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【 CASE REPORT 】

Pneumatosis Intestinalis Developed in a Patient with Giant Cell Arteritis While in a Clinically Sustained Remission Phase

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Abstract:
We herein report a patient with giant cell arteritis (GCA) who developed pneumatosis intestinalis (PI) while she was in a clinically sustained remission phase. A 79-year-old woman with GCA involving the thoracic aorta and its first branches to the posterior tibial arteries had been treated with high-dose prednisolone. Nine weeks after initiating treatment and while in clinically sustained remission with a normal CRP level, PI and pneumoperitoneum were incidentally found during scheduled positron emission tomography-computed tomography, which also revealed slight residual inflammation of GCA. This is a very rare case of PI complicated by GCA, and we discuss the possible relationships.

Key words: pneumatosis intestinalis, pneumoperitoneum, giant cell arteritis, vasculitis, steroids

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Introduction

Pneumatosis intestinalis (PI) is a rare medical condition characterized by the presence of gas within the intestinal wall. PI has been reported in a wide spectrum of conditions, ranging from emergent life-threatening conditions to expectant management (1). Among the various causes of PI, connective tissue diseases (CTDs) are infrequent (2). Nevertheless, PI has been reported in patients with systemic sclerosis (SSc) (3, 4), systemic lupus erythematosus (SLE) (5), and other CTDs (6, 7). However, no report has yet described a case of PI presenting in a patient with giant cell arteritis (GCA), one of the most common vasculitides affecting large vessels in elderly patients, causing a variety of symptoms.

We herein report a case of PI complicated by GCA in a clinically remitting state and discuss the possible risks for the occurrence of PI based on the existing literature.

Case Report

A 79-year-old woman with abdominal distension was hospitalized emergently in our department due to the detection of PI and pneumoperitoneum.

Six months before the admission, she had begun to experience pain involving her left jaw, left ear, left temporal area, and left thigh, as well as intermittent claudication. The Dental and Oral, Otorhinolaryngology, and Orthopedics Departments were all consulted. Serial C-reactive protein (CRP) levels were elevated, fluctuating from 3.8-8.9 mg/dL; however, the specific causes of the symptoms could not be determined.

She was referred to our department and hospitalized. She complained of transient vision loss with movement of her head. Laboratory testing revealed a CRP level of 10.42 mg/dL, and enhanced computed tomography (CT) revealed an abnormal arterial wall thickness of the aorta and its first branches. ^{18}F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)-CT also showed an increased uptake of FDG by arteries from the common carotid, vertebral, and subclavian arteries as well as the ascending and descending aorta to the posterior tibial arteries (Fig. 1a). A biopsy specimen from the left temporal artery revealed granulomas with accumulated polynuclear cells with destruction of the

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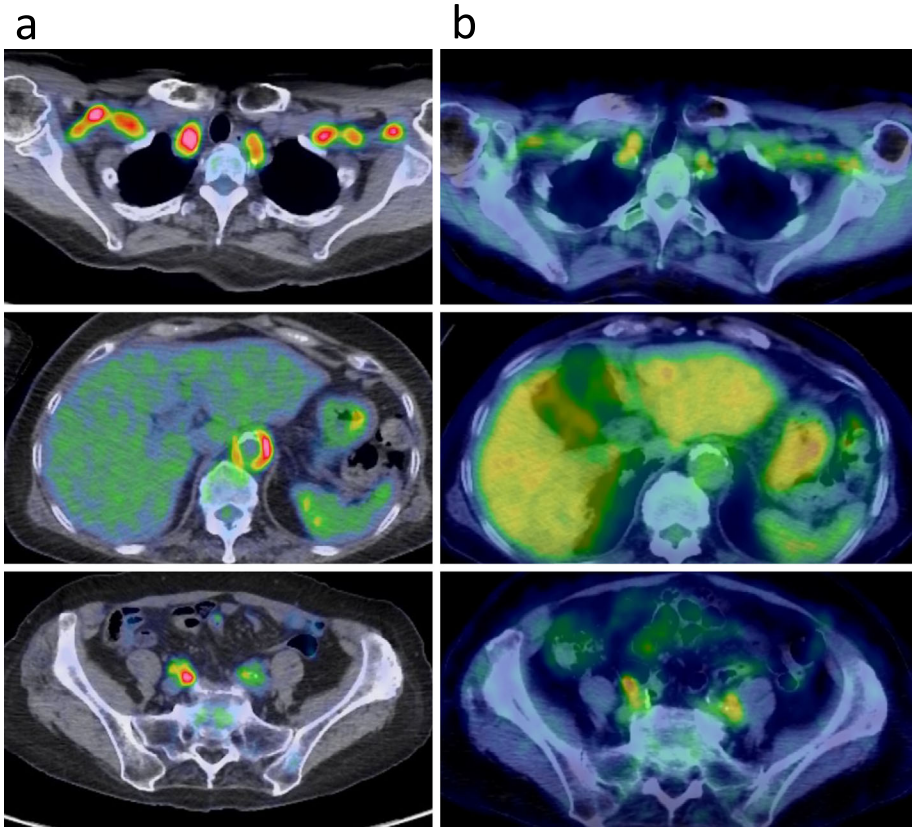

