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Whipple's Disease in a 61-Year-Old Patient. Clinical Follow-Up

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Aim: to present a clinical observation of a patient with Whipple's disease, demonstrating the difficulties in diagnosing the disease.
Key points. A clinical observation of Whipple's disease in a 61-year-old man is described. The onset of the disease was manifested as polyarthritis three years before diagnosis. The further course of the disease occurred during the pandemic of a new coronavirus infection COVID-19, which made the diagnostic search difficult. Clinical manifestations of fever, arthralgias, diarrhea, lymphadenopathy, anaemia and weight loss raised suspicion of Whipple's disease. Key to the diagnosis were endoscopic studies with multiple small bowel biopsies, which allowed histological identification of PAS-positive macrophages in the small bowel mucosa. Therapy with ceftriaxone for 14 days, therapy with trimethoprim-sulfamethoxazole (160 mg/800 mg twice a day) for 14 months resulted in positive clinical dynamics, improvement of laboratory parameters, disappearance of PAS-positive macrophages in the small intestinal mucosa, indicating remission of the disease.
Keywords: Whipple's disease, PAS-positive macrophages, lymphadenopathy, joint syndrome, diarrhea, anaemia
Conflict of interest: the authors declare no conflict of interest.

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Болезнь Уиппла у пациента в возрасте 61 года. Клиническое наблюдение

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Цель: представить клиническое наблюдение пациента с болезнью Уиппла, демонстрирующее сложности диагностики заболевания.
Основные положения. Описано клиническое наблюдение болезни Уиппла у мужчины в возрасте 61 года. Дебют заболевания проявился по типу полиартрита за 3 года до установления диагноза. Дальнейшее течение заболевания происходило в период пандемии новой коронавирусной инфекции COVID-19, что затруднило диагностический поиск. Клинические проявления в виде лихорадки, суставного синдрома, диареи, лимфаденопатии, анемии и снижения массы тела позволили заподозрить болезнь Уиппла. Ключевым моментом для диагноза явились эндоскопические исследования с множественной биопсией тонкой кишки, что позволило гистологически выявить PAS-положительные макрофаги в слизистой оболочке тонкой кишки. Терапия цефтриаксоном на протяжении 14 дней, терапия триметоприм-сульфаметоксазолом (160 мг/800 мг 2 раза в день) на протяжении 14 месяцев привели к положительной клинической динамике, улучшению лабораторных показателей, исчезновению PAS-положительных макрофагов в слизистой оболочке тонкой кишки, что свидетельствует о ремиссии заболевания.
Ключевые слова: болезнь Уиппла, PAS-положительные макрофаги, лимфаденопатия, суставной синдром, диарея, анемия
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Whipple's disease is a rare systemic infectious disease with a chronic course caused by the Gram-positive bacterium *Tropheryma whipplei* (*T. whipplei*; Greek: *trope* — food, *eryma* — barrier) [1, 2]. Primary infection with *T. whipplei* occurs in childhood, asymptomatically or in the clinic with gastroenteritis, pneumonia, with further clearance of the pathogen [3, 4]. Human-to-human or nosocomial transmission has not been reported [5]. According to a study performed in Italy in 2015, the prevalence of Whipple's disease was estimated at 3 cases per 1 million population, with 30 % being female [6]. More recent data suggest an increasing incidence of Whipple's disease worldwide, with an incidence of 1 to 6 new cases per 10 million population.

The pathogenesis of Whipple's disease is based on the blockage of the lymphatic apparatus of the mucosa, the lymphatic vessels of the mesentery and the lymph nodes of the small intestine by PAS-positive macrophages. As a result, the functional activity of macrophages is disturbed. In the absence of the production of specific antibodies by macrophages to the presence of foreign bacteria, the latter begin to proliferate actively, leading to the development of a massive cellular infiltrate that subsequently blocks lymphatic drainage and disrupts fat transport. Furthermore, *T. whipplei* spreads from the lymph nodes to the synovial membranes, pleura, pericardium and brain, contributing to the gradual progression of the disease and the duration of the pathological process [7, 8]. Classically, Whipple's disease is characterised by the development of migratory arthralgia (73–80 %), chronic digestive disorders with diarrhea (72–81 %), abdominal pain (23–60 %), weight loss (79–93 %), lymphadenopathy (35–66 %), hypoalbuminemia, anaemia [9].

However, other more common forms of *T. whipplei* infection have recently been recognised, including localised forms that affect heart valves or the central nervous system without intestinal symptoms, and asymptomatic forms that occur in about 4 % of Europeans [10].

In the early stages, the first sign of classic Whipple's disease in 80–90 % of cases is seronegative arthritis and/or arthralgia, often with fever, elevation of acute phase proteins [11]. In the second stage, in the period of the developed clinical picture, the small intestine is affected with the appearance of a gastrointestinal syndrome accompanied by diarrhea, weight loss and metabolic disorders. In most cases, there is an increase in lymph nodes and skin manifestations such as hemorrhages and erythema nodosum. The third stage is characterised by cachexia and symptoms of central nervous system, respiratory, cardiac and ocular damage. The diagnosis is more often made by morphological examination of the small intestine, less often by polymerase chain reaction. It should be stressed that the presence of arthralgia, weight loss and diarrhea in a middle-aged man suggests Whipple's disease [12].

