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Clinical Case: A Patient with Weakness, Skin Rashes, Increased Transaminase Activity and Bilirubin Levels

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Aim: to increase physicians' awareness of differential diagnosis of autoimmune hepatitis and diffuse connective tissue disease using a clinical case as an example.
Key points. The article describes a clinical observation of a 34-year-old patient with dermatomyositis occurring against the background of atopic dermatitis and Gilbert's syndrome, imitating autoimmune liver disease and complicated by the development of drug-induced liver injury. The complexity of diagnosis was determined by the development of skin lesions against the background of changes already present as a result of the atopic dermatitis, laboratory data (increased transaminase activity, bilirubin levels, and detection of antinuclear and anti-smooth muscle autoantibodies indicating a suspected liver disease), and the disappearance of a number of typical signs of the disease as a result of previously prescribed immunosuppressive therapy. The diagnosis was established through a thorough retrospective analysis of the clinical manifestations and anamnesis of the disease (a change in the nature of skin rashes and the predominance of increased activity of aspartate transaminase were noteworthy); the key moment for making the diagnosis was the detection of increased activity of creatine kinase and myositis-specific antibodies Jo-1. Morphological examination of liver tissue did not find signs of autoimmune hepatitis and liver fibrosis, but revealed centrilobular intracellular cholestasis and lymphohistiocytic infiltration, proliferative changes in the biliary epithelium, probably caused by drug-induced liver injury due to azathioprine intake. The issues of diagnostics and differential diagnosis of autoimmune hepatitis are considered, the strict necessity of morphological examination of the liver for diagnosis is discussed. Secondary liver injury in diffuse connective tissue disease and azathioprine-induced liver injury are analyzed.
Conclusion. Differential diagnosis of elevated serum transaminases should include not only liver disease, but also muscle tissue injury. When diagnosing autoimmune hepatitis, histological examination plays a key role, and verification of the diagnosis is impossible without morphological data.
Keywords: autoimmune liver disease, autoimmune hepatitis, dermatomyositis, polymyositis, liver damage, drug-induced liver injury, azathioprine
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Клиническое наблюдение: пациент со слабостью, кожными высыпаниями, повышением активности трансаминаз и уровня билирубина

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Цель: повысить осведомленность врачей о дифференциальной диагностике аутоиммунного гепатита и диффузных заболеваний соединительной ткани на примере клинического наблюдения.
Основные положения. Описано клиническое наблюдение пациента 34 лет с дерматомиозитом, протекавшим на фоне атопического дерматита и синдрома Жильбера, имитировавшим аутоиммунное заболевание

печени и осложнившимся развитием лекарственного поражения печени. Сложность диагностики определялась развитием поражения кожи на фоне уже имевшихся вследствие атопического процесса изменений, лабораторными данными (повышение активности трансаминаз, уровня билирубина и обнаружение антинуклеарных и антигладкомышечных аутоантител, указывавших на предполагаемое заболевание печени), исчезновением ряда типичных признаков заболевания вследствие ранее назначенной иммуносупрессивной терапии. Диагноз установлен благодаря тщательному ретроспективному анализу клинической картины и анамнеза заболевания (обращало на себя внимание изменение характера кожных высыпаний, мышечная слабость и преобладание повышения активности аспартатаминотрансферазы). Ключевым моментом для постановки диагноза явилось обнаружение повышенной активности креатинкиназы и миозит-специфических антител Jo-1. Морфологическое исследование ткани печени не обнаружило признаков аутоиммунного гепатита и фиброза печени, но выявило центролобулярный внутриклеточный холестаз и лимфогистиоцитарную инфильтрацию, пролиферативные изменения билиарного эпителия, вероятно, обусловленные лекарственным поражением печени вследствие приема азатиоприна. Рассмотрены вопросы диагностики и дифференциальной диагностики аутоиммунного гепатита, обсуждена строгая обязательность морфологического исследования печени для постановки диагноза. Проанализированы вторичные поражения печени при диффузных заболеваниях соединительной ткани и азатиоприн-индуцированное поражение печени.

Заключение. Дифференциальный диагноз при повышении сывороточных трансаминаз должен включать в себя не только заболевания печени, но и патологию мышечной ткани. При постановке диагноза аутоиммунного гепатита гистологическое исследование играет ключевую роль, и верификация диагноза невозможна без морфологических данных.

Ключевые слова: аутоиммунные заболевания печени, аутоиммунный гепатит, дерматомиозит, полимиозит, поражение печени, лекарственное поражение печени, азатиоприн

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Description of the clinical case

Patient M., 34 years old. We have been observing him since March 2024. During the initial examination, he complained of a rash in the back and neck area, accompanied by moderate itching, and moderate general weakness.

Anamnesis morbi. Since childhood, he suffered from atopic dermatitis, periodically received local therapy with topical corticosteroids. Since the age of 20, routine examinations revealed a moderate increase in serum bilirubin to 30 μmol/L (reference interval — 5.0–21.0 μmol/L), mainly due to indirect bilirubin.

In July 2023, after an episode of alcohol consumption, weakness appeared in the proximal muscles of the upper limbs when performing routine physical activity, which at that time was assessed as general weakness. Thus, the patient noted that he could not continue to exercise (push-ups, pull-ups on a horizontal bar), or lift a child in his arms as before. Then, he experienced intense pain in the right gluteal region, swelling in the area of small joints of the hands and feet, accompanied by morning stiffness lasting up to several hours. In August 2023, after intense physical activity, he experienced severe general weakness, an increase in body temperature to 38.6 °C with chills. Febrile fever was observed for a month, general and muscle weakness progressed, limiting daily activity, and diarrhea developed.

