REVIEW
3535 Peroxisome proliferator-activated receptor gamma as a therapeutic target for hepatocellular carcinoma: Experimental and clinical scenarios
Katoch S, Sharma V, Patial V

3555 Gut microbiota alteration and modulation in hepatitis B virus-related fibrosis and complications: Molecular mechanisms and therapeutic inventions
Li YG, Yu ZJ, Li A, Ren ZG

MINIREVIEWS
3573 Combination approaches in hepatocellular carcinoma: How systemic treatment can benefit candidates to locoregional modalities
da Fonseca LG, Araujo RLC

3586 Update on endoscopic ultrasound-guided liver biopsy
Rangwani S, Ardeshna DR, Mumtaz K, Kelly SG, Han SY, Krishna SG

3595 Non-alcoholic fatty liver disease-related hepatocellular carcinoma: Is there a role for immunotherapy?
Mattos ÂZ, Debes JD, Vogel A, Arrese M, Reveleo X, Pase THS, Manica M, Mattos AA

3608 Potassium-competitive acid blockers and gastroesophageal reflux disease
Leowattana W, Leowattana T

3620 Making the case for multidisciplinary pediatric aerodigestive programs
Kanotra SP, Weiner R, Rahhal R

3627 Therapeutic potential of mesenchymal stem cells in the treatment of acute liver failure
Harrell CR, Pavlovic D, Djonov V, Volarevic V

3637 Effective combinations of anti-cancer and targeted drugs for pancreatic cancer treatment
Nishimoto A

ORIGINAL ARTICLE
Basic Study
3644 Mechanism of electroacupuncture and herb-partitioned moxibustion on ulcerative colitis animal model: A study based on proteomics
Retrospective Study

3666 How has the disease course of pediatric ulcerative colitis changed throughout the biologics era? A comparison with the IBSEN study
Kwon Y, Kim ES, Choe YH, Kim MJ

3682 Gastric mucosal precancerous lesions in Helicobacter pylori-infected pediatric patients in central China: A single-center, retrospective investigation
Yu M, Ma J, Song XX, Shao QQ, Yu XC, Khan MN, Qi YB, Hu RB, Wei PR, Xiao W, Jia BL, Cheng YB, Kong LF, Chen CL, Ding SZ

Observational Study

3695 Secular trends of intrahepatic cholangiocarcinoma in a high endemic area: A population-based study
Lin CR, Lee YK, Chiang CJ, Yang YW, Chang HC, You SL

3706 Family-based Helicobacter pylori infection status and transmission pattern in central China, and its clinical implications for related disease prevention

Scientometrics

3720 Global research on Clostridium difficile-associated diarrhoea: A visualized study
Zyoud SH

Case Report

3732 Delayed immune-related sclerosing cholangitis after discontinuation of pembrolizumab: A case report
Tanaka T, Sakai A, Tsujimae M, Yamada Y, Kobayashi T, Masuda A, Kodama Y

Letter to the Editor

3739 Prednisolone induced pneumatosis coli and pneumoperitoneum
Goh SSN, Shelat V

3743 Is patient satisfaction sufficient to validate endoscopic anti-reflux treatments?
Bortolotti M

3747 Endoluminal vacuum-assisted therapy as a treatment for anastomotic leakage in colorectal surgery
Chiarello MM, Bianchi V, Fransvea P, Brisinda G
ABOUT COVER
Editorial Board Member of World Journal of Gastroenterology, Giovanna Ferraioli, MD, FAIUM, Researcher, Department of Clinical Surgical, Diagnostic and Pediatric Sciences, Medical School University of Pavia, Viale Brambilla 74, Pavia 27100, Italy. giovanna.ferraioli@unipv.it

AIMS AND SCOPE
The primary aim of World Journal of Gastroenterology (WJG, World J Gastroenterol) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING
The WJG is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports, Index Medicus, MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJG as 5.374; IF without journal self cites: 5.187; 5-year IF: 5.715; Journal Citation Indicator: 0.84; Ranking: 31 among 93 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG’s CiteScore for 2021 is 8.1 and Scopus CiteScore rank 2021: Gastroenterology is 18/149.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Yu-Xi Chen; Production Department Director: Xu Guo; Editorial Office Director: Jia-Ru Fan.
Prednisolone induced pneumatosis coli and pneumoperitoneum

Serene S N Goh, Vishal Shelat

**Abstract**

Pneumatosis intestinalis (PI) is defined as the presence of gas within the submucosal or subserosal layer of the gastrointestinal tract. It is a radiologic sign suspicious for bowel ischemia, hence non-viable bowel must be ruled out in patients with PI. However, up to 15% of cases with PI are not associated with bowel ischemia or acute abdomen. We described an asymptomatic patient with prednisolone-induced PI and modified the Naranjo score to aid in a surgeon’s decision-making for emergency laparotomy vs non-operative management with serial assessment in patients who are immunocompromised due to long-term steroid use.