Figure 1. **^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-computed tomography (CT) findings during the first (a) and second hospitalizations (b). (a) The accumulation of FDG during the first hospitalization was observed in the aorta and its first branches, abdominal aorta, and common iliac arteries on FDG-PET-CT. (b) The FDG uptake was reduced but persisted on the second PET-CT scan compared to the first PET-CT scan.**

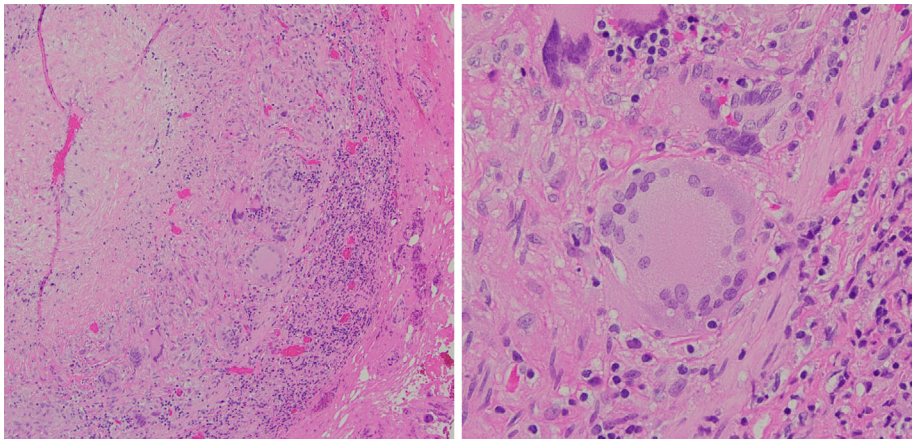

Figure 2. **A temporal artery biopsy obtained at the first admission. Granulomas with accumulated polynuclear cells showing destruction of the vessel wall were detected.**

vessel wall, findings consistent with arteritis (Fig. 2).

Based on these findings, she was diagnosed with GCA, and prednisolone (PSL) was started at 45 mg/day (1 mg/kg). The symptoms were resolved promptly. She was discharged on hospital day 10 because she exhibited an abnormal affect due to dementia. She underwent regular follow-up evaluations. The PSL was tapered to 20 mg/day, and her CRP value was negative for 7 weeks.

Two months after the first admission, she underwent scheduled follow-up PET-CT to confirm whether or not radiographic remission of GCA had been achieved (Fig. 1b). PI and pneumoperitoneum were incidental findings at this scan (Fig. 3a-c), so she was admitted to our department for a second time.

At the second hospital admission, she mentioned that she had noticed abdominal distention. Her height and weight