In September 2023, he sought medical help. He was examined by a therapist, gastroenterologist, infectious disease specialist, and rheumatologist on an outpatient basis. Clinical blood test showed no significant changes. Blood biochemistry as of August 21, 2023: aspartate aminotransferase (AST) — 346 U/L (upper limit of normal (ULN) — 10.8 times), alanine aminotransferase (ALT) — 196 U/L (6.3 ULN), total bilirubin — 22.6 μmol/L, uric acid — 485.2 μmol/L (reference interval — 142.0–416.0 μmol/L), total cholesterol — 6.0 mmol/L (reference interval — 2.8–5.2 mmol/L), C-reactive protein — 13.2 mg/L (reference interval < 5.0 mg/L), IgG — 15 mg/L (within normal limits). Other laboratory parameters (glucose, creatinine, alkaline phosphatase, gamma-glutamyl transferase, ceruloplasmin, rheumatoid factor, thyroid-stimulating hormone, general urine analysis parameters) are within the normal range. Creatine kinase was not determined during this period. Viral hepatitis markers (HBsAg, anti-HCVAb) were negative. Fecal calprotectin 197 μg/L (normal range < 80.0 μg/L). HLA-B27 antigen was negative. Chest fluorography dated August 21, 2023, showed signs of moderate basal pneumofibrosis. ECG — without clinically significant changes. Gastroscopy and ileocolonoscopy did not reveal any clinically significant changes in the mucous

membrane. Ultrasound of the abdominal organs: heterogeneity of the liver structure, mild splenomegaly, increased echogenicity of the pancreas.

In September 2023, the indirect immunofluorescence revealed antinuclear antibodies with nuclear speckled (AC-2, 4) pattern in a titer of 1:160, and antibodies to smooth muscles in a titer of 1:80. Antibodies to mitochondria, to liver and kidney microsomes type 1 were not detected. A diagnosis of autoimmune hepatitis (AIH) type 1 was established, and prednisolone was recommended at 60 mg/day with a gradual (over 2 months) dose reduction to 10 mg/day, ursodeoxycholic acid at a dose of 750 mg/day. During the treatment, the patient noted an improvement in his general condition, relief of weakness, fever, diarrhea, and joint pain, which was accompanied by normalization of C-reactive protein, a decrease in serum transaminases without their normalization (October 27, 2023: ALT — 1.6 ULN, AST — 1.8 ULN).

In November of the same year, when the dose of prednisolone was reduced, itchy skin rashes appeared in the dorsal surface of the neck, upper half of the back, which were regarded as an exacerbation of atopic dermatitis. However, the patient noted that the rashes had previously been of a different nature. He independently canceled prednisolone, which was accompanied by a resumption of general weakness, joint pain, and muscle weakness. In blood tests on December 9, 2023: an increase in ALT — 2.4 ULN, AST — 8.7 ULN, IgG — 12 mg/L (withing normal limits), C-reactive protein — 6.65 mg/L. In December 2023, prednisolone was resumed at a dose of 30 mg/day, followed by a dose reduction to 10 mg/day, azathioprine 50 mg/day, ursodeoxycholic acid — 500 mg/day, then 750 mg/day were prescribed. With therapy, weakness significantly decreased, a decrease in serum transaminases was noted without their normalization (February 27, 2024: ALT — 1.4 ULN, ACT — 2.5 ULN). In the clinical blood test — eosinophilia (0.53×10^9/L). Shear wave elastometry was performed: liver stiffness is 8.28 kPa (corresponds to moderate fibrosis, F2), spleen — 9.3 kPa.

The peculiarities of the *anamnesis vitae* include the fact that the patient's mother also came to us with complaints of weakness, increased activity of transaminases and alkaline phosphatase for six months. No other significant factors for diagnosis were found in the anamnesis.

Physical examination: the patient's condition was satisfactory, consciousness was clear. The body type was normosthenic, the body mass index was 24.4 kg/m^2. The skin lesion was widespread, polymorphic, and affected the dorsum of the neck, upper back, and the extensor surfaces of the hands and knee joints. On the skin of the neck, it was represented by an extensive lichenification focus against the background of erythema with a cyanotic tint. The focus of congestive erythema was also located on the skin of the shoulder girdle and the interscapular region of the back and had the shape of a triangle (the shawl sign) (Fig. 1). Against the background of erythema there were separate, sometimes grouped lichenoid slightly lilac papules, which gave the lesion an uneven color. Similar foci of lilac erythema were present on the back of the hands and the extensor surface of the knee joints (Gottron sign). The affected and visibly unaffected skin was dry, in places, especially on the back of the neck, covered with scanty bran- and powder like scales. The skin of the palms was characterized by an emphasized skin pattern (deeper creases and higher folds) and focal weakly expressed hyperkeratosis, against the background of which there were a few superficial fissures. There was no edema. The peripheral lymph nodes were not enlarged.