The earliest and very often the only (in 75 % of cases) sign of Whipple's disease is a joint syndrome, which precedes the clinical picture of the disease by an average of 6.7 years. The difficulty in the timely diagnosis of Whipple's disease is due to the multisystem involvement of organs and, consequently, the variability of the clinical syndromes. More than 2000 clinical cases of Whipple's disease have been reported in the world literature, reflecting both lesions of different organs and variants of different disease courses. In 2013. E. Maresi et al. published a review of 1000 clinical observations from 1957 to 2012 [13].

A team of authors involved in the diagnosis and treatment of Whipple's disease in Marseille (Centre National de R f rence Rickettsia, Coxiella, Bartonella) systematised the data and published them in clinical reviews [9, 14].

Data on 191 patients with Whipple's disease with a classic clinical picture were presented in a published review by U. Gunther et al. [15]. Experience in the treatment of patients with Whipple's disease has been accumulated at the Central Research Institute of Gastroenterology since 1987. The expansion of diagnostic methods for Whipple's disease has contributed to an increase in the number of clinical reports from different centers [16, 17]. The global medical community continues to gain experience in the diagnosis and treatment of Whipple's disease [18–22].

Patient K., 61 years old, Russian, native of Kirov Region, by profession — woodworker in a cottage workshop, admitted to Kirov Regional Clinical Hospital on July 12, 2022 with complaints of increased body temperature up to 37–38 °C, weakness, pain in joints accompanied by swelling and redness, stiffness of the body at the beginning of movements, swelling of the legs up to the middle third of the shins, nausea, loss of appetite, decrease in body weight by more than 20 kg during the last year, loose stools up to 5–6, sometimes up to 10 or more times a day, watery, without pathological impurities.

From the medical history: the patient considered himself ill since April 2019, when he began noticing periodic pains in the knees, ankles, joints of the hands, accompanied by swelling, hyperemia, which were not treated. In September 2019, he consulted the district GP and was diagnosed with polyarthritis. The blood test (September 17, 2019) revealed acceleration of ESR up to 75 mm/h,

increase in the level of C-reactive protein up to 40 mg/L. The patient was referred to a rheumatologist consultation to clarify the genesis of the existing changes and to clarify the diagnosis. Rheumatologist consultation on September 23, 2019: no data suggesting the presence of rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus. It was recommended to continue the examination to exclude pathology of the organs of the gastrointestinal tract. On October 28, 2019, first esophagogastroduodenoscopy (EGDS) was performed (conclusion — erythematous gastropathy).

A colonoscopy was performed on October 30, 2019, showing no pathology. According to the results of MRI of the abdominal cavity made on November 25, 2019, mesenteric lymphadenopathy was detected for the first time. Radiological examination of thoracic organs dated December 12, 2019 — without pathology; the phthisiologist did not reveal any data in favour of the diagnosis of tuberculosis. HIV, hepatitis B and C viruses were excluded. Further screening was suspended due to the pandemic of a new coronavirus infection COVID-19.

In the period from January 2020 to September 2021, the patient's condition worsened, with increasing weakness, fatigue, decreased tolerance to physical exertion, anxiety, and a decrease in body weight of more than 20 kg; he did not seek medical help and was not treated. In October 2021, against the background of a sharp deterioration of the condition accompanied by an increase in body temperature to 37–38 °C, increasing weakness, loss of appetite, nausea, pain in the joints accompanied by swelling and redness, stiffness in the body at the beginning of movements, periodic swelling of the legs up to the middle third of the shins, frequent unformed stools up to 4–5 times a day, the patient continued the examination again.

On November 28, 2021, chest CT scan revealed right-sided interstitial pneumonia, 8 % lung lesions. With confirmed COVID-19 coronavirus infection complicated by right-sided interstitial pneumonia, the patient was admitted to a specialised hospital, where against the background of therapy (favipiravir, apixaban, glucocorticosteroids, baricitinib, antibiotics) the diarrhea syndrome became more pronounced, stool frequency increased up to 10 times a day. Treatment with vancomycin and metronidazole helped to improve the patient's condition, which was considered antibiotic-associated (*C. difficile*-associated) diarrhea. According to the data of laboratory tests from November 29, 2021: anaemia of mild degree (haemoglobin — 115 g/L, leukocytes — 8.87×10^9/L, ESR — 61 mm/h; bilirubin, ALT, AST — within normal limits, C-reactive protein — 87 mg/L, total protein — 48.1 g/L, rheumatoid factor — normal, HIV, markers of hepatitis B and C — negative. The patient was discharged in satisfactory condition and follow-up with a general practitioner was recommended.