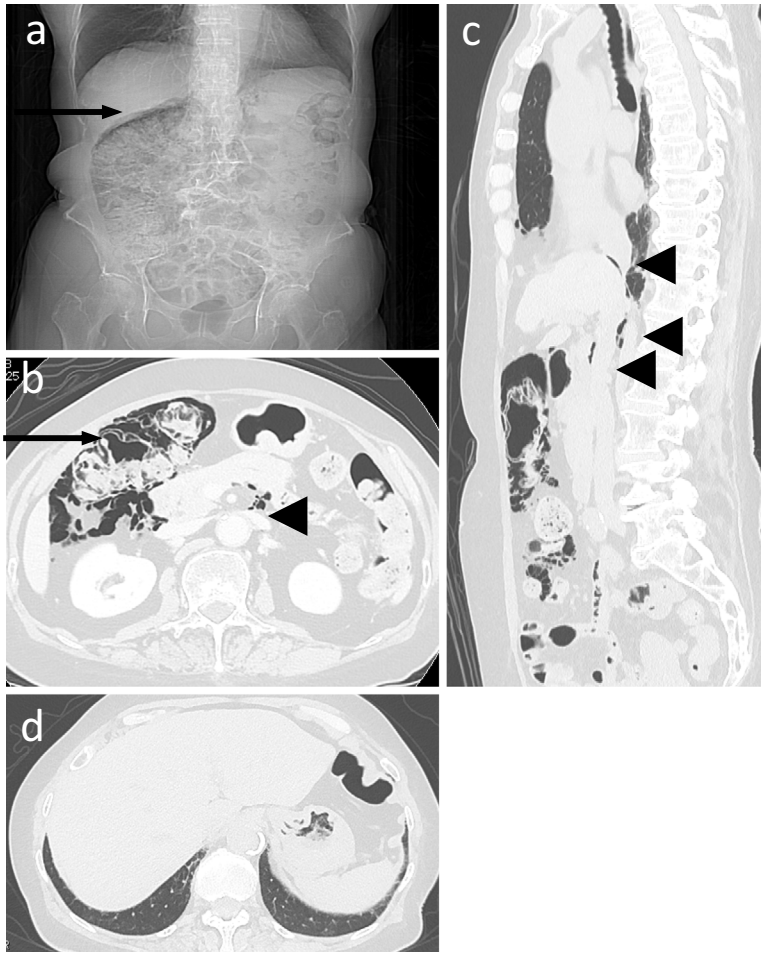

Figure 3. **Abdominal X-ray (a) and computed tomography (b, c) findings on the second hospital admission. The accumulation of gas within the intestinal wall (arrow) of the ascending and transverse colon on abdominal X-ray and computed tomography (CT). Free air (arrow heads) in the peritoneal cavity and retroperitoneum was detected. There were no findings suggestive of interstitial pneumonia on chest plain CT (d).**

were 151 cm and 54.3 kg, respectively. Her blood pressure was 102/52 mmHg, heart rate 55 bpm, and temperature 36.3℃. A physical examination showed a soft but distended abdomen without abnormal bowel sounds or tenderness. The laboratory findings are shown in Table. Chest X-ray and chest CT revealed no findings suggestive of interstitial pneumonia or mediastinal emphysema (Fig. 3d). PET-CT showed a reduced but still sustained FDG uptake in the arterial walls (Fig. 1b), even though CRP levels were negative either at the time of admission or during the seven weeks prior to the second admission. Based on these findings, inflammation of arteritis was not considered to have completely subsided.

The clinical course from the first admission is shown in Fig. 4. After the second admission (on day 65 after the first treatment was initiated), she stopped eating due to PI and pneumoperitoneum, so intravenous nutrition was started. The same dose of PSL was administered intravenously instead of orally. Although the CRP level had been persistently negative for at least 7 weeks before the second admission, she complained of a fever, numbness of the lower extremities, and left thigh pain; the CRP level rose to 4.75 mg/dL on day 75. Based on these symptoms and abnormal laboratory findings, it was deemed unlikely that the GCA had subsided completely, despite two consecutive months of negative CRP levels, and relapse was considered probably. The PSL dose was increased to 30 mg/day, and 2 mg/day of tacrolimus was added. Tacrolimus was selected over other immunosuppressive drugs, such as methotrexate or tocilizumab, because the patient had relatively high risk of infection, intestinal perforation due to tocilizumab use, and low adherence to methotrexate (MTX) use because of her age. The fever and thigh pain quickly resolved with the decrease in her CRP level to 0.52 mg/dL and she was discharged on day 80 with reduced but sustained abdominal distension and the presence of PI.