No objective signs of decreased muscle strength were found: manual muscle testing with assessment of eight muscle groups on one side showed 80 points (against the background of ongoing systemic glucocorticoid therapy). Muscle palpation

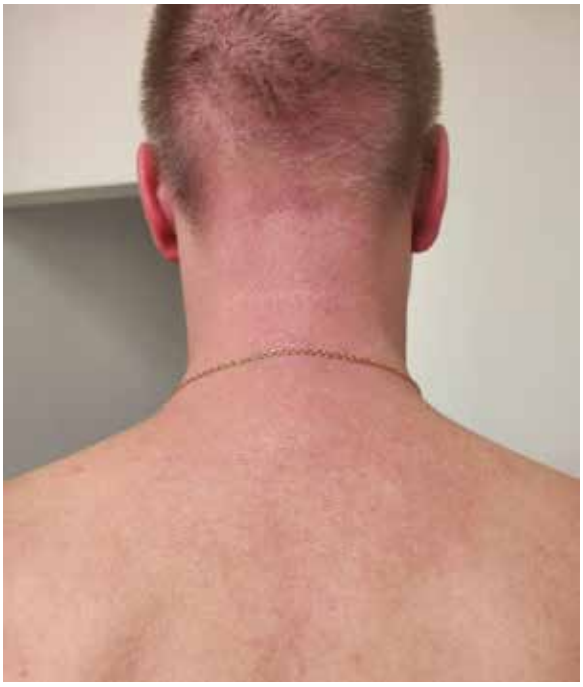

Figure 1. The "shawl" sign in Patient M., 34 years old, with atopic dermatitis

Рисунок 1. Симптом «шали» на фоне атопического дерматита у пациента М., 34 года

was painless. The range of active and passive movements in the joints was preserved, swollen and painful joints were not determined. During auscultation of the lungs — crepitation in the lower thirds of both lung fields (not determined during further observation). The abdomen was soft, painless on palpation. The liver was not enlarged, the edge was elastic, smooth, painless. The spleen was not palpated on percussion from the IX to the XII rib. The tone of the colon was unchanged, palpation was painless. No clinically significant changes were detected on the part of other organs and systems.

Examination data. The presence of skin rashes untypical for atopic dermatitis, muscle weakness and joint syndrome in the anamnesis, the predominance of AST over ALT made us suspect a disease from the group of idiopathic inflammatory myopathies and refer the patient for further examination. An increase in serum creatine kinase of 373 U/L (reference interval — 24–195 U/L) was detected. An enzyme immunoassay revealed antisynthetase antibodies (anti-Jo-1) in the serum over 200 U/mL. A preliminary diagnosis of dermatomyositis/polymyositis was established.

Heredity was clarified: at the same time, we detected primary sclerosing cholangitis with features of AIH in the patient's mother (the diagnosis was established based on cholangiographic and morphological data) as well as Gilbert's syndrome (confirmed by genetic testing).

To finally exclude AIH, a liver biopsy was performed in April 2024 (during this period, ALT and AST remained elevated — less than 2 ULN). Morphological examination revealed minimal manifestations of cholestatic liver damage in the form of intracellular centrilobular cholestasis, mild proliferative changes in the biliary epithelium, mild lymphohistiocytic infiltration of the parenchyma of the centrilobular parts of the liver lobules, and steatosis of less than 5 % of hepatocytes. Periportal "necroinflammatory" activity and signs of fibrosis were absent (Fig. 2).

Further examination was aimed at clarifying the damage to internal organs, differential diagnostics with other connective tissue diseases and selection of therapy. It was decided to refrain from objectifying muscle damage (electromyography, magnetic resonance imaging, biopsy of the skin-muscle flap), since restoration of muscle strength was noted against the background of therapy, and studies during this period would have been uninformative.

The patient was examined by a dermatologist: skin changes were assessed as manifestations of dermatomyositis against the background of atopic dermatitis. Clinical blood test, general urine analysis — without significant changes. According to the biochemical blood test, normalization of transaminases was achieved (ALT — 18.5 U/L, AST — 35.1 U/L); total bilirubin — 47.9 μmol/L (indirect bilirubin — 42.7 μmol/L); creatine kinase — 756 U/L; uric acid — 494 μmol/L; lactate dehydrogenase — 242 U/L (reference interval < 248 U/L); alkaline phosphatase — within normal limits. Serum IgM, IgG, complement components C3 and C4 — within reference intervals. Rheumatoid factor and antibodies to cyclic citrullinated peptide were not detected. X-rays of the hands and feet did not reveal any pathological changes. CT-scan of the chest organs, respiratory function tests, and echocardiography did not reveal any clinically significant changes. Gastroscopy revealed signs of erosive esophagitis stage A (according to the Los Angeles classification), and therefore proton pump inhibitors were prescribed in a standard dose.

Discussion

Dermatologist's opinion. The presence of two itchy dermatoses in a patient undoubtedly presented a significant diagnostic challenge. In addition, the possibility of cholestatic genesis of itching should have been considered in a patient with suspected liver disease.

Atopic dermatitis is a multifactorial genetically determined inflammatory skin disease characterized by itching, chronic relapsing course, age-related features of localization and morphology of lesions. Clinical manifestations of atopic dermatitis vary with age, and in adults the exudative component is usually less pronounced. Atopic dermatitis rashes in adults are more often represented by erythema, papules, scaling, infiltration, lichenification, multiple excoriations and fissures [1]. Such morphological diversity of rashes can significantly mask the skin symptoms of another disease. This patient had a SCORAD (SCORing Atopic Dermatitis) index of 35, which corresponded to moderate severity of atopic dermatitis [2]. The patient and his routine caregivers were accustomed to the presence of persistent refractory pruritus and polymorphic inflammatory lesions. In addition, many of the patient's skin lesions were located in atopic dermatitis "favorite" areas.