In December 2021, due to the deterioration of the patient's condition (increasing weakness, persistence of the diarrhea syndrome, joint pain), the diagnostic search was continued to clarify the diagnosis. In the blood test from December 23, 2021: increasing anaemia (haemoglobin — 92 g/L), mean corpuscular haemoglobin — 24.4 pg, platelets — 380×10^9/L, leucocytes — 5.49×10^9/L, ESR — 73 mm/h. Biochemical blood test: bilirubin, liver transaminases — normal, serum iron level decreased to 2.0 μmol/L, total protein decreased to 48.1 g/L, C-reactive protein level remained high — 28.4 mg/L (norm — 0–5 mg/L). According to the results of ultrasound of abdominal cavity organs performed on December 20, 2021, expressed lymphadenopathy of abdominal cavity and retroperitoneal lymph nodes was revealed. EGDS (November 24, 2021) showed signs of gastritis. Colonoscopy (December 20, 2021) showed polyps of the descending colon; conclusion of histological examination (December 27, 2021) — hyperplastic polyps of the descending colon. MRI-enterography (December 30, 2021) detected no pathological changes of the small intestine.

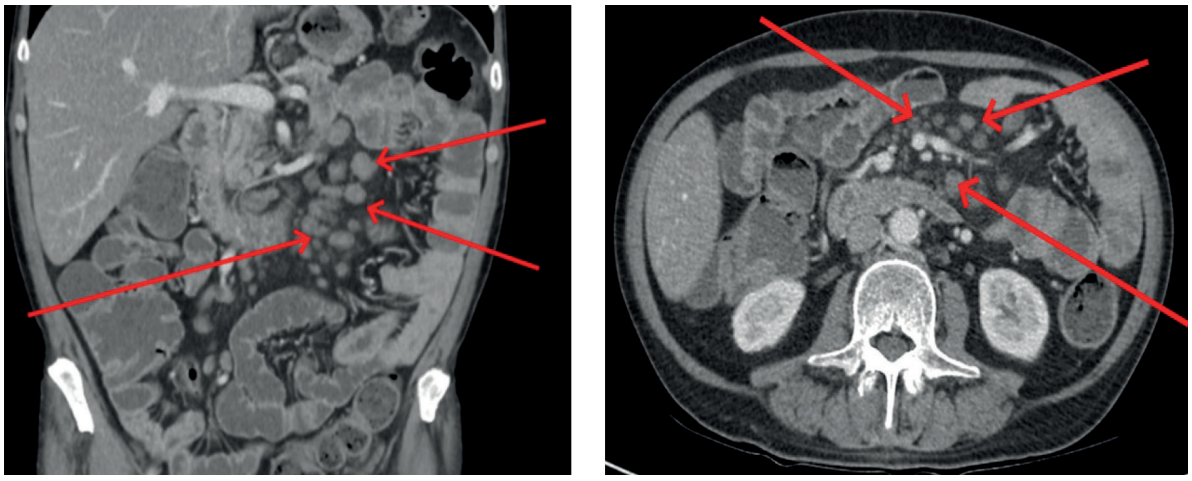
In January 2022, the patient's examination was continued at the Centre of Oncology and Medical Radiology (Kirov), where positron emission tomography (PET-CT) of the whole body (from the occipital bone to the middle third of the thigh) was performed. According to its result, lymphadenopathy of the abdominal cavity and retroperitoneal lymph nodes was detected, there was no evidence of oncological diseases, including neuroendocrine tumours. Laparoscopic puncture biopsy of retroperitoneal lymph nodes was performed in the Department of Surgery, histological examination was performed in the Morphological Laboratory of the Kirov Research Institute of Haematology and Blood Transfusion. Conclusion (February 10, 2022): histological and immunohistochemical picture showed no evidence of lymphoproliferative disease; pathological changes corresponded to granulomatous process/sarcoid reaction (tuberculosis? sarcoidosis?) combined with signs of fatty degeneration. Further examination of the patient was continued in N.N. Blokhin Oncology Centre (Moscow), where another PET-CT was performed on April 5, 2022, which concluded: enlargement of lymph nodes of mediastinum, abdominal cavity, retroperitoneum with metabolic activity. To diagnose malignant tumours of the gastrointestinal tract, markers of gastrointestinal tumours were studied: chromogranin A — 121.48 μg/L (norm — up to 100 μg/L),

