EJCRIM
European Journal
of Case Reports
in Internal Medicine

WHIPPLE'S DISEASE COMPLICATED BY SEVERE PULMONARY HYPERTENSION AND RIGHT VENTRICULAR FAILURE

Marwan Joma[1], Abdulrahman M. Karam[1], Bisher Sawaf[1], Wasef Sayeh[2], Waqar Khan[3], Fadi Safi[4], Yaseen Alastal[2]

[1] Department of Internal Medicine, University of Toledo College of Medicine and Life Sciences, Toledo, USA
[2] Division of Gastroenterology, University of Toledo College of Medicine and Life Sciences, Toledo, USA
[3] Department of Pathology, ProMedica Toledo Hospital, Toledo, USA
[4] Division of Pulmonary and Critical Care Medicine, Department of Medicine, The University of Toledo, Toledo, USA

Corresponding author's e-mail: abdulrahman.karam@utoledo.edu

Received: 27/03/2026
Accepted: 03/04/2026
Published: 30/04/2026

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Written informed consent was obtained from the patient for publication and any accompanying images.
This article is licensed under a CC Attribution-NonCommercial-NoDerivatives 4.0 License

How to cite this article: Joma M, Karam AM, Sawaf B, Sayeh W, Khan W, Safi F, Alastal Y. Whipple's disease complicated by severe pulmonary hypertension and right ventricular failure. *EJCRIM* 2026;**13**:doi:10.12890/2026_006600

ABSTRACT

Whipple's disease is a rare, chronic systemic infection caused by *Tropheryma whipplei* that commonly presents with gastrointestinal manifestations but may involve multiple extraintestinal organs. Cardiac involvement, particularly culture-negative endocarditis, is described; however, pulmonary complications such as pulmonary hypertension (PH) are uncommon. We report a case of Whipple's disease presenting with severe pre-capillary pulmonary hypertension and right ventricular (RV) failure with reversibility following antimicrobial therapy. A 62-year-old woman with seropositive rheumatoid arthritis on adalimumab, presented with one month of profuse watery diarrhoea, abdominal pain, dizziness and weakness. Imaging revealed diffuse mesenteric and para-aortic lymphadenopathy. Upper endoscopy demonstrated oedematous whitish granular villi in the duodenum, and biopsies showed periodic acid–Schiff–positive, acid-fast bacillus–negative foamy macrophages diagnostic of Whipple's disease. Transthoracic echocardiography revealed RV dilation and dysfunction with pulmonary hypertension, which was confirmed on right heart catheterisation as severe pre-capillary PH with elevated pulmonary vascular resistance and normal wedge pressure. The patient developed RV-predominant cardiogenic shock requiring inotropic and vasopressor support. Following initiation of intravenous ceftriaxone her haemodynamics improved rapidly, with normalisation of cardiac output and marked reduction in pulmonary pressures on repeat catheterisation. Gastrointestinal symptoms resolved, immunosuppressive therapy was discontinued, and she was discharged on prolonged antimicrobial therapy. This case underscores PH as a rare but potentially reversible manifestation of Whipple's disease. Recognition of this entity is critical, as PH-specific vasodilator therapy alone is often ineffective, whereas early targeted antimicrobial treatment can result in rapid and profound clinical and haemodynamic recovery, even in cases presenting with severe RV failure.

KEYWORDS

Whipple's disease, pulmonary hypertension, ventricular failure

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

LEARNING POINTS

- Whipple's disease should be considered in the differential diagnosis of otherwise unexplained pre-capillary pulmonary hypertension, particularly when accompanied by chronic diarrhoea, arthralgia or systemic features.
- Unlike idiopathic pulmonary arterial hypertension, Whipple's disease-associated pulmonary hypertension is often driven by a reversible inflammatory process and may present with severe right ventricular failure and haemodynamic compromise.
- Recognition of this rare entity is critical, as pulmonary hypertension-specific vasodilator therapy alone is frequently insufficient, whereas timely initiation of targeted antimicrobial treatment can result in rapid and profound clinical and haemodynamic recovery.