Dermatomyositis also often involves persistent itching [3], and the rash is usually polymorphic, although it is often distinguished by a specific color. Traditionally, the shade of red typical of dermatomyositis rashes is compared to the color of the heliotrope flower ("heliotrope rash") [4]. This generally accepted color characteristic is quite ambiguous, since the color of heliotrope

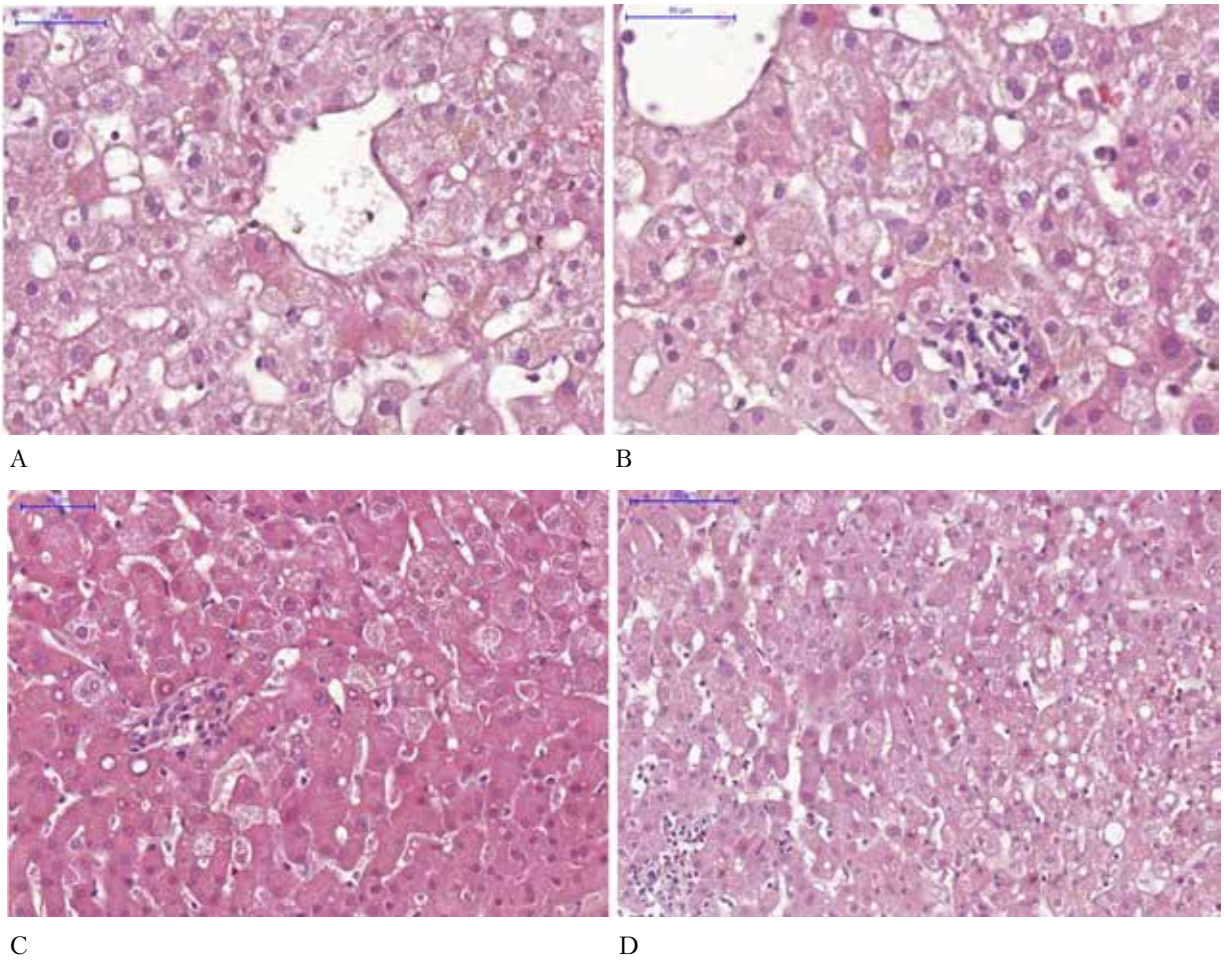

Figure 2. Pathological changes in the liver of Patient M., 34 years old: centrilobular intracellular cholestasis (A); scant lymphohistiocytic infiltration of the parenchyma of the centrilobular part of the liver lobule around degeneratively altered hepatocytes with abundant chologenic pigmentation of the cytoplasm (B); mild reactive proliferative changes in the biliary epithelium, absence of pathological fibrosis of cellular infiltration of the stroma of the portal tract, absence of periportal "necroinflammatory" changes (C); mild medium- and large-droplet fatty degeneration of hepatocytes (D); hematoxylin and eosin staining; the length of the scale segment: A, B, C — 500 μm, D — 100 μm