serotonin — 505 ng/mL (norm — 50–220 ng/mL), gastrin — 17 pg/mL (norm — 13–115 pg/mL). In the general blood analysis: anaemia increased (haemoglobin — 75 g/L), ESR — 60 mm/h. C-reactive protein — 62.5 mg/L, total protein — 44.6 g/L, albumin — 26.8 g/L. The patient was discharged due to exclusion of oncological nature of symptoms. Two weeks after discharge from the Oncology Centre on May 10, 2022, due to progressive deterioration of the condition (increasing weakness, periodic increase in body temperature up to 37–38 °C, joint pains, diarrhea, decrease in body weight by 20 kg over the last year) the patient was admitted to the therapeutic department of Kirov City Hospital No. 7 for treatment of enteritis of unspecified etiology. The examination was continued. In the general blood analysis dated May 10, 2022: anaemia (haemoglobin — 75 g/L), thrombocytosis (411 × 10^9/L), ESR — 55 mm/h. There was found an increase of C-reactive protein level up to 62.5 mg/L; AST, ALT, bilirubin, creatinine, urea — normal; potassium decreased to 2.8 mmol/L (norm — 3.5–5.1 mmol/L), total protein — to 44.6 g/L, albumin — to 26.5 g/L. Based on the course of treatment (enzymes, metronidazole, vancomycin, albumin) the patient was discharged on May 20, 2022, and less than a month later (June 06, 2022) he was again hospitalised in the Therapy Department of the Kirov City Hospital No. 7 without improvement of condition and without dynamics of general and biochemical parameters of blood analysis. On July 12, 2022, the patient was admitted to the Gastroenterological Department of the Kirov Regional Clinical Hospital for clarification of the diagnosis, examination and decision on repeated intra-abdominal lymph node sampling for histological examination. At the time of admission, the patient's general condition was average. Consciousness was clear. Posture was active. Physique was normosthenic. The skin was pale and dry. Turgor was reduced. Subcutaneous adipose tissue was moderately developed, BMI — 20.3 kg/m^2 (weight — 60 kg, height — 172 cm). Peripheral oedema in the lower third of the lower legs. Enlarged cervical, axillary and inguinal lymph nodes up to 1–1.5 cm were palpable. The thyroid was not enlarged. The thorax was regular in shape. Both halves participated equally in the act of breathing. There was vesicular breathing in the lungs, no wheezing, the respiratory rate was 18 per minute. The boundaries of the heart were not expanded. Heart sounds were clear and rhythmic. Heart rate — 82 per minute. Blood pressure — 95/60 mmHg. Pulse — 82 per minute, rhythmic, normal filling and tone. The abdomen was of normal shape, soft, painless on palpation. The liver was not enlarged, dimensions according to Kurlov: 9 × 8 × 7 cm. The spleen was not palpable. Pasternatsky's symptom was negative on both sides.

Total protein decreased to 57.3 g/L, albumin — to 24.2 g/L; C-reactive protein increased to 82.25 mg/L. Altered electrolyte balance was noted: hypokalemia (K — 3.41 mmol/L; norm — 3.5–5.1 mmol/L), hypocalcemia (ionised Ca — 1.08 mmol/L; norm — 1.13–1.32 mmol/L), increased level of chlorine (Cl — 110.3 mmol/L; norm — 98–106 mmol/L), normal sodium level — 139.8 mmol/L. Antibodies to tissue transglutaminase IgG, to deaminated gliadin peptides IgG, to endomysium — negative. The diagnostic search was continued to exclude lymphoproliferative and infectious diseases. Coombs test (direct, indirect) — negative. Antibodies to HIV-1, HIV-2, antibodies to *Treponema pallidum*, Vidal's reaction (antibodies to paratyphoid A and B, typhoid), markers of viral hepatitis — negative results. Stool elastase 100 mcg/g; coprogram — neutral fat ++. Stool culture for *C. difficile* —no growth detected. Stool culture for group of pathogenic microorganisms — no growth of anaerobic flora detected. A CT scan of the chest, abdominal cavity and retroperitoneal space was performed on July 7, 2022. In the lungs there was diffuse thickening of the intralobular interstitium, small foci along the interlobular pleura. The heart was not enlarged. The cranio-caudal size of the liver — 200 mm, the density of the parenchyma — 14–18 HU. The bile ducts were not dilated. The gallbladder was not enlarged. Pancreas: head — 20 mm, body — 19 mm, tail — 15 mm. Wirsung duct — up to 1 mm. Spleen — 73 × 54 × 81 mm. The walls of the large and small intestine were not dilated. Aorta — not dilated. Paraaortic lymph nodes — up to 16 mm in cross section. Several mesenteric lymph nodes — up to 15 mm. Conclusion: interstitial focal changes in the lungs; diffuse changes in the liver; transperitoneal and mesenteric lymphadenopathy (Fig. 1).

Video colonoscopy on July 14, 2022: the terminal parts of the ileum (about 15.0 cm) were examined — the mucosa was friable, diffusely brightly hyperemic, vascular pattern was not visible, pitting white plaque was considered as a sign of enteritis (Fig. 2). Bauhin's valve was rosette-shaped, closed, unchanged. Colonic walls were elastic, tone was preserved, mucosa with smeared vascular pattern. Biopsies were taken from the small and large intestine.

EGD dated July 13, 2022, concluded: esophagus was passable, cardia is closed; stomach walls were elastic, folds of medium height; pylorus was round, closed; duodenal mucosa was loose, hyperemic, with white plaque. A biopsy was taken from the duodenum (Fig. 3).