INTRODUCTION

Whipple's disease is a rare, chronic systemic infection caused by *Tropheryma whipplei*, a Gram-positive actinomycete first described by George Whipple in 1907[1]. It typically presents with gastrointestinal symptoms such as chronic diarrhoea, steatorrhea, weight loss and malabsorption. However, Whipple's disease can also involve extraintestinal organs including the joints, central nervous system, cardiovascular system and lymphatic tissue[2].

Cardiac manifestations, particularly culture-negative endocarditis, have been increasingly reported[3]. However, pulmonary complications are less commonly recognised. For instance, pulmonary hypertension (PH) linked to Whipple's disease is extremely uncommon, with only a few cases reported. Patients may present with marked right ventricular (RV) dysfunction and severe haemodynamic compromise. The significance of treating the underlying infection is highlighted by the fact that PH-specific vasodilator therapy by itself is frequently ineffective unless combined with targeted antibiotic therapy[4-7].

We report a case of Whipple's disease in a 62-year-old female with severe PH and RV failure. The condition improved dramatically following antimicrobial treatment.

CASE DESCRIPTION

A 62-year-old woman with seropositive rheumatoid arthritis on adalimumab, type 2 diabetes mellitus, paroxysmal atrial flutter and chronic iron-deficiency anaemia presented with one month of watery diarrhoea occurring up to 30 times daily, accompanied by diffuse abdominal pain, dizziness and weakness. She denied fever, haematochezia or recent travel. On admission, blood pressure was 84/60 mmHg, which improved with fluid resuscitation.

Laboratory findings showed leucocytosis (11.4 $\times 10^9$/l), hyponatraemia (131 mmol/l) and elevated troponin (47 to 35 ng/l). An electrocardiogram revealed new anterior T-wave inversions. A computed tomography (CT) of the abdomen and pelvis demonstrated diffuse low-density mesenteric and para-aortic lymphadenopathy without obstruction *(Fig. 1)*.

Given persistent diarrhoea and concern for inflammatory or infectious enteropathy, the patient underwent an esophagogastroduodenoscopy and a colonoscopy. The esophagogastroduodenoscopy revealed oedematous whitish granular villi in the examined duodenum *(Fig. 2A)*; the colonoscopy also showed similar mucosal changes in the terminal ileum *(Fig. 2B)*. A duodenal biopsy showed lamina propria expansion by PAS-positive foamy macrophages, and a terminal ileum biopsy demonstrated diffuse mucosal infiltration by sheets of foamy macrophages, consistent with Whipple's disease *(Fig. 3)*.

Echocardiography revealed a moderately dilated right ventricle with reduced systolic function and moderate PH (estimated RV systolic pressure ≈ 45 mmHg) *(Fig. 4A)*. Right heart catheterisation confirmed severe pre-capillary PH (mean pulmonary artery pressure 33 mmHg, wedge 10 mmHg, pulmonary vascular resistance 5.17 Wood units). The patient subsequently developed RV-predominant cardiogenic shock requiring milrinone, vasopressin and inhaled epoprostenol. After initiation of intravenous ceftriaxone, her haemodynamics gradually improved. Repeat catheterisation 10 days later demonstrated near-