Рисунок 2. Патологические изменения печени пациента М., 34 года: центролобулярный внутриклеточный холестаз (A); скудная лимфогистиоцитарная инфильтрация паренхимы центролобулярного отдела печеночной дольки вокруг дегенеративно измененных гепатоцитов с обильной хологенной пигментацией цитоплазмы (B); слабо выраженные реактивные пролиферативные изменения билиарного эпителия, отсутствие патологического фиброза клеточной инфильтрации стромы портального тракта, отсутствие перипортальных «некровоспалительных» изменений (C); слабо выраженная средне- и крупнокапельная жировая дистрофия гепатоцитов (D); окраска гематоксилином и эозином; длина масштабного отрезка: A, B, C — 500 мк, D — 100 мк

flowers varies widely. In practice, we most often observe a dark purple rash with shades of light madder or magenta in dermatomyositis. Our patient's rash was atypically light in color, and was camouflaged by long-standing dyschromia of the skin, scaling, and lichenification foci typical of adult atopic dermatitis. In atopic dermatitis, due to disruption of the skin microbiome, erythema foci often occur on the skin of seborrheic zones, one of which is the upper back, which complicates the recognition of the shawl sign. Skin lesions on the back of the hands are also typical of diseases that manifest with an eczematous reaction (i.e., atopic dermatitis). Of course, one cannot ignore long-term topical glucocorticoid therapy, which significantly affects the severity of inflammatory infiltration, as well as the prescription of systemic glucocorticoids for suspected AIH. These drugs significantly affect appearance of the affected skin, complicating differential diagnostics.

However, the peculiarities of the localization of the rash (for example, over the extensor surface of the knee joints) and their new characteristics (change in the color of erythema, the appearance of new papula elements) made it possible to suspect dermatomyositis.

Rheumatologist's opinion. We examined the patient during glucocorticoid therapy, which had changed the clinical manifestations of the disease and their severity. Previous treatment with systemic glucocorticoids did not allow us to reliably objectify the already largely regressed muscle and, possibly, lungs damage. In addition, skin rash characteristic of dermatomyositis was observed against the background of previously changed skin due to long-term atopic dermatitis. The diagnosis was established primarily due to a thorough retrospective assessment of complaints and anamnesis. Anamnestic data showed a classic onset of dermatomyositis in the form of progressive muscle weakness and skin rash. In addition, the patient's history of symmetrical polyarthritis, represented by swelling and stiffness of the small joints of the hands and feet, as well as general weakness and fever. Subsequently, the clinical assumption of dermatomyositis/polymyositis was confirmed by laboratory data.

The detection of myositis-specific antibodies (anti-Jo-1) suggested a high probability of developing a certain phenotype of inflammatory myopathy — antisynthetase syndrome, which has features that distinguish it from other idiopathic inflammatory myopathies. Thus, pulmonary involvement, at the onset of which is low or asymptomatic, is detected in 90 % of cases of anti-Jo-1 positivity, and clinical signs (dyspnea, cough) can occur much later than skin and muscle symptoms [5]. During examination, the patient had crepitation in the lungs, and at the onset of the disease, basal pneumofibrosis was suspected during a screening X-ray examination. However, further instrumental examinations (performed during therapy) did not reveal any evidence of lung damage, which suggests regression of that early-stage lesion without the development of significant fibrosis. When assessing the disease activity after a course of glucocorticoids, sufficient for the treatment of AIH, but not for dermatomyositis treatment, 4 points were obtained (class B according to the Myositis Intention to Treat Activity Index, MITAX [6]), which indicated persistent disease activity.

Primary idiopathic dermatomyositis was confirmed: based on compliance with the 2017 EULAR/ACR criteria for adult and juvenile idiopathic inflammatory myopathies [7], the diagnosis of inflammatory myopathy in this patient is reliable (probability ≥ 90 %) — 11.3 points were scored. In addition, three out of five classification criteria for dermatomyositis were identified (A. Bohan and J.B. Peter, 1975) [8]: specific skeletal muscle damage, characteristic skin changes, elevated levels of ALT, AST, creatine kinase, which made it possible to confirm the diagnosis. Clinical and laboratory activity (MITAX-B) remained. Given the persistence of signs of muscle inflammation caused by the low initial dose of glucocorticoids for dermatomyositis, the dose of prednisolone was increased at a rate of 1 mg/kg/day with a recommendation to gradually reduce the dose at the outpatient stage after normalization of myolysis markers. Taking into account the data of the histological examination of the liver (cholestatic lesion), it was decided to refrain from continuing the use of azathioprine and to plan further selection of steroid-sparing therapy.

Pathologist's opinion. According to the Consensus of International AIH Pathology Group on the histological criteria of AIH, the diagnosis is considered probable if there is: portal lymphoplasmacytic hepatitis with more than mild periportal activity and/or more than mild lobular hepatitis, or predominantly lobular hepatitis in combination with portal lymphoplasmacytic hepatitis, periportal hepatitis, or portal fibrosis in the absence of evidence of other liver diseases. Emperipolesis and hepatocellular rosettes are no longer considered specific for AIH [9].

In this case, the histological examination was performed against the background of immunosuppressive therapy. However, the patient still had laboratory signs of disease activity. In addition, it is known that normalization of transaminases precedes the stabilization of the morphological picture in AIH by several months [10].

Morphological examination revealed intracellular cholestasis and proliferative changes in the biliary epithelium without an increase in laboratory markers of cholestasis, weak inflammatory infiltration in the centrilobular zone, the absence of periportal "necroinflammatory" activity and missing of plasma cells in pathological cellular infiltration. These changes suggest drug-induced liver damage and exclude the presence of AIH.

