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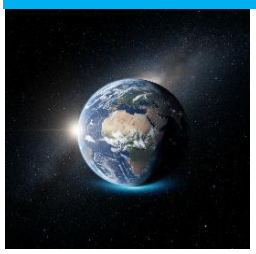

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SYPHILITIC HEPATITIS MIMICKING AUTOIMMUNE LIVER DISEASES - A NARRATIVE REVIEW

Artur Merc
ORCID: https://orcid.org/0009-0002-1651-018X
artur.merc@gmail.com
Independent Public Health Care Facility in Myślenice, ul. Szpitalna 2, 32-400 Myślenice

Jan Łozowski
ORCID: https://orcid.org/0009-0006-1355-0740
janlozowski02@gmail.com
Gabriel Narutowicz Municipal Hospital in Kraków, ul. Prądnicka 35-37, 31-202 Kraków, Poland

Łukasz Szymański
ORCID: https://orcid.org/0009-0001-7172-9953
szymanskilukasz@onet.pl
Frydrychowice Health Center

Julia Białas
ORCID: https://orcid.org/0009-0008-5128-1611
julia.bialas@10g.pl
District Hospital in Limanowa Name of the Divine Mercy, ul. Józefa Piłsudskiego 61, 34-600 Limanowa, Poland

Przemysław Piątek
ORCID: https://orcid.org/0009-0000-8121-7647
przemek.piatek@onet.pl
Father Rafał Hospital SPZOZ in Proszowice, Kopernika 13, 32-100 Proszowice, Poland

Joanna Paluchowska
ORCID: https://orcid.org/0009-0002-7762-7410
joanna.paluchowska@student.uj.edu.pl
Ludwik Rydygier Specialist Hospital in Kraków, Kraków, Poland

Natalia Gołąbek
ORCID: https://orcid.org/0009-0008-1849-5706
nataliagolabek@onet.pl
The University Hospital in Krakow, ul. Macieja Jakubowskiego 2, 30-688 Kraków, Poland

Milena Mordarska
ORCID: https://orcid.org/0009-0002-3318-8006
milenamordarska06@gmail.com
The University Hospital in Krakow, ul. Macieja Jakubowskiego 2, 30-688 Kraków, Poland

Alicja Kodura
ORCID: https://orcid.org/0009-0004-8410-1673
alicja@kodura.pl
Specialist Hospital Stefan Żeromski in Kraków, Osiedle Na Skarpie 66, 31-913 Kraków, Poland

Alicja Piwowarczyk
ORCID: https://orcid.org/0009-0005-8850-3925
alicja.m.piwowarczyk@gmail.com
Independent Public Health Care Facility in Myślenice, ul. Szpitalna 2, 32-400 Myślenice

Corresponding author:

Artur Merc

Email: artur.merc@gmail.com

Abstract

Background: Syphilis, often referred to as the "great imitator," is a re-emerging systemic infection caused by the spirochete *Treponema pallidum*. In its secondary stage, it can manifest as syphilitic hepatitis (SH), a rare condition that frequently presents with a cholestatic or mixed pattern of liver injury. Due to complex immunological mechanisms, including molecular mimicry and polyclonal B-cell activation, SH can induce false-positive autoantibodies, allowing it to closely mimic autoimmune liver diseases such as primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH).

Aim: This narrative review aims to analyze the clinical, serological, and histopathological overlap between syphilitic hepatitis and autoimmune liver diseases, highlighting the diagnostic challenges and evaluating the potential of *T. pallidum* to act as an environmental trigger for true, irreversible AIH.

Material and methods: A targeted review of current medical literature was conducted, focusing on systematic reviews, case reports and case series of patients presenting with SH who initially exhibited features of autoimmune liver diseases, including positive antimitochondrial antibodies (AMA), antinuclear antibodies (ANA), and anti-smooth muscle antibodies (ASMA). The analysis synthesized clinical presentations, autoantibody profiles, histopathological findings, and patient responses to targeted antibiotic versus empirical immunosuppressive therapies.