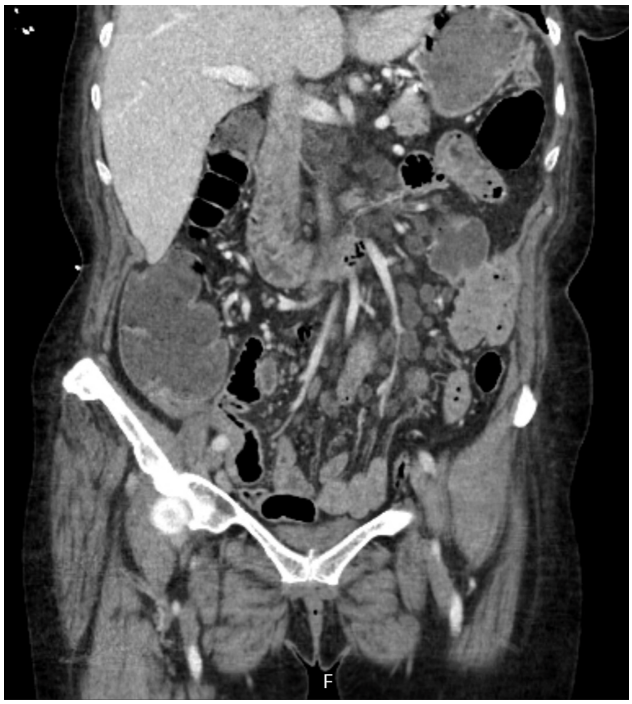


Figure 1. *CT of abdomen and pelvis demonstrating diffuse low-density mesenteric and para-aortic lymphadenopathy.*

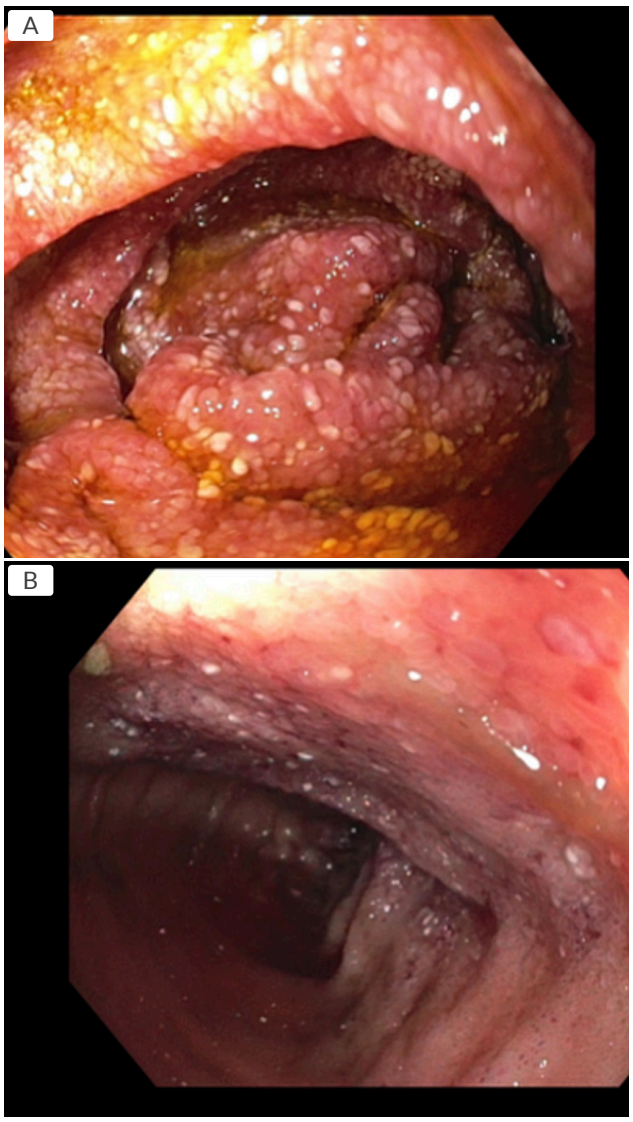


Figure 2. A) Esophagogastroduodenoscopy showing oedematous whitish granular villi in the duodenum; B) Colonoscopy demonstrating similar mucosal changes in the terminal ileum.

normal filling pressures and cardiac output with only mild residual PH *(Fig. 4B)*. Her diarrhoea and abdominal pain resolved, and adalimumab was discontinued. She was discharged on ceftriaxone with plans to transition to oral doxycycline plus hydroxychloroquine for 12–18 months.

DISCUSSION

Whipple's disease (WD) is a rare systemic infection caused by *Tropheryma whipplei*, most often presenting with chronic diarrhoea, abdominal pain, weight loss and arthralgia. Although gastrointestinal manifestations predominate, extraintestinal involvement including cardiac, neurologic and lymphatic disease is well documented[8]. PH, however, remains exceptionally uncommon with fewer than 20 reported cases in the literature.

