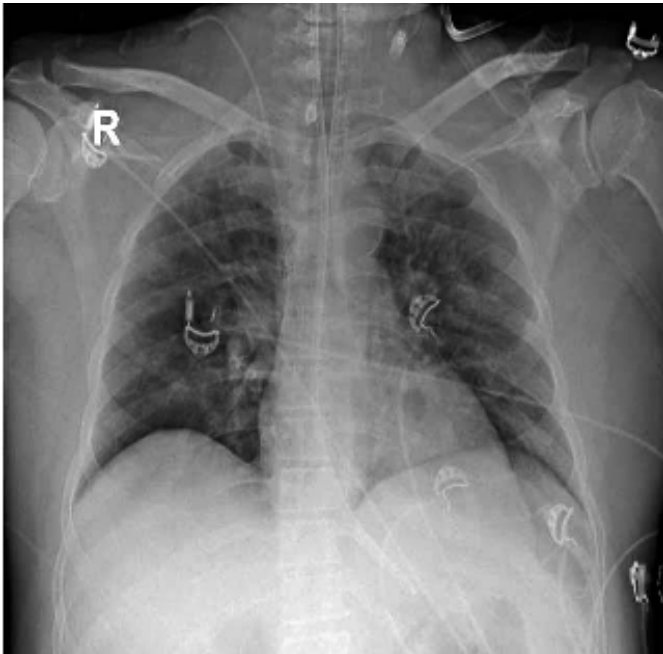
Fig. 1.

Fig. 2.

had diverticulosis. Indications for abdominal CT were immediate for all patients. One patient had perforation of small bowel, while four patients had large bowel perforation. Chest X-ray showed multifocal bilateral lung opacities (Fig 1),and CT scan found in all patients free air and liquid in the peritoneal cavity (Fig. 2). At the time of CT diagnosis of bowel perforation, the average serum lactate was 4,50 mmol/L, average arterial was with an average value of 7, 20, average serum bicarbonate was 18,00. One patient was treated at time of diagnosis with unfractionated heparin. COVID-19 specific therapy included a variety of different regimens. In this case all patient were treated with steroids and azithromycin. After diagnosis of bowel perforation, all patient underwent an exploratory laparotomy and treated with bowel resection and ostomy packaging. The resolution was demonstrated in three patients while two patients expired after six days for failure acute respiratory.

Discussion

We reported case series of bowel perforation. In our series 40% of patients who were diagnosed of bowel perforation died. For those who died, average time to death after bowel perforation diagnosis was 6 days. Based on pre-COVID-19 studies on predictive factors for pathologic bowel perforation, our results support that the diagnosis of bowel perforation in COVID-19 patients is of clinically significance. Multiple studies have shown that serum lactate is the most consistent predictor of clinically significant bowel perforation. One study showed that lactate level greate that 2.0 mmol/L at time of diag-
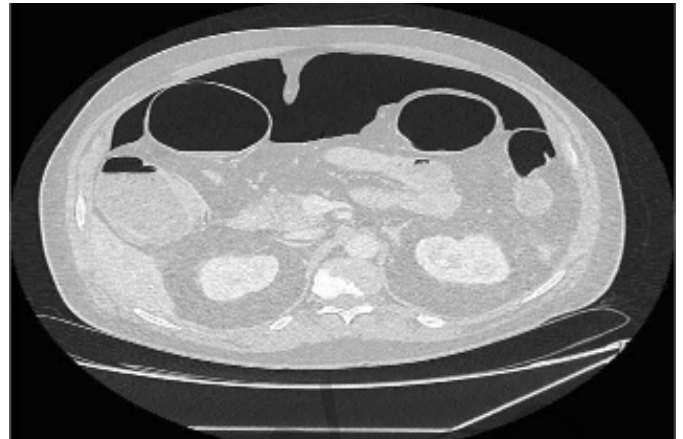
nosis has been associated with over 80% mortality [2]. In our case series, this was true in 60% of patients. The presence of bowel diverticulosis has also been shown to be a predictor which was present in 100% of our patients. The pathophysiology of this process is unclear as many aspects of COVID-19 remain unknown. Recent COVID-19 autopsy studies have shown a 40% prevalence of deep venous thrombosis, presence of microtrombi in multiple organ systems, as well evidence of intestinal endothelitis suggesting both macro and microvascular clotting predisposition and consequent hypoxic intestinal damage [3-4]. Two patients with surgical intervention had undergone exploratory laparotomy the same day of bowel perforation diagnosis and died after six days [5].Three patients had resolution of bowel perforation without surgical intervention. This manifestation of disease has significant implications on possible treatment modalities of interest. Recently cytokine storm has been purported to be partly responsible for the high morbidity and mortality seen in COVID-19 [6]. Interleukin-6 inibitors are being investigated for their potential in stemming hyperinflammation and its deleterious effects. Tocilizumab, an IL-6 inhibitors, has a known elevated risk of intestinal perforation. Intestinal perforation has also been reported with sarilumab, another inhibitor [7-8]. In our group, five patients had received an IL-6 inhibitor with an average time from administration to bowel perforation diagnosis of 10,4 days [9-10]. Of five patients, four receveid tocilizumab and one received sarilumab.