A B

Figure 1. CT of the chest, abdomen and retroperitoneum: retroperitoneal (A) and mesenteric (B) lymphadenopathy (arrows)

Рисунок 1. КТ органов грудной клетки, брюшной полости и забрюшинного пространства: забрюшинная (A) и мезентериальная (B) лимфаденопатия (стрелки)

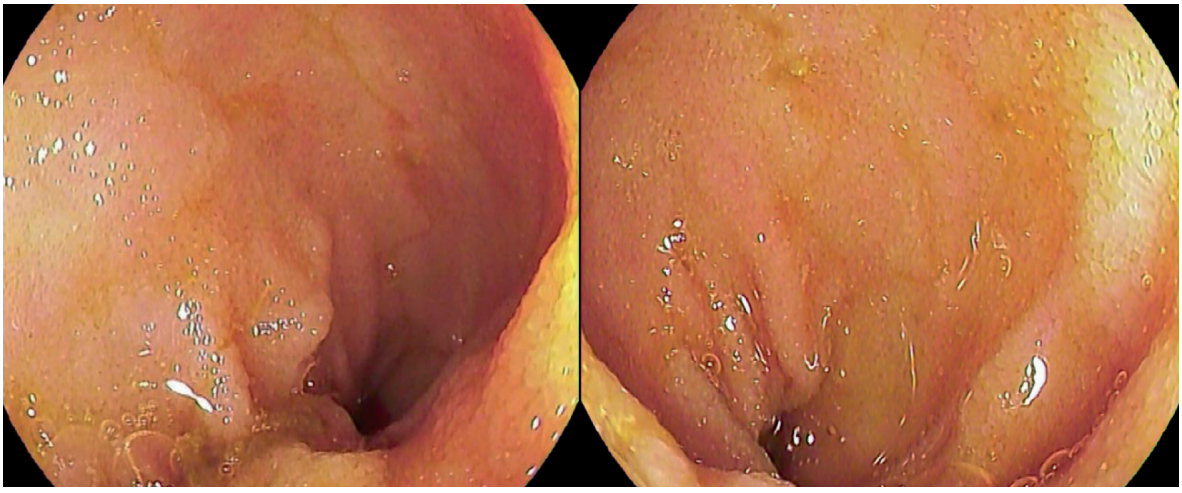


Figure 2. Endoscopic view of the ileum mucosa

Рисунок 2. Эндоскопическая картина слизистой оболочки подвздошной кишки

The results of a histological examination of the duodenal mucosa demonstrated a change in histoarchitectonics due to deformation of the villi, accumulation of foamy macrophages between the crypts and in the stroma, and the presence of a large number of PAS-positive microorganisms in the cytoplasm of macrophages, which indicates Whipple's disease (Fig. 4).

On July 19, 2022, a biopsy of two whole lymph nodes of the jejunal mesentery was performed using a LigaSure™ Maryland 5-mm device (Medtronic, Ireland). Histological examination revealed a pronounced macrophage-histiocytic reaction ($CD68^+$, CD163, $HLA\text{-}DR^+$, $CD11c^+$, $Vimentin^+$, $CD45^+$) with cells located in the lumens of dilated sinuses, in the stroma of the lymph node and between connective tissue cords. A significant proportion of macrophages with granular eosinophilic cytoplasm containing foamy inclusions (PAS-positive foamy macrophages and histiocytes in reaction

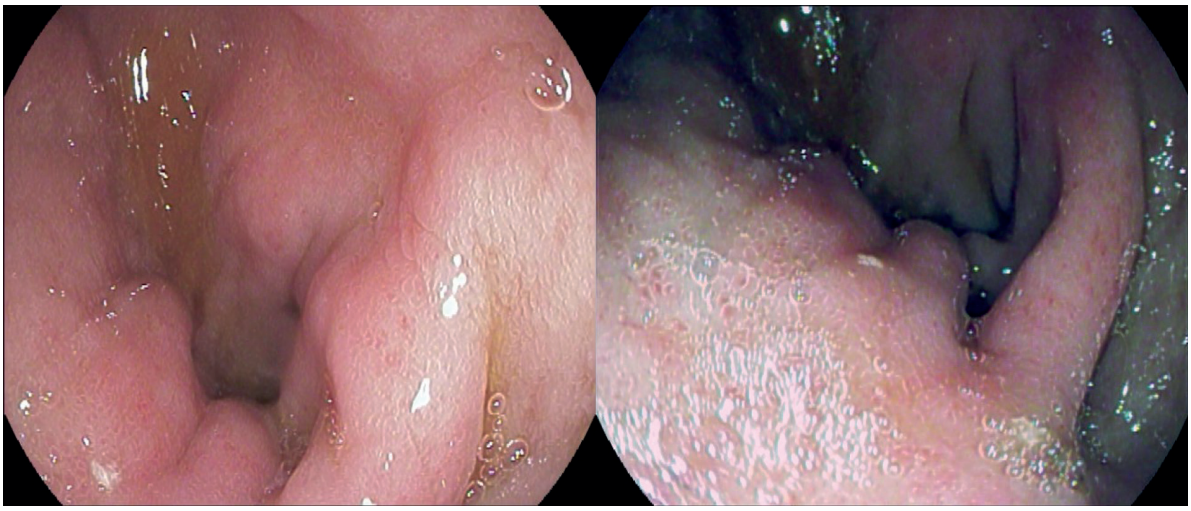
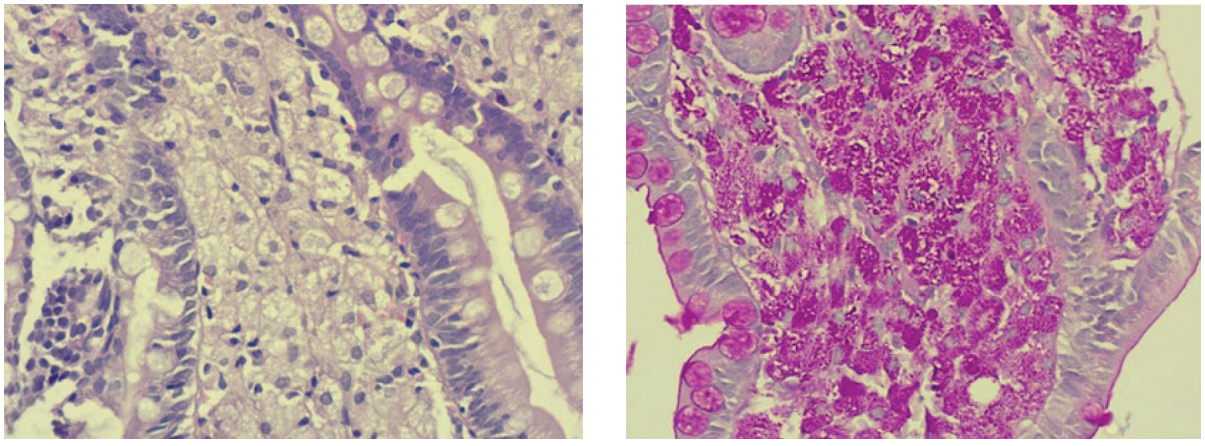