Across reported cases, patients vary widely in age and presenting symptoms[4-14]. Many experience months of gastrointestinal or rheumatologic complaints before developing dyspnoea or right-sided heart failure[5,7,10]. In some patients, PH precedes the diagnosis of WD whereas in others, gastrointestinal or systemic symptoms prompt the diagnostic evaluation leading to biopsy confirmation[8]. Duodenal biopsy showing PAS-positive foamy macrophages remains the diagnostic gold standard[8].

A consistent feature among modern WD-associated PH cases is severe, predominantly pre-capillary pulmonary hypertension characterised by elevated pulmonary vascular resistance and RV dysfunction. Proposed pathophysiologic mechanisms include inflammatory injury to the pulmonary endothelium, macrophage infiltration and cytokine-mediated vasoconstriction. In several reports, *Tropheryma whipplei* DNA has been identified within pulmonary vascular tissue, suggesting a direct infectious component. Importantly, unlike idiopathic pulmonary arterial hypertension, WD-related PH is typically reversible once appropriate antimicrobial therapy is initiated.

Our patient demonstrated this reversible inflammatory phenotype. She presented with marked RV dilation and dysfunction, elevated pulmonary pressures and reduced cardiac output. Initial haemodynamics showed a mean pulmonary artery pressure of 33 mmHg, wedge pressure of 10 mmHg and pulmonary vascular resistance of 5.17 Wood units. A repeat study demonstrated a mean pulmonary

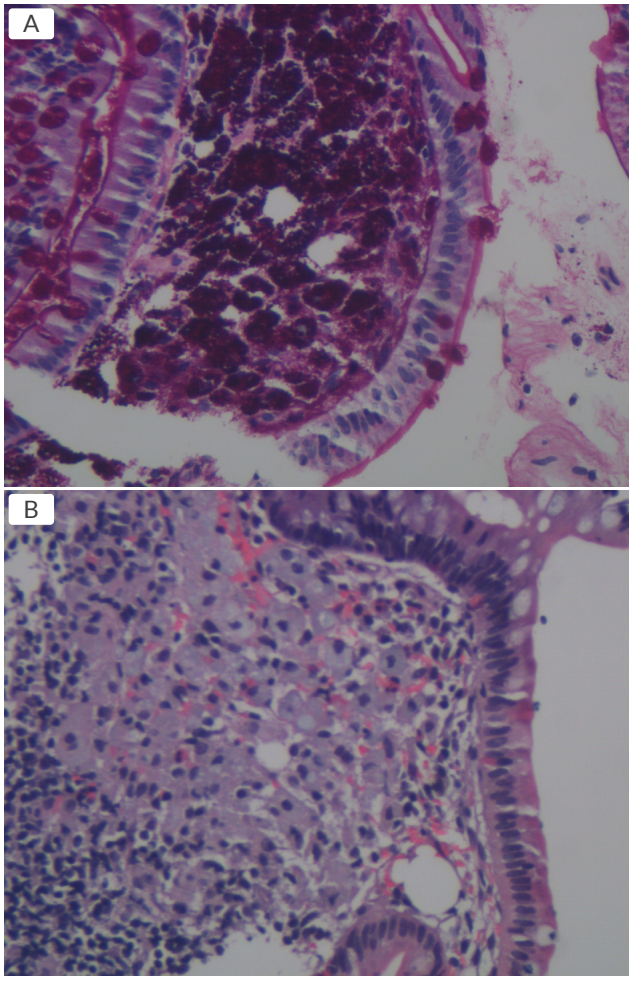


Figure 3. A) Duodenal biopsy showing lamina propria expansion by PAS-positive foamy macrophages; B) Terminal ileum biopsy demonstrating diffuse mucosal infiltration by sheets of foamy macrophages.