Discussion

We herein report a case of PI complicated by GCA. There have been some reports on PI with CTDs (6-9). The major primary diseases associated with PI among CTDs are SSc (3, 4) and polymyositis/dermatomyositis (6), followed

Table. **Laboratory Findings at the Second Admission.**

[Urinalysis]		[Chemistry]		[Immunology]	
Gravity	1.012	TP	5.5 g/dL	CRP	0.03 mg/dL
pH	6.5	Alb	3.5 g/dL	IgG	697 mg/dL
Protein	(-) mg/dL	BUN	16.7 mg/dL		
Sugar	(-) mg/dL	Cre	0.82 mg/dL		
Urobil	Normal	eGFR	47.1 mL/min/1.73m^2	ANA*	<40
RBC	4.6 /μL	UA	5.6 mg/dL	MPO-ANCA*	<0.5 IU/mL
WBC	13.6 /μL	Na	143 mmol/L	PR3-ANCA*	<0.5 IU/mL
		K	5.6 mmol/L	Anti-CCP ab*	<0.5 U/mL
[CBC]		Cl	101 mmol/L	RF*	6 U/mL
RBC	476 10^4/μL	Ca	9.6 mg/dL		
HB	14.6 g/dL	AST	21 U/L		
Ht	43.5 %	ALT	30 U/L		
MCV	91.4 fL	LDH	262 U/L		
MCH	30.7 pg	γ-GTP	23 U/L		
MCHC	33.6 g/dL	ALP	139 U/L		
WBC	9,420 /μL	T-Bil	0.9 mg/dL		
Neutro	79.7 %	CK	69 U/L		
Lymph	17.3 %				
Mono	2.6 %				
Eosino	0.2 %				
Baso	0.2 %				
Plate	18.4 10^4/μL				

*: these data were obtained at the first admission.

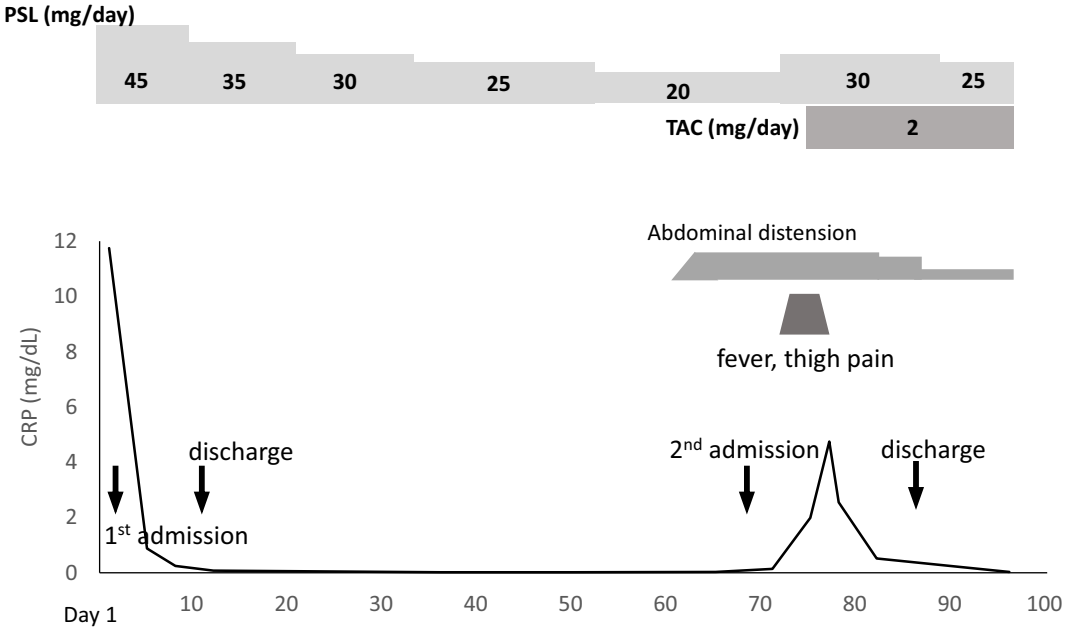

Figure 4. **Clinical course of this patient from the first hospitalization. CRP: C-reactive protein, PI: pneumatosis intestinalis, PSL: prednisolone, TAC: tacrolimus, PET-CT: positron emission tomography-computed tomography**

by SLE (5, 7, 10) and mixed connective tissue disease (9). After we experienced this case, we searched the English literature though PubMed using the key search terms 'pneumatosis intestinalis', 'pneumoperitoneum', and 'giant cell arteritis'. Only one case report was detected, focusing on the occurrence of PI probably due to peudolipomatosis of the colon and cecum complicated in a patient with GCA (11). Thus, our case is considered the first case of PI in GCA with no other cause.