**Key Words:** Benign pneumatosis; Pneumatosis coli; Pneumatosis intestinalis; Prednisolone

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Goh SSN, Shelat V. Prednisolone induced pneumatosis coli and pneumoperitoneum. *World J Gastroenterol* 2022; 28(28): 3739-3742


**TO THE EDITOR**

We read with interest the report by Azzaroli et al[1], who conservatively managed two patients with benign pneumatosis intestinalis (PI). We would like to share a similar
A 71-year-old lady with dysphagia and diplopia symptoms was diagnosed with Neuromyelitis Optica (NMO). Treatment with prednisolone 20 mg once daily improved her diplopia. Nasogastric tube (NGT) feeding was commenced due to malnourishment from dysphagia. The chest radiograph for NGT placement showed pneumoperitoneum, and she was referred urgently to the surgical unit. She was asymptomatic, afebrile with normal hemodynamics. Abdomen was soft and non-tender. Leukocyte count, procalcitonin, lactate, and arterial blood gas were normal. A computed tomography of abdomen and pelvis (CTAP) with intravenous and NGT contrast confirmed pneumoperitoneum and pneumatosis coli from cecum to splenic flexure (Figure 1). There was no contrast extravasation, portal venous gas, inflammatory pathology, or mesenteric ischemia. Non-operative management with nil enteral feeding, serial abdominal examination, serum tests, and abdominal radiographs (AXR) was done. The patient remained asymptomatic with normal serum tests. A repeat CTAP showed minimal improvement of pneumoperitoneum. A follow-up AXR two weeks later showed worsening of pneumatosis coli. Hyperbaric oxygen therapy (HBOT) was arranged. Five HBOT sessions were performed at 2.2 atmospheric pressure for 90 min. Her abdominal girth reduced from 79 to 73 cm with minimal AXR improvement. Prednisolone was weaned over next five days and she was discharged well on oral diet. At two-weeks outpatient follow-up, AXR showed improvement (Figure 1).

Corticosteroid therapy remains the cornerstone for the treatment of autoimmune diseases. The true incidence of benign PI as an ADR secondary to corticosteroids is unknown[2,3]. The hypothesis is due to atrophy of lymphoid follicles in the bowel wall. Although PI occurred after prednisolone’s commencement in our patient, we did not initially stop prednisolone in balancing risk vs benefits for NMO therapy. When PI worsened, HBOT was offered due to concerns for secondary bowel ischemia from PI. The HBOT regimen was similar to that described by Feuerstein et al[4], who suggested at least three sessions. As our patient's PI improved but did not resolve fully after 5 HBOT sessions, we reduced prednisolone dose. After two weeks of cessation, PI resolved, similar to a report described by Choi et al[5].

According to the Naranjo score (adverse drug reaction probability scale) of 6, PI was probably caused by prednisolone in our patient. Naranjo score recommends isolation of drug in toxic concentrations in body fluid, response to placebo administration, and drug rechallenge to evaluate for the occurrence of symptoms. These three criteria are not routinely done due to practical and safety reasons[6]. We propose a modified Naranjo score (Tables 1 and 2) for prednisolone-induced pneumatosis which replaces these three criteria with the following: (1) No symptoms or signs of abdominal pathology; (2) Serum investigations for inflammatory markers (e.g., C-reactive protein and procalcitonin) must be normal; and (3) Imaging studies should rule out hollow viscus perforation or inflammatory abdominal pathology as a cause for PI. With the modified Naranjo score, the causal link of PI due to prednisolone becomes definite. We propose validation of modified Naranjo score.
**Table 1 Modified Naranjo score-pneumatosis intestinalis specific score**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/No/Do not know</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there previous conclusive reports on this reaction?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Did the adverse event appear after the suspected drug was administered?</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Are there alternative causes (other than the drug) that could on their own have caused the reaction?</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Was the reaction more severe when the dose was increased or less severe when the dose was decreased?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Did the patient have a similar reaction to the same or similar drugs in any previous exposure?</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Did any objective evidence confirm the adverse event?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Were there any symptoms or signs of abdominal pathology? (instead of isolation of drug in toxic concentrations in body fluid)</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Were the serum inflammatory markers normal? (instead of drug rechallenge to evaluate for reoccurrence of symptoms)</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>Did imaging studies rule out hollow viscus perforation or inflammatory abdominal organ pathology? (instead of response to placebo administration)</td>
<td>Yes</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total score** 9 (definite)

**Table 2 Interpretation of scores**

<table>
<thead>
<tr>
<th>Total score</th>
<th>Interpretation of scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 9</td>
<td>Definite</td>
</tr>
<tr>
<td>5 to 8</td>
<td>Probable</td>
</tr>
<tr>
<td>1 to 4</td>
<td>Possible</td>
</tr>
<tr>
<td>≤ 0</td>
<td>Doubtful</td>
</tr>
</tbody>
</table>

**FOOTNOTES**

**Author contributions:** Goh SSN wrote the letter; Shelat V revised the letter.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Country/Territory of origin:** Singapore

**ORCID number:** Serene S N Goh 0000-0003-4916-2142; Vishal Shelat 0000-0003-3988-8142.

**S-Editor:** Fan JR

**L-Editor:** A

**P-Editor:** Fan JR

**REFERENCES**