Results: SH can perfectly mimic PBC through severe cholestasis and cross-reactivity leading to false-positive AMA results. Similarly, it can mimic AIH by presenting with marked transaminitis and false-positive ANA and ASMA. Histologically, SH is highly heterogeneous and can show interface hepatitis or neutrophilic cholangitis, while direct spirochete detection via biopsy is frequently negative due to rapid Kupffer cell phagocytosis. Crucially, while antibiotic therapy typically resolves the pathogen-induced serological mimicry, empirical immunosuppression without antibiotic coverage can lead to catastrophic dissemination, such as fulminant syphilitic retinitis and neurosyphilis. Furthermore, emerging evidence suggests that the immunological disruption caused by SH, including molecular mimicry and regulatory T-cell manipulation, can permanently break self-tolerance, triggering true AIH in genetically susceptible individuals even after successful

spirochete eradication.

Conclusions: Syphilitic hepatitis is a critical differential diagnosis in patients presenting with acute liver injury and positive autoantibodies . Accurate diagnosis relying on established clinical criteria rather than solely on direct histopathological images is essential to avoid detrimental immunosuppressive therapy. Clinicians must also remain aware of the subsequent development of true autoimmune hepatitis following the resolution of the initial infection.

Keywords: Treponema pallidum, syphilis, primary biliary cholangitis, syphilitic hepatitis, molecular mimicry

Introduction

Syphilis is one of the most impactful sexually transmitted diseases of all time. It is caused by a spirochete *Treponema pallidum*. Primary syphilis usually presents as a skin lesion, called a chancre. If left untreated, the disease progresses to secondary syphilis, often seen as a characteristic rash and then to latent and tertiary syphilis which affects the nervous system and circulatory system. [1, 2, 3] Liver damage is usually observed in patients with early stages of syphilis due to disseminated bacteremia and a systemic inflammatory response. It is estimated that liver involvement occurs in about ten percent of patients but is often overlooked as a diagnosis due to its nonspecific clinical presentation. [1, 2, 4]

Syphilis is also known as The Great Imitator as it has various other presentations, which may mimic other diseases. Recent data suggests that it may be underdiagnosed due to its non-specific symptoms [1, 4] In this narrative review we decided to focus on a very specific and dangerous diagnostic trap: syphilitic hepatitis mimicking Primary Biliary Cholangitis (PBS) and Autoimmune Hepatitis (AIH).

Syphilitic hepatitis diagnosis criteria consist of: 1) the presence of abnormal liver enzyme parameters; 2) serological evidence of active syphilis infection; 3) the absolute exclusion of other, more common causes of liver injury; 4) the complete normalization of liver enzyme levels after the implementation of appropriate targeted antimicrobial therapy. [5]

Despite the clear guidelines, the diagnostic process is often difficult, as the clinical, serological, and histopathological features of syphilitic hepatitis can mimic primary autoimmune liver diseases. *Treponema pallidum* infection has been repeatedly documented as a factor generating laboratory profiles indistinguishable from primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH), accompanied by highly reactive autoantibody titers and characteristic inflammatory infiltrates in microscopic examination. [6] Therefore in this narrative review we decided to focus on a very specific and dangerous diagnostic trap: syphilitic hepatitis mimicking Primary Biliary Cholangitis (PBS) and Autoimmune Hepatitis (AIH).

Methodology

This narrative review was developed based on an analysis of current medical literature covering atypical and mimicking cases of syphilitic hepatitis. The search was performed in Google Scholar and PubMed databases using the keywords: “syphilitic hepatitis”, “syphilis”, “primary biliary cholangitis”, “autoimmune hepatitis” and “mimicry”. We also conducted a citation search.