Figure 3. Endoscopic view of the duodenal mucosa

Рисунок 3. Эндоскопическая картина слизистой оболочки двенадцатиперстной кишки

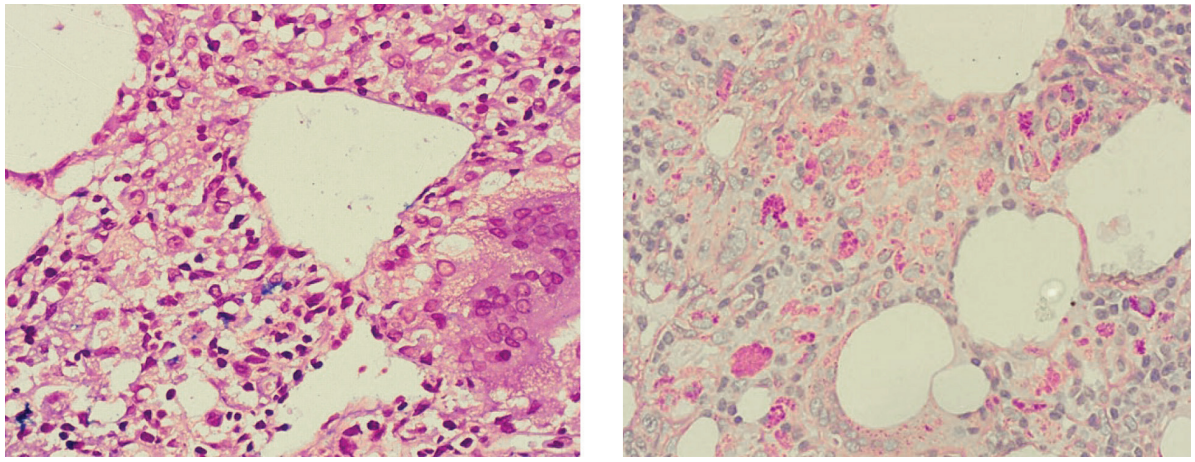


A B

Figure 4. Microscopic specimen of the mucous membrane of the duodenum: A — the histoarchitecture of the mucous membrane is changed due to deformation of the villi, most of which are thickened, expansion of the mucous and submucosal space, lymphangiectasia; between the crypts and in the stroma there are diffuse accumulations of foamy macrophages (×200, hematoxylin and eosin staining); B — in the cytoplasm of macrophages there is a large number of PAS-positive microorganisms (×400, PAS reaction to glycogen)

Рисунок 4. Микропрепарат слизистой оболочки двенадцатиперстной кишки: А — гистоархитектоника слизистой оболочки изменена за счет деформации ворсинок, большая часть которых утолщена, расширение слизистого и подслизистого пространства, лимфангиэктазия; между криптами и в строме диффузные скопления пенистых макрофагов (×200, окраска гематоксилином и эозином); В — в цитоплазме макрофагов большое количество PAS-положительных микроорганизмов (×400, PAS-реакция на гликоген)

to glycogen), small Gram-positive structures/microorganisms with positive PAS reaction, reaction to HLA-DR and Gram were detected in the cytoplasm of the cells. There were multiple lipid depositions (glycogen reaction — positive). Conclusion: no evidence of lymphoproliferative disease. The pathomorphological features were consistent with a granulomatous inflammatory process associated with signs of fatty degeneration typical of Whipple's disease (Fig. 5).