Study	Age	Sex	Condition diagnosed first	PH timing relative to WD	Disease progression timeline	Initial antibiotic regimen	Follow-up oral regimen	WD treatment response	PH response
Lyle et al.[7]	54	M	WD (diagnosed after long symptoms)	Present before treatment	One year symptoms; PH resolved 9 months into therapy	Ceftriaxone IV × 2 weeks	TMP-SMX × 1 year	Not detailed	Complete resolution of PH and TR
Jutant et al.[13] – Patient 1	54	M	WD symptoms first	Developed before treatment	Improved after one year	Broad-spectrum IV antibiotics	Doxycycline + hydroxychloroquine	Rapid improvement	Complete recovery
Jutant et al.[13] – Patient 2	59	M	WD symptoms first	Developed before treatment	Rapid deterioration, death within 24 h	Broad-spectrum IV antibiotics	None (died before oral therapy)	No improvement	Fatal outcome
Hoskote et al.[9]	45	F	Whipple's disease	Present at WD diagnosis	Not reported	Ceftriaxone IV × 6 weeks	TMP-SMX × 1 year	Clinical, endoscopic, histologic improvement	Complete resolution of PH
Peschard et al.[10]	57	F	Whipple's disease	Developed before treatment	5-year course	TMP-SMX (initial regimen)	Not reported	Histologic remission	Rapid PH resolution
Zahra et al.[11]	43	F	Initially misdiagnosed as sarcoidosis, then PH, then WD	PH developed before WD treatment	12-month improvement timeline	Ceftriaxone IV × 2 weeks	Co-trimoxazole × 12 months	GI symptoms resolved, weight gain	PASP reduced from 80 to 42 mmHg (partial improvement)
Camboulive et al.[8]	Not reported	M	WD and PH diagnosed concomitantly	Concurrent with WD	Not reported	IV antibiotics (not specified)	Doxycycline + hydroxychloroquine × 1 year	Rapid improvement	Complete haemodynamic reversal
Villa et al.[4]	72	F	Whipple's disease	PH detected after admission, before therapy	PH resolved by day 40 of therapy	Ceftriaxone IV × 14 days	TMP-SMX orally twice daily	Rapid improvement	PASP 95 → 29 mmHg (complete reversal)
Riemer et al.[12]	58	M	Whipple's disease (systemic WD)	Present at diagnosis	PH resolved over 3 months	Penicillin G + gentamicin × 10 days	TMP-SMX × 1 year	Complete symptomatic resolution	Complete PH resolution
Morrison et al.[6]	49	M	Whipple's disease (diagnosed years earlier)	PH developed ~14–18 years after initial WD diagnosis	WD diagnosed 1963; intermittent relapses; PH progressed 1981–83 despite WD remission	Tetracycline courses; later penicillin; brief TMP-SMX (stopped for eosinophilia)	Penicillin maintenance; PH managed with nifedipine + oxygen	Histologic remission; WD controlled	Significant but partial hemodynamic improvement with vasodilator therapy; PH not antibiotic-responsive
Najm et al.[14]	23	M	Initially presumed sarcoidosis, later confirmed WD	PH concurrent with active WD flare	Severe PH at presentation; deterioration on vasodilators; major improvement after WD therapy; 1-year follow-up RHC improved	Ceftriaxone 2 g/day IV × 4 weeks	TMP-SMX 160/800 mg daily + rifampin 300 mg BID × 1 year	Dramatic systemic improvement (GI, ocular, lymphatic); inflammatory markers normalised	PAP 102/47/66 → 45/15/27 mmHg; PVR 11 → 3.2 WU; RV function normalised; vasodilators discontinued
Baloira et al.[5] – case 1	72	M	GI symptoms first	PH during WD symptoms	8 months GI sx → 4 months dyspnoea	Ceftriaxone IV × 4 weeks	TMP-SMX × 1 year	Complete resolution	PH normalised by 10 months
Baloira et al.[5] – case 2	66	M	Musculoskeletal first	PH before WD diagnosis	1 year arthralgia, 2 months diarrhoea	Ceftriaxone IV × 2 weeks	TMP-SMX × 1 year	Rapid improvement	sPAP 112→41 mmHg at 6 months

Table 1. *Literature review – summary of published cases of WD-associated PH.*

Abbreviations: GI sx, gastrointestinal symptoms; PAP, pulmonary artery pressure; PASP, pulmonary artery systolic pressure; PVR, pulmonary vascular resistance; sPAP, systolic pulmonary artery pressure; TMP-SMX, trimethoprim/sulfamethoxazole; PH, pulmonary hypertension.