Eligible studies involving systematic reviews, meta analyses, original studies, case reports and case series were analyzed, with a particular focus on patients whose clinical and biochemical presentation initially led diagnostics towards autoimmune liver diseases. The selected evidence includes situations of evident induction of autoantibodies, such as ANA, ASMA (anti-smooth muscle), and AMA (antimitochondrial), incorporating data from various publications. A synthesis of clinical and histopathological features and treatment strategies based on systematic reviews and literature reviews was performed to isolate precise differentiating criteria.

The search was limited to publications in English. The timeframe spanned from 2004 to January 2026, with a special focus on the last decade to capture the most recent data.

Literature Review

Literature Review: Syphilis mimicking PBC

The syphilitic hepatitis may present similarly to primary biliary cholangitis, which is a chronic autoimmune cholestatic liver disease, which often progresses despite treatment. [7] There have been several case reports on this matter, however we decided to present the most vivid ones.

A case report published in 2025 described a 20 year old male patient presenting with vomiting, jaundice, choluria, fecal acolia, fever and epigastric pain. The patient had been admitted to the hospital for further investigation. A couple weeks prior to admission he noticed genital skin lesions a few weeks after sexual intercourse. He was diagnosed with syphillis but never got the right treatment.

First laboratory tests had shown mildly elevated ALT 53 IU/L, AST 65 IU/L, GGTP 59 IU/L, total bilirubin 16.9mg/dL and significantly elevated ALP 327 IU/L. The further diagnostics ruled out various infections as well as genetic diseases. The investigation was significant for reactive antibodies: high level of IgG 1955, antimuscle smooth (ASMA) 1:40 and antimitochondria (AMA) 1:80, which are commonly seen in PBC.

The authors mention that imaging (CT, MRI) did not reveal the potential diagnosis and the presence of cholangiocarcinoma was ruled out. Furthermore they raised a hypothesis of primary biliary cholangitis or syphilis hepatitis mimicking autoimmune liver disease. The clinicians decided to treat the patient for late latent syphilis with benzathine penicillin, resulting in resolving the symptoms and ultimately normalising the liver function tests. The IgG titer was significantly lower (1356) and both ASMA and AMA were non reactive after the syphilis treatment.

As the authors note, overlooking the syphilis infection would result in treating the patient for PBC with ursodeoxycholic acid, allowing the undetected syphilis to run its natural course. [7]

Another example of syphilis mimicking PBC was described in 2020. The authors presented a case of a 54-year old man with a history of hypertension, diabetes mellitus, hyperlipidemia

and human immunodeficiency virus infection, who presented with jaundice, diffuse abdominal pain, vomiting and an erythematous, macular rash located on his upper body and limbs, including palms. He also had a history of unprotected sex in the previous 6 months.
The laboratory results were significant for AST 91 IU/L, ALT 120 IU/L, ALP 832 IU/L, total bilirubin 6.4 mg/dL. The Viral hepatitis panel was negative, CT scan showed no signs of biliary obstruction. At one point the liver injury was associated with antiretroviral drugs, the regimen was changed to less hepatotoxic drugs and the patient was discharged with plans to follow up with his primary care physician.
He presented 1 week later to his primary care physician with the same symptoms as prior and similar laboratory test results suggesting cholestatic liver injury.
Further workup was significant for a positive syphilis immunoglobulin IgG and RPR of 1:256 and an anti-M2 AMA IgG of 83.5 U (positive >25 U) which was suspicious for syphilis hepatitis vs underlying PBC. He was started on doxycycline for 2 weeks for the treatment of secondary syphilis. Once he completed the antibiotic therapy a complete resolution of the symptoms occured. 2 months after the treatment the liver function tests were normal, both RPR and AMA returned negative. Once the rapid plasma regain titer returned negative, a repeat AMA IgG was tested and negative.
The resolution of both liver enzyme abnormalities and elevated AMA IgG following the eradication of syphilis established the diagnosis of syphilis hepatitis, demonstrating that the AMA IgG result was a false positive. [8]