A B

Figure 5. Microscopic picture of the lymph node of the mesentery of the small intestine: A — lymphatic tissue is atrophied, dilated sinuses and accumulations of foamy macrophages are identified (×400, Gram stain); B — in the cytoplasm of macrophages there is a large number of PAS-positive microorganisms (×400, PAS reaction to glycogen)

Рисунок 5. Микроскопическая картина лимфатического узла брыжейки тонкой кишки: А — лимфатическая ткань атрофирована, определяются расширенные синусы и скопления пенистых макрофагов (×400, окраска по Граму); В — в цитоплазме макрофагов большое количество PAS-положительных микроорганизмов (×400, PAS-реакция на гликоген)

The patient was diagnosed with Whipple's disease with enlargement of the retroperitoneal and mesenteric lymph nodes, chronic course. Malabsorption, protein-losing diarrhea with impaired protein metabolism (hypoproteinemia, hypoalbuminemia), electrolyte imbalance. Moderate iron deficiency anaemia. Ceftriaxone 2 g per day intravenously for 14 days, trimethoprim/sulfamethoxazole 160 mg/800 mg per day were added to the current therapy (glucocorticosteroids, albumin, iron preparations, enzymes). The patient's condition began to improve, body temperature normalised, stool became clear, and the patient was discharged from the hospital on August 19, 2022. The patient was and still is monitored by the GP, control visits are once in three months.

Against the background of the improvement of the patient's state of health already noted in the gastroenterology department in August 2022, in the following three months the patient gained weight, the joint syndrome disappeared, the laboratory parameters of blood improved. Control visit on September 5, 2023. The condition was satisfactory, appetite maintained. BMI — 25.7 kg/m^2 (weight — 76 kg, height — 172 cm). General blood test (September 12, 2023): haemoglobin — 137 g/L, ESR — 15 mm/h. C-reactive protein — 2.9 mg/L, total protein — 71.4 g/L, albumin — 38 g/L. Drug therapy (trimethoprim/sulfamethoxazole 160 mg/800 mg daily) was continued until the endoscopic control examination with biopsy.

EGD was performed on November 15, 2023. The esophagus was passable, the mucosa — pink and elastic. The cardia was incompletely closed. Gastric mucosa was slightly swollen, elastic, peristalsis was circular. The mucous membrane of the duodenal bulb was edematous, in the postbulbar parts — pale pink, elastic, finely tufted. A needle biopsy of the duodenal mucosa was performed (Fig. 6).

Histological examination (November 18, 2023): the histological structure was preserved, no phagocytic macrophages were detected; the histoarchitecture was not changed, a few lymphocytes and plasma cells were detected (Fig. 7).

Video colonoscopy was performed on November 15, 2023. The colon was examined along its entire length, the endoscope was passed into the dome of the cecum and the terminal ileum. The ileal mucosa was pink. A biopsy of the mucous membrane of the terminal ileum was performed. The lumen of the examined sections of the colon was not deformed, the folds were pronounced, and the intestinal tone was preserved. The mucous membrane was light pink, elastic, the vascular pattern could be seen in all sections (Fig. 8).

Conclusion

The diagnosis of Whipple's disease in a patient aged 61 years was made during the pandemic of the new coronavirus infection COVID-19, which

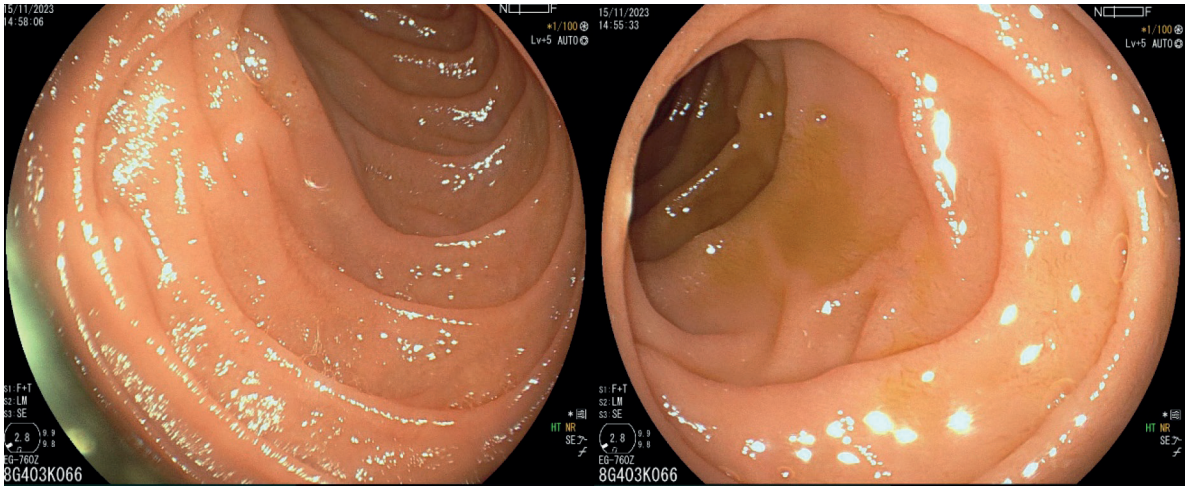
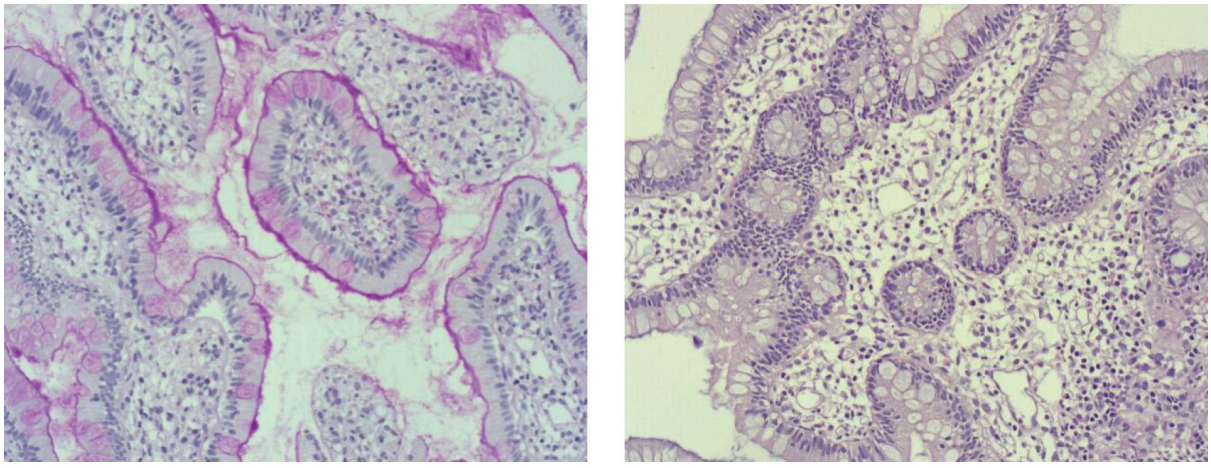