Hepatologist's opinion. Clinical observation demonstrates the need for careful differential diagnostics of AIH and rheumatological pathology. Difficulties may be caused by the prominence of non-specific complaints in the clinical features of the diseases considered. Thus, in the presented observation, the patient complained of symmetrical proximal muscle weakness in the upper limbs, which was initially assessed as general, hepatogenic weakness.

It is known that in autoimmune liver diseases no diagnostic test has absolute specificity and much depends on the subjective assessment of individual criteria [11]. Thus, an increase in transaminases, IgG, and the detection of autoantibodies typical for AIH can be observed in dermatomyositis/polymyositis, Sjogren's disease, and imitate AIH.

Serum transaminases and IgG are non-specific markers of various diseases not only of the liver. High levels of AST, ALT without determining creatine kinase is usually perceived as signs of liver disease, but they can act as an indicator of muscle damage [12]. Thus, an increase in ALT, AST [13], along with an increase in lactate dehydrogenase and creatine kinase is characteristic of idiopathic inflammatory myopathies, which include dermatomyositis/polymyositis. Creatine kinase, aldolase, ALT, AST and lactate dehydrogenase are enzymes of muscle origin, the levels of which increase with increasing activity of myositis [14].

It was the predominance of AST activity over ALT in a series of biochemical blood tests that forced us to direct the diagnostic search towards identifying myopathy.

But previously elevated ALT and AST values were interpreted as markers of hepatocellular damage. Hyperbilirubinemia probably contributed to this interpretation. However, it was observed in the patient earlier, and was represented by indirect bilirubin, which suggests a background condition - Gilbert's syndrome. The patient is recommended to undergo further genetic testing — detection of mutations in the *UGT1A1* gene — to verify this condition.

Characteristic antibodies for AIH (antinuclear antibodies, antibodies to smooth muscles, to soluble liver antigen and to liver and kidney microsomes type 1) [15] are not strictly specific for AIH and can be detected in other liver diseases, as well as in healthy individuals and in rheumatological patients with various diagnoses [16, 17]. For example, for the diagnosis of AIH type 1, antinuclear antibodies in a titer of 1 : 80 (observed in the patient) has a specificity of 36.1 %, a sensitivity of 91.8 % and a positive predictive value of 54.9 % [18].

During the initial examination of a patient with suspected AIH, morphological examination of the liver biopsy is mandatory [19–21]. Histological examination is necessary not only to exclude alternative or concomitant liver diseases, assess the severity of inflammatory activity and indicate the stage of fibrosis [22] but also to make sure that the cause of the disease is liver damage. Since the source of transaminases, elevated IgG and autoantibodies can be the processes in other organs. That is why, using modified criteria for the diagnosis of AIH (including autoantibodies, IgG level, absence of viral hepatitis and histological features), without morphological data we will never reach a total of more than 6 points, which is sufficient to establish "probable AIH", but does not allow us to confirm the diagnosis of AIH [23].

This patient had a Simplified AIH Score [23] of 4, which is not consistent with the diagnosis of AIH.

What about the patient's liver? Liver damage in dermatomyositis/polymyositis has been reported [24, 25], but it is quite rare compared to damage to the main target organs (lungs, heart, esophagus). It is believed that liver damage in dermatomyositis/polymyositis should be discussed only if transaminase activity is increased to a greater extent than creatine kinase and aldolase, ALT predominates over AST, and when alternative causes of liver pathology are excluded [14, 26, 27].

The patient received azathioprine for several months. It is known that azathioprine can cause drug-induced liver injury (DILI), which usually develops 2–12 months after the start of therapy, occurs with various phenotypes, including cholestatic hepatitis, and in most cases is reversible upon its discontinuation [28, 29]. In DILI, morphological cholestasis in most cases is not accompanied by an increase in serum alkaline phosphatase [30]. We tend to interpret the changes in the patient's liver as azathioprine-induced DILI. The revealed medium- and macrovesicular fatty degeneration of hepatocytes could be associated with prednisolone intake. However, since steatosis affected less than 5 % of hepatocytes, in this case we cannot talk about fatty liver disease of a specific (drug-induced) etiology [31, 32]. When assessing the probability of DILI using the electronic tool RECAM [33], which is a modified computer version of the Roussel Uclaf Causality Assessment Method (RUCAM) [34], the result obtained corresponds to possible DILI. However, it should be noted that RECAM was developed based on data from the American (Drug-Induced Liver Injury Network (DILIN)) and Spanish DILI registries, which impose minimal requirements for tests (such as ALT activity > 5 ULN) for registering cases of DILI. And its informative value for a number of DILI phenotypes, including those not accompanied by a sharp increase in serum transaminases and/or alkaline phosphatase, is questionable [33].

It is interesting that the mother and son developed autoimmune diseases at the same time and at different ages, which illustrates a genetic predisposition to autoimmune processes and, probably, the presence of a common external trigger for their manifestation.

A clinical diagnosis has been formulated.

Main: Dermatomyositis (MITAX class B)

Associated: Drug-induced liver injury (intrahepatic cholestasis), azathioprine-induced (RECAM — 2 points), mild severity.

Atopic dermatitis, moderate course (SCORAD — 35 points), erythematous-squamous form with lichenification.

Gastroesophageal reflux disease: erosive esophagitis, stage A by Los Angeles classification.

Gilbert's syndrome.

Conclusion

Differential diagnosis with elevated serum transaminases should include not only liver disease, but also muscle tissue pathology. When diagnosing AIH, histological examination data play a key role, and verification of the diagnosis is impossible without liver biopsy.