© EFIM 2026 - European Journal of Case Reports in Internal Medicine - Doi: 10.12890/2026_006600

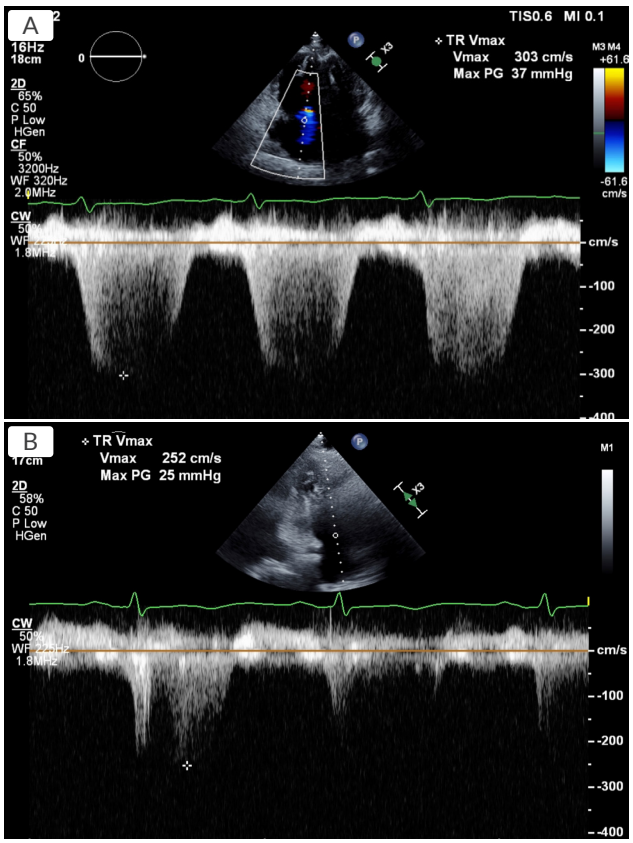


Figure 4. A) Transthoracic echocardiogram showing RV dilation and dysfunction with elevated estimated RV systolic pressure; B) Haemodynamic improvement on repeat right heart catheterisation following antimicrobial therapy.

artery pressure of 31 mmHg, elevated pulmonary vascular resistance and markedly reduced mixed venous saturation. Following initiation of intravenous ceftriaxone, her condition improved rapidly. Subsequent catheterisation demonstrated near-normal filling pressures, only mild residual PH and normalisation of cardiac output and cardiac index. This clinical trajectory mirrors the outcomes described in other published WD-PH cases, further emphasising the importance of early antibiotic therapy.

Table 1 summarises published cases of WD-associated PH and highlights the consistent reversibility of haemodynamic compromise when antimicrobial therapy is administered promptly. These observations underscore several important points: clinicians should consider WD in cases of unexplained PH, particularly when accompanied by chronic diarrhoea, arthralgia or mesenteric lymphadenopathy; early endoscopic evaluation with duodenal biopsy is crucial; and timely initiation of antibiotics is essential to optimise outcomes.

CONCLUSION

PH associated with WD represents a rare but potentially reversible manifestation of systemic infection. This case highlights the importance of recognising WD as a cause of unexplained PH, particularly when accompanied by chronic diarrhoea or rheumatologic symptoms. Early diagnosis through duodenal biopsy and prompt initiation of targeted antimicrobial therapy can lead to rapid haemodynamic and clinical improvement, even in cases presenting with severe RV failure. Multidisciplinary evaluation involving gastroenterology, cardiology, pulmonology and infectious diseases is essential to ensure timely diagnosis and optimal outcomes.