A variety of underlying etiologies have been proposed to explain the abnormal accumulation of gas in PI; however, several theories have been advanced (1, 6, 12), including (1)

the mechanical theory, in which increased intestinal pressure due to intestinal obstruction results in a break in the integrity of the gastric mucosa and serves as the driving force in PI; (2) the pulmonary theory, in which pulmonary alveolar rupture caused by pulmonary diseases, such as chronic obstructive disease or interstitial pneumonitis, produce gas dissecting interstitially along the bronchopulmonary bundles to the mediastinum and retroperitoneally along the aorta and the mesenteric vessels to the bowel wall; (3) the bacterial theory, in which the gas is produced by gas-forming bacteria that enter the mucosal barrier or increased mucosal permeability and produce gas within the bowel wall; and (4) the chemical or nutritional deficiency theory, in which malnutrition increases bacterial fermentation in the intestine, thus producing large volumes of gas and subsequently the submucosal dissection of gas. Recently, the development of PI during treatment with a-glucosidase inhibitors (a-GIs) has been reported (8, 13, 14). It is thought that the cessation of a-GI therapy is the key to successful treatment of PI (13).

In our patient, additional etiologies presenting as PI were considered.

The first is vasculitis caused by GCA. According to several reports (5, 10), vasculitis can cause PI in patients with SLE. Intestinal ischemia provoked by vasculitis may permit invasion of gas-producing bacteria into the intestinal wall. In our case a wide range of arteries were involved (aorta and its primary branches, abdominal aorta, bilateral femoral arteries, and posterior tibial arteries). Therefore, the superior mesenteric artery, which supplies the ascending and transverse colon, may also be involved.

The second is vulnerability of the intestinal wall resulting from the active inflammation. In our patient, it took over six months for treatment to be administered, and the FDG uptake persisted for more than two months after corticosteroid (CS) therapy with a negative CRP level. The difficulty of evaluating aortitis activity based on the CRP is highlighted here. In our patient, PET-CT was useful for detecting inflammation. Thus, an active inflammatory period might be sufficient to develop intestinal wall vulnerability. As mentioned in the European Allaiance of Associations for Rheumatology (EULAR) recommendations, PET-CT can be used as a supporting modality for the diagnosis of GCA (15), but its utility for monitoring the disease activity is still unclear (16-18). The feasibility of PET-CT examinations is not always high because they cannot be performed frequently in terms of cost and radiation exposure. Based on our experience with the present patient, we feel that it is necessary to collect and analyze cases to propose the best use of PET-CT in the future.

The third is atrophy of the intestinal wall due to CS. CS depletes lymphatic tissue in the Peyer's patch cells of the intestine, thus enabling gas entry into the intestinal wall (19). Mizoguchi et al. (5) reported a case of PI that resolved after tapering CS therapy for lupus enteritis, suggesting that high-dose CS therapy for bowel vasculitis may be a risk factor for developing PI. Whether or not the dose or the duration of CS treatment affects the onset of PI is unclear. Indeed, some reports have concluded that high-dose CS therapy worsens PI (5, 20), while other reports have shown that PI is resolved by CS therapy (10). In our patient, CS was increased to 30 mg/day to decrease GCA and the associated symptoms, and the CRP level rapidly decreased to the normal range. PI was not exacerbated, but several weeks were required for attenuation.

Conclusion

We reported a very rare case of PI in a patient with GCA with long-lasting active inflammation, even after the CRP level normalized. The flare in GCA activity following the reduction in the CS dose, may be explained by the incomplete resolution of inflammation, which was not detected by CRP but rather by PET-CT and may be related to the occurrence of PI.

We obtained written informed consent from this patient for the publication of her case prior to submission of this manuscript.

The authors state that they have no Conflict of Interest (COI).