References / Литература

1. Атопический дерматит: клинические рекомендации. 2024. [Atopic dermatitis: Clinical guidelines. 2024. (In Russ.)]. URL: https://www.medznat.ru/uploads/file/post/ru/9359/17297545049359.pdf
2. Severity scoring of atopic dermatitis: The SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186(1):23–31. DOI: 10.1159/000247298
3. *Kim H.J., Zeidi M., Bonciani D., Pena S.M., Tiao J., Sahu S., et al.* Itch in dermatomyositis: The role of increased skin interleukin-31. *Br J Dermatol.* 2018;179(3):669–78. DOI: 10.1111/bjd.16498
4. *Xu A., Fu Q.* Heliotrope rash. *BMJ*. 2023;382:e075978. DOI: 10.1136/bmj-2023-075978
5. *Трисветова Е.Л.* Диагностика интерстициальных заболеваний легких при системных заболеваниях соединительной ткани. *Медицинские новости.* 2021;7(322):22–8. [*Trisvetova E.L.* Diagnosis of interstitial lung diseases in systemic connective tissue diseases. *Meditsinskie novosti.* 2021;7(322):22–8. (In Russ.)].
6. *Isenberg D.A., Allen E., Farewell V., Ehrenstein M.R., Hanna M.G., Lundberg I.E., et al.; International Myositis and Clinical Studies Group (IMACS).* International consensus outcome measures for patients with idiopathic inflammatory myopathies. Development and initial validation of myositis activity and damage indices in patients with adult onset disease. *Rheumatology (Oxford).* 2004;43(1):49–54. DOI: 10.1093/rheumatology/keg427
7. *Lundberg I.E., Tjärnlund A., Bottai M., Werth V.P., Pilkington C., de Visser M., et al.; International Myositis Classification Criteria Project Consortium, the Euromyositis Register, and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland).* 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Arthritis Rheumatol.* 2017;69(12):2271–82. DOI: 10.1002/art.40320
8. *Bohan A., Peter J.B.* Polymyositis and dermatomyositis (second of two parts). *N Engl J Med*. 1975;292(8):403–7. DOI: 10.1056/NEJM197502202920807
9. *Lohse A.W., Sebode M., Bhathal P.S., Clouston A.D., Dienes H.P., Jain D., et al.* Consensus recommendations for histological criteria of autoimmune hepatitis from the International AIH Pathology Group: Results of a workshop on AIH histology hosted by the European Reference Network on Hepatological Diseases and the European Society of Pathology: Results of a workshop on AIH histology hosted by the European Reference Network on Hepatological Diseases and the European Society of Pathology. *Liver Int.* 2022;42(5):1058–69. DOI: 10.1111/liv.15217
10. *Manns M.P., Czaja A.J., Gorham J.D., Krawitt E.L., Mieli-Vergani G., Vergani D., et al.; American Association for the Study of Liver Diseases.* Diagnosis and management of autoimmune hepatitis. *Hepatology*. 2010;51(6):2193–213. DOI: 10.1002/hep.23584
11. *Woodward J., Neuberger J.* Autoimmune overlap syndromes. *Hepatology.* 2001;33(4):994–1002. DOI: 10.1053/jhep.2001.23316
12. *Hounoki H., Shinoda K., Ogawa R., Taki H., Tsuneyama K., Tobe K.* Simultaneously developed polymyositis and autoimmune hepatitis. *BMJ Case Rep*. 2011;2011:bcr0920114763 DOI: 10.1136/bcr.09.2011.4763
13. *Hirschfield G.M., Gill P., Neuberger J.* The liver in systemic disease: A clinician's guide to abnormal liver tests. Hoboken, NJ: John Wiley & Sons, Inc.; 2023. DOI: 10.1002/9781119802181
14. *De Santis M., Crotti C., Selmi C.* Liver abnormalities in connective tissue diseases. *Best Pract Res Clin Gastroenterol.* 2013;27(4):543–51. DOI: 10.1016/j.bpg.2013.06.016
15. *Vergani D., Alvarez F., Bianchi F.B., Cançado E.L., Mackay I.R., Manns M.P., et al.; International Autoimmune Hepatitis Group.* Liver autoimmune serology: A consensus statement from the committee for autoimmune serology of the International Autoimmune Hepatitis Group. *J Hepatol*. 2004;41(4):677–83. DOI: 10.1016/j.jhep.2004.08.002
16. *Ткаченко О.Ю., Лапин С.В., Мазинг А.В., Тотолян Арег А.* Русскоязычная адаптация международной номенклатуры типов свечения ядра и цитоплазмы клетки (ICAP) для стандартизации выявления антинуклеарного фактора. *Медицинская иммунология.* 2020;6:1195–214. [*Tkachenko O.Yu., Lapin S.V., Mazing A.V., Totolian Areg A.* Russian-language version of the International Nomenclature of International Consensus on Antinuclear Antibody (ANA) Patterns (ICAP). *Medical Immunology (Russia).* 2020;6:1195–214. (In Russ.)]. DOI: 10.15789/1563-0625-RVO-2067
17. *Damoiseaux J., von Mühlen C.A., Garcia-De La Torre I., Carballo O.G., de Melo Cruvinel W., Francescantonio P.L., et al.* International consensus on ANA patterns (ICAP): The bumpy road towards a consensus on reporting ANA results. *Auto Immun Highlights*. 2016;7(1):1. DOI: 10.1007/s13317-016-0075-0
18. *Galaski J., Weiler-Normann C., Schakat M., Zachou K., Muratori P., Lampalzer S., et al.* Update of the simplified criteria for autoimmune hepatitis: Evaluation of the methodology for immunoserological testing. *J Hepatol*. 2021;74(2):312–20. DOI: 10.1016/j.jhep.2020.07.032
19. *European Association for the Study of the Liver.* EASL Clinical Practice Guidelines: Autoimmune hepatitis. *J Hepatol.* 2015;63(4):971–1004. DOI: 10.1016/j.jhep.2015.06.030
20. *Винницкая Е.В., Сандлер Ю.Г., Абдурахманов Д.Т., Бакулин И.Г., Белоусова Е.А., Буеверов А.О. и др.* Ключевые положения Российского консенсуса по диагностике и лечению аутоиммунного гепатита. *Фарматека.* 2017;5(17):47–55. [*Vinnitskaya E.V., Sandler Yu.G., Abdurakhmanov D.T., Bakulin I.G., Belousova E.A., Buyeverov A.O., et al.* Main provisions of the Russian consensus on diagnosis and treatment of autoimmune hepatitis. *Farmateka.* 2017;5(17):47–55. (In Russ.)].
21. *Винницкая Е.В., Сандлер Ю.Г., Бакулин И.Г., Парфенов А.И., Ильченко А.Ю., Никитин И.Г. и др.* Актуаль-