Another case was reported in 2025. It described a 52-year old, previously healthy male patient presenting with fatigue, pruritus and a rash and a history of high risk sexual behaviour. Initial laboratory results showed elevated ALP, mild transaminitis and a positive AMA (M2 subtype), suggesting PBC. Liver biopsy was performed revealing bile duct destruction and lymphocytic infiltration, typical for PBC. Later on the patient developed a rash on his palms and soles, raising suspicion for hepatitis, which was confirmed by RPR and a reactive treponemal test. The liver function tests were significantly lower after the treatment for syphilis. The authors suggest that the diagnosis should be syphilis hepatitis overlapping preexisted PBC, which was supported by reactive AMA test and the biopsy result. There is no information whether or not the AMA was reactive after the syphilis treatment. [6]

Literature Review: Syphilis mimicking AIH

While the cholestatic pattern of injury in syphilitic hepatitis is widely described and relatively well recognized, some patients may present with severe cytolytic or mixed injury. Such a biochemical phenotype, combined with an appropriate serological constellation, almost flawlessly mimics autoimmune hepatitis (AIH). [9] When early stages of syphilis present similarly, it may appear difficult to distinguish the infection from the severe autoimmune disease.

An illustrative case from the Yale School of Medicine involved a 23-year-old male with severe abdominal pain and jaundice. Laboratory testing revealed elevated antimitochondrial (AMA M2: 66.4 units), antinuclear (ANA: 1:160), and anti-smooth muscle antibodies (ASMA: 31 units), initially suggesting autoimmune hepatitis (AIH). However, a liver biopsy showed neutrophilic cholangitis and pericholangitis. A second pathology review noted these changes were atypical for AIH and consistent with hepatic syphilis. Subsequent immunohistochemical staining definitively visualized *Treponema pallidum* spirochetes in

the liver tissue, and serology confirmed active syphilis (RPR 1:256). Treatment with benzathine penicillin G completely normalized liver enzymes within two months, proving the autoantibodies were a transient consequence of the infection. Recognizing this prevented the erroneous initiation of massive corticosteroid therapy. [9]

A separate dimension of difficulty is the masking of advanced syphilitic lesions in the form of ambiguous tumors and granulomas coupled with immunological markers. This is illustrated by the case of a 34-year-old man prophylactically taking antiretroviral drugs (PrEP) and declaring anal intercourse with a monogamous partner. He presented to the hospital with severe epigastric pain and systemic symptoms. As in the previous story, severe impairment of liver function was found with a significant elevation of AST, ALT, and ALP, associated with the isolated presence of anti-smooth muscle antibodies (SMA). The difference lies in the imaging studies. Magnetic resonance cholangiopancreatography (MRCP) revealed a dense conglomerative mass measuring 4.2 by 5.2 centimeters in the liver hilum and retroperitoneal space, which surrounded the portal vein. The biopsy revealed massive granulomatous inflammation, consistent with a rare form of gummatous syphilis of the liver. Although this time immunohistochemistry came back negative showing no presence of spirochetes, reactive syphilis titers directed the team to proper treatment with penicillin G. As a result of the correct therapy the mass resolved and autoimmune titers underwent complete resorption. [3]

A striking example of the dangers of unwarranted immunosuppression involves a 62-year-old male who initially presented with elevated cholestatic liver enzymes. A liver biopsy revealed granulomatous hepatitis, and after ruling out viral etiologies, autoimmune hepatitis was presumed, prompting the initiation of prednisone. Four months into this immunosuppressive therapy, the patient suffered a severe, bilateral drop in vision. He was diagnosed with bilateral panuveitis, punctate inner retinitis, and placoid chorioretinitis. Subsequent serological testing was strongly positive for syphilis, and a lumbar puncture confirmed neurosyphilis. The immunosuppression had allowed the unrecognized syphilis infection to progress to fulminant syphilitic retinitis. Fortunately, the initiation of systemic penicillin led to a marked resolution of the posterior uveitis and significant visual improvement without recurrence. [10]