Conclusion

We describe a case series of COVID-19 patients who developed bowel perforation. We believe it is a clinically significant manifestation of disease that is likely underdiagnosed. Clinical suspicion should be high in COVID-19 patients with clinical decompression rising serum lactate, or worsening abdominal exam. Futher surgical and pathology data is necessary to determine exact pathophysiology.

Riassunto

I pazienti affetti da infezione da SARS-COV2 possono sviluppare complicanze fra cui la perforazione intestinale che presenta un elevato rischio di mortalità. Alcuni studi hanno evidenziato che elevati livelli sierici di lattati sono un fattore che aumenta il rischio di perforazione e di mortalità. Da un punto di visto fisiopatologico molti aspetti non sono ancora ben chiari. Rilievi autoptici hanno evidenziato lo sviluppo di un processo infiammatorio a carico dell'endotelio dei vasi mesenteriali con conseguente danno ipossico e perforativo dell'intestino. Inoltre i pazienti trattati con inibitori dell'interleuchina 6 hanno mostrato un elevato rischio di perforazione intestinale.

References

1. Zhu N, Zhang D, et al.: *A novel coronavirus from patients with pneumonia in China 2020.* N Engl J Med, 2020; 382:727-33.

2. Kotfis K, Skonieczena-Zydecka K: *COVID-19: gastrointestinal symptoms and potential COVID-19: Gastrointestinal symptoms and potential sources of 2019-nCov transmission.* Anaesthesiol Intensive, 2020; 52:1.

3. Conde G, Quintana Pajaro LD, Quintero Marzola ID, Ramos Villegas Y, Moscote Salazar YL: *Neurotropism of SARS-Cov 2: Mechanisms and manifestations.* J Neurol Sci, 2020; 116824.

4. Sambataro G, Giuffre' M, Sambataro D, PalermoA, Vignini G, Cesareo R, Crimi N, Torrisi S, Vancheri C, Malatino L, et al.: *The model for early COVID-19 recognition score: A proof-of-concept for a simple and low-cost tool to recognize a possible viral etiology in community-acquired pneumonia patients during covid-19.* Outbreak diagnostics, 2020; 10:619.

5. Magro F, Lopes J, Borralho P, Lopes S, Coelho R, Cotter J, De Castro FD, De Sousa H.T., Salgado M, Andrade P, et al.: *Comparision of different histological indexes in the assessment of UC activity and their accuracy regarding endoscopic outcomes and faecael calprotectin levels.* Gut, 2018; 68:594-603.

6. Cabas P, Di Bella S, Giuffre' M, Trombetta C, Luzzati R, Antonello RM, Parenzan K, Liguori G: *Community pharmacists exposure to COVID-19.* Res Soc Adm Pharm, 2020.

7. Gupta AK, Vazquez OA, Lopez-Viego M: *Cureus. Idiopathic pneumatosis of small bowel and bladder.* 2020; 12;0.

8. Thair M, Arshid S, Fontes B, Castro MS, Luz IS, Botelho KLR, Sidoli S, Schwammle V, Roepstorff P, Fontes W: *Analysis of the effect of intestinal ischemia and reperfusion on the rat neutrophilis proteome.* Front Mol Biosci, 2018; 5:89.

9. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernageal AS, Mehra MR, Schuepbach RA, Moch H: *Endothelial cell infection and endothelitis in COVID-19.* Lancet, 2020; 395:1417-18.

10. Gu Jinyang, Han Bing, Wang Jian. *COVID-19: Gastrointestinal manifestation and potential fecal-oral transmission.* Gastroenterology, 2020; 158(6):1518-19.