Figure 6. Endoscopic picture of the duodenal mucosa after 14 months of therapy

Рисунок 6. Эндоскопическая картина слизистой оболочки двенадцатиперстной кишки спустя 14 месяцев терапии



A B

Figure 7. Microscopic picture of the duodenal mucosa after 14 months of therapy: A — the histological structure is preserved, no phagocytic macrophages were detected (×200, PAS reaction to glycogen); B — histoarchitecture is not changed, a few lymphocytes and plasma cells are detected in the mucosa (×200, hematoxylin and eosin staining)

Рисунок 7. Микроскопическая картина слизистой оболочки двенадцатиперстной кишки спустя 14 месяцев терапии: А — гистологическая структура сохранена, фагоцитирующих макрофагов не обнаружено (×200, PAS-реакция на гликоген); В — гистоархитектоника не изменена, в слизистой определяются немногочисленные лимфоциты и плазмоциты (×200, окраска гематоксилином и эозином)

is a feature of this observation. The detected coronavirus infection not only aggravated the clinical manifestations and course of the disease, but also complicated the diagnostic search. The key to establishing the diagnosis was endoscopic examination with multiple biopsies of the small intestine, which allowed histological identification of PAS-positive macrophages in the small intestinal mucosa. Therapy with ceftriaxone for 14 days and maintenance therapy with trimethoprim/sulfamethoxazole (160 mg/800 mg 2 times a day) for 14 months led to positive clinical dynamics, improvement in laboratory parameters, and the disappearance of PAS-positive macrophages in the intestine, which indicates remission of the disease.

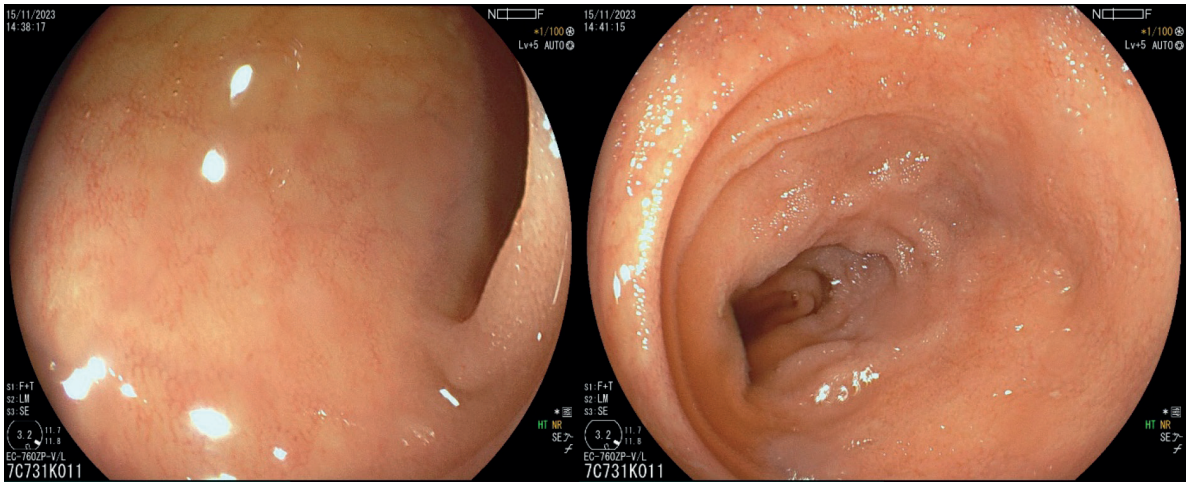


Figure 8. Endoscopic picture of the ileal mucosa after 14 months of therapy

Рисунок 8. Эндоскопическая картина слизистой оболочки подвздошной кишки спустя 14 месяцев терапии

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