Literature Review: Syphilitic hepatitis triggering AIH

While the discourse most often focuses on syphilitic hepatitis generating false-positive and transient masking autoantibodies, emerging scientific evidence points to the existence of a phenomenon with an infinitely higher degree of complexity. *Treponema pallidum* infection can transcend the imitation stage and act as an absolute ultimate environmental trigger, provoking the occurrence of fully true, permanent, irreversible, and idiopathic Autoimmune Hepatitis in genetically predisposed individuals. Such a transition from a phase of transient infectious mimicry to a critical breaking point where a permanent autoimmune pathology arises in the body diametrically modifies the patient's trajectory, effectively pushing the physician into the necessity of juggling separate therapeutic goals - an antibiotic to kill spirochetes and a steroid to control the patient's autoimmune reactions. [4]

The phenomenon of post-infectious autoimmune disease is perfectly illustrated by a 49-year-old hypertensive patient who initially presented with severe acute hepatotoxicity (AST 1280 U/L, ALT 1652 U/L, total bilirubin >19.9 mg/dL). While early immunology showed an isolated ANA elevation (1:160) with normal IgG, an emergency liver biopsy revealed massive inflammatory infiltrates and intertwined spirochetes. Intramuscular benzathine penicillin successfully eradicated the *Treponema pallidum* infection, prompting a rapid clinical recovery. However, exactly ten weeks later, a secondary systemic collapse occurred. The patient was readmitted with severe jaundice, recurrent transaminitis (AST 1007 U/L, ALT >1000 U/L), and a drastically altered immunological profile: IgG surged to a pathological 2275 mg/dL, accompanied by new atypical p-ANCA (1:320) and persistent ANA. A second biopsy confirmed complete bacterial clearance but revealed fundamentally rearranged liver architecture with extensive interface hepatitis, the defining hallmark of Autoimmune Hepatitis. This abrupt shift objectively documents a mechanism, where an initial syphilis infection served as the elusive trigger for a permanent autoimmune process. The resulting immunological disease has been shortly inhibited by prednisone, which only confirmed the diagnosis.[4]

Differential diagnosis

Syphilitic hepatitis vs primary biliary cholangitis comparison

Primary biliary cholangitis (PBC) is a classic autoimmune disease whose pathogenesis involves the gradual, chronic destruction of small intrahepatic bile ducts. Patients with PBC can be asymptomatic or may present with jaundice, pruritus, and fatigue. Few patients may complain of vague right upper quadrant pain and mild cognitive impairment. Physical examination may reveal liver enlargement and, in case of cholestasis, jaundice. [11] The diagnostic criteria consist of 1) biochemical: prominently elevated alkaline phosphatase (at least 1.5 times the upper limit of normal), 2) serologically: positive result of antimitochondrial antibody (AMA) with a titer of 1:40 or higher and 3) histopathological: nonsuppurative destructive cholangitis or "florid duct lesion" and destruction of interlobular bile ducts with a predominance of lymphocytic infiltration. A definitive diagnosis requires fulfilling at least two out of these three criteria. [11, 12]

Syphilitic hepatitis extremely often presents with an identical cholestatic laboratory profile and, as described above, can induce false-positive AMA, making it a perfect, almost textbook imitator of PBC.

Clinical presentation of SH is nonspecific. The analyses of 97 cases showed that the most representative clinical symptoms of syphilitic hepatitis were rashes occuring in 77.9% of the patients, followed by fatigue or poor appetite being a complaint of 56.7% of the patients. [1] Some authors point out that the other common symptoms may include malaise, pain in the right hypochondrium, fever, nausea, vomiting, anorexia and pruritus. Physical examination may be remarkable for liver enlargement with possible pain on palpation as well as jaundice. [13]

The pattern of liver function tests abnormalities is commonly cholestatic with a marked increase in ALP and less often GGTP. However, other patterns are often described showing , with rather mild transaminitis (ALT > AST) and slightly elevated bilirubin level [1, 3, 7]

Significant reduction of the alkaline phosphatase level as well as rapid resolution of the symptoms after antibiotic treatment was reported as an indication for etiologic role of syphilis in liver injuries. [7]

Summary of Differentiating Parameters

Differentiating syphilitic hepatitis from true primary biliary cholangitis requires maintaining the highest degree of clinical vigilance and precise integration of history with laboratory data.