REFERENCES

1. Whipple GH. A hitherto undescribed disease characterized anatomically by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues. *Bull Johns Hopkins Hosp* 1907;18:382–393.
2. Marth T, Raoult D. Whipple's disease. *Lancet* 2003;**361**:239-246. doi: 10.1016/S0140-6736(03)12274-X
3. Geissdörfer W, Moos V, Moter A, Loddenkemper C, Jansen A, Tandler R, et al. High frequency of Tropheryma whipplei in culture-negative endocarditis. *J Clin Microbiol* 2012;**50**:216–222. doi: 10.1128/JCM.05531-11
4. Villa A, Nucera G, Kostihova A, Mazzola A, Marino P. Reversible pulmonary hypertension associated with Whipple's disease. *Case Rep Pulmonol* 2012;**2012**:382460. doi: 10.1155/2012/382460
5. Baloira A, Núñez M, Tumbeiro M, Parente-Lamelas I, Bastos M, Gutiérrez M. Pulmonary hypertension associated with Whipple disease. *Eur Respir Rev* 2014;**23**:533–536. doi: 10.1183/09059180.00005714
6. Morrison DA, Gay RG, Feldshon D, Sampliner RE. Severe pulmonary hypertension in a patient with Whipple's disease. *Am J Med* 1985;**79**:263–267. doi: 10.1016/0002-9343(85)90020-8
7. Lyle PL, Weber RD, Bogarin J, Kircher T. Reversible pulmonary hypertension in Whipple disease: a case report with clinicopathological implications and literature review. *BMJ Case Rep* 2009;**2009**:bcr06.2008.0095. doi: 10.1136/bcr.06.2008.0095
8. Camboulive A, Jutant EM, Savale L, Jaïs X, Sitbon O, Mussini C, et al. Reversible pulmonary hypertension associated with multivisceral Whipple's disease. *Eur Respir J* 2021;**57**:2003132. doi: 10.1183/13993003.03132-2020
9. Hoskote SS, Georgescu A, Ganjhu L, Zeizafoun N, Polsky B. Resolution of Whipple disease-induced pulmonary hypertension following antibiotic therapy. *Am J Ther* 2014;**21**:e143-e147. doi: 10.1097/MJT.0b013e3182691cdc
10. Peschard S, Brinkane A, Bergheul S, Crickx L, Gaudin B, Morcelet M, et al. Maladie de Whipple associée à une hypertension artérielle pulmonaire. Réaction de Jarisch-Herxheimer après antibiothérapie [Whipple disease associated with pulmonary arterial hypertension. Jarisch-Herxheimer reaction after antibiotic therapy]. *Presse Med* 2001;**30**:1549–1551. French.
11. Zahra SA, McCabe C, Price L, Brown MM, Nashat H, Wort SJ. 7-043 Pulmonary hypertension and Whipple's disease: a diagnostic challenge. *Heart* 2025;**111**:A240–A241. doi: 10.1136/heartjnl-2025-BCS.234
12. Riemer H, Hainz R, Stain C, Dekan G, Feldner-Busztin M, Schenk P, et al. Severe pulmonary hypertension reversed by antibiotics in a patient with Whipple's disease. *Thorax* 1997;**52**:1014–1015. doi: 10.1136/thx.52.11.1014.
13. Jutant EM, Roche A, Boucly A, Camboulive A, Jevnikar M, Jaïs X, et al. Whipple's disease: a rare and life-threatening cause of pulmonary hypertension. *Eur Respir J* 2021;**58**:PA3599. doi: 10.1183/13993003.congress-2021.PA3599
14. Najm S, Hajjar J, Nelson RP Jr, Moorthy RS, Wolf KM, Lahm T. Whipple's disease-associated pulmonary hypertension with positive vasodilator response despite severe hemodynamic derangements. *Can Respir J* 2011;**18**(5):e70–e72. doi: 10.1155/2011/365645