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22. *Mack C.L., Adams D., Assis D.N., Kerkar N., Manns M.P., Mayo M.J., et al.* Diagnosis and management of autoimmune hepatitis in adults and children: 2019 Practice guidance and guidelines from the American Association for the Study of Liver Diseases. *Hepatology.* 2020;72(2):671–722. DOI: 10.1002/hep.31065
23. *Hennes E.M., Zeniya M., Czaja A.J., Pares A., Dalekos G.N., Krawitt E.L., et al.* Simplified criteria for the diagnosis of autoimmune hepatitis. *Hepatology.* 2008;48(1):169–76. DOI: 10.1002/hep.22322
24. *Takahashi A., Takeda I., Kanno T., Nakahara T., Odajima H., Kasukawa R.* CD8-positive T cell-induced liver damage was found in a patient with polymyositis. *Intern Med.* 2006;45(18):1059–63. DOI: 10.2169/internalmedicine.45.1710
25. *Takahashi A., Abe K., Yokokawa J., Iwadate H., Kobayashi H., Watanabe H., et al.* Clinical features of liver dysfunction in collagen diseases. *Hepatol Res.* 2010;40(11):1092–7. DOI: 10.1111/j.1872-034X.2010.00707.x
26. *Wada T., Abe G., Kudou T., Ogawa E., Nagai T., Tanaka S., et al.* Liver damage in patients with polymyositis and dermatomyositis. *Kitasato Med J.* 2016;46:40–6.
27. *Noda S., Asano Y., Tamaki Z., Takekoshi T., Sugaya M., Sato S.* A case of dermatomyositis with "liver disease associated with rheumatoid diseases" positive for anti-liver-kidney microsome-1 antibody. *Clin Rheumatol.* 2010;29(8):941–3. DOI: 10.1007/s10067-010-1397-3
28. *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet].* Azathioprine. Last Update: August 21, 2017. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012. URL https://www.ncbi.nlm.nih.gov/books/NBK548332/
29. *Björnsson E.S., Gu J., Kleiner D.E., Chalasani N., Hayashi P.H., Hoofnagle J.H.; DILIN Investigators.* Azathioprine and 6-mercaptopurine-induced liver injury: Clinical features and outcomes. *J Clin Gastroenterol.* 2017;51(1):63–9. DOI: 10.1097/MCG.0000000000000568
30. *Kleiner D.E., Chalasani N.P., Lee W.M., Fontana R.J., Bonkovsky H.L., Watkins P.B., et al.; Drug-Induced Liver Injury Network (DILIN).* Hepatic histological findings in suspected drug-induced liver injury: Systematic evaluation and clinical associations. *Hepatology.* 2014;59(2):661–70. DOI: 10.1002/hep.26709
31. *Rinella M.E., Lazarus J.V., Ratziu V., Francque S.M., Sanyal A.J.; Kanwal F., et al.; NAFLD Nomenclature consensus group.* A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology.* 2023;78(6):1966–86. DOI: 10.1097/HEP.0000000000000520
32. *Liebe R., Esposito I., Bock H.H., Vom Dahl S., Stindt J., Baumann U., et al.* Diagnosis and management of secondary causes of steatohepatitis. *J Hepatol.* 2021;74(6):1455–71. DOI: 10.1016/j.jhep.2021.01.045
33. *Hayashi P.H., Lucena M.I., Fontana R.J.* RECAM: A new and improved, computerized causality assessment tool for DILI diagnosis. *Am J Gastroenterol.* 2022;117(9):1387–9. DOI: 10.14309/ajg.0000000000001836
34. *Danan G., Benichou C.* Causality assessment of adverse reactions to drugs – I. A novel method based on the conclusions of international consensus meetings: Application to drug-induced liver injuries. *J Clin Epidemiol.* 1993;46(11):1323–30. DOI: 10.1016/0895-4356(93)90101-6

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