References

1. St Peter SD, Abbas MA, Kelly KA. The spectrum of pneumatosis intestinalis. Arch Surg **138**: 68-75, 2003.
2. Adachi W, Matsushita T, Yashiro Y, Imura J, Shiozawa H, Kishimoto K. Clinical characteristics of pneumoperitoneum with pneumatosis intestinalis detected using computed tomography: a descriptive study. Medicine (Baltimore) **99**: e22461, 2020.
3. Kaneko M, Sasaki S, Teruya S, et al. Pneumatosis cystoides intestinalis in patients with systemic sclerosis: a case report and review of 39 Japanese cases. Case Rep Gastrointest Med **2016**: 2474515, 2016.
4. Jenkins M, Courtney H, Pope E, Williamson J. A case report and approach to management in pneumatosis intestinalis. Ann Med Surg (Lond) **23**: 25-27, 2017.
5. Mizoguchi F, Nanki T, Miyasaka N. Pneumatosis cystoides intestinalis following lupus enteritis and peritonitis. Intern Med **47**: 1267-1271, 2008.
6. Suzuki E, Kanno T, Hazama M, Kobayashi H, Watanabe H, Ohira H. Four cases of pneumatosis cystoides intestinalis complicated by connective tissue diseases. Intern Med **56**: 1101-1106, 2017.
7. Dovrish Z, Arnson Y, Amital H, Zissin R. Pneumatosis intestinalis presenting in autoimmune diseases: a report of three patients. Ann N Y Acad Sci **1173**: 199-202, 2009.
8. Saito M, Tanikawa A, Nakasute K, Tanaka M, Nishikawa T. Additive contribution of multiple factors in the development of pneumatosis intestinalis: a case report and review of the literature. Clin Rheumatol **26**: 601-603, 2007.
9. Koppikar S, Yu D, Ropeleski M, Robertson D. Recurrent benign pneumatosis intestinalis in a patient with mixed connective tissue disease. Arch Rheumatol **33**: 478-481, 2018.
10. Cabrera GE, Scopelitis E, Cuellar ML, Silveira LH, Mena H, Espinoza LR. Pneumatosis cystoides intestinalis in systemic lupus erythematosus with intestinal vasculitis: treatment with high dose prednisone. Clin Rheumatol **13**: 312-316, 1994.
11. Iwamuro M, Tanaka T, Kawabata T, et al. Pseudolipomatosis of the colon and cecum followed by pneumatosis intestinalis. Intern Med **57**: 2501-2504, 2018.

12. Wu LL, Yang YS, Dou Y, Liu QS. A systematic analysis of pneumatosis cystoids intestinalis. World J Gastroenterol **19**: 4973-4978, 2013.
13. Tsujimoto T, Shioyama E, Moriya K, et al. Pneumatosis cystoides intestinalis following alpha-glucosidase inhibitor treatment: a case report and review of the literature. World J Gastroenterol **14**: 6087-6092, 2008.
14. Lin WC, Wang KC. Pneumatosis cystoides intestinalis secondary to use of an α-glucosidase inhibitor. Radiology **290**: 619, 2019.
15. Hellmich B, Agueda A, Monti S, et al. 2018 update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis **79**: 19-30, 2020.
16. Martinez-Rodriguez I, Jimenez-Alonso M, Quirce R, et al. ^{18}F-FDG PET/CT in the follow-up of large-vessel vasculitis: a study of 37 consecutive patients. Semin Arthritis Rheum **47**: 530-537, 2018.
17. Henes JC, Mueller M, Pfannenberg C, Kanz L, Kotter I. Cyclophosphamide for large vessel vasculitis: assessment of response by PET/CT. Clin Exp Rheumatol **29**: S43-S48, 2011.
18. Slart R, Writing G, Reviewer G, et al. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging **45**: 1250-1269, 2018.
19. Ammons MA, Bauling PC, Weil R 3rd. Pneumatosis cystoides intestinalis with pneumoperitoneum in renal transplant patients on cyclosporine and prednisone. Transplant Proc **18**: 1868-1870, 1986.
20. Ezuka A, Kawana K, Nagase H, Takahashi H, Nakajima A. Improvement of pneumatosis cystoides intestinalis after steroid tapering in a patient with bronchial asthma: a case report. J Med Case Rep **7**: 163, 2013.