Diagnostic Parameter	Syphilitic Hepatitis Mimicking PBC	Primary Biliary Cholangitis (PBC)
Demographic Profile and Risk	Often men, MSM individuals, patients with HIV coinfection, history of high-risk behaviors.	Strong dominance of middle-aged women (approx. 90% of cases).
Dermatological Manifestation	Diffuse maculopapular rash with specific involvement of palms and soles; possible mucous membrane and genital ulcers.	Xanthelasma, hyperpigmentation in areas of chronic scratching, excoriations.
Autoantibody Profile	Presence of false-positive AMA (M2 subtype) and less frequently ANA. Titers normalize shortly after antibiotic use.	Highly positive, persistent, and lifelong AMA antibodies (M2 subtype).
Biochemical Dynamics	Acute onset of severe cholestasis (very high ALP, hyperbilirubinemia); rapid decline after treatment.	Insidious, very slow and chronically progressive increase in ALP and GGT, often without hyperbilirubinemia in initial phases.

Response to Therapy	Rapid and complete clinical and biochemical remission after benzathine penicillin G (or doxycycline) administration.	No response to antibiotic therapy. The condition requires chronic use of ursodeoxycholic acid (UDCA).
Dominant Histological Picture	Inflammatory infiltrates around portal tracts, edema, *endarteritis obliterans* (obliterative endarteritis), sporadic presence of spirochetes.	Chronic nonsuppurative destructive cholangitis, progressive ductopenia (loss of ducts).

Table 1. Summarises data collected from following publications [1, 5, 6, 7, 8, 11, 12, 13]

4.2. Syphilitic hepatitis vs Autoimmune hepatitis comparison

While the cholestatic pattern of injury in syphilitic hepatitis is widely described and relatively well recognized, some patients may present with severe cytolytic or mixed injury. Such a biochemical phenotype, combined with an appropriate serological constellation, almost flawlessly mimics autoimmune hepatitis (AIH). [9] True AIH is a chronic inflammatory liver disease defined by: 1) histologically interface hepatitis, 2) biochemically elevated aminotranferases, 3) serologically high IgG titers and presence of autoantibodies (most commonly ANA, ASMA, less often anti-LKM1). [19] When early stages of syphilis present similarly, it may appear difficult to distinguish the infection from the severe autoimmune disease.

Summary of Differentiating Parameters

Differentiating syphilitic hepatitis from autoimmune hepatitis requires combining the detailed history with clinical symptoms, laboratory results as well as histopathological findings. It is crucial for further treatment strategies because AIH treatment demands exclusion of any infections.

Diagnostic Feature	Syphilitic Hepatitis Mimicking AIH	Autoimmune Hepatitis (AIH)
Dynamics of Disease Onset	**Usually an acute, rapid onset, intertwined with distinct systemic symptoms (enlarged lymph nodes, body rashes).**	**Onset ranges from highly insidious, asymptomatic to acute, with a strongly fluctuating course.**
Serological Specificity	**False-positive, often isolated ANA or ASMA, low titers. Serum IgG immunoglobulin level normal or slightly elevated.**	**Persistently strongly positive titers of ANA, ASMA, or targeted anti-LKM1 antibodies. Spectacularly and pathologically elevated IgG concentration.**
Histopathological Pattern	**Massive portal tract edema with neutrophilic cholangitis (pericholangitis), obliterative endarteritis, rare plasma cells.**	**Dense, literally boiling interface hepatitis dominated by plasma cells, visible hepatocyte rosettes, and emperipolesis phenomenon.**
Pathogen Visualization	**Possible confirmation of the existence of *Treponema pallidum* spirochetes using targeted immunohistochemical stains or dark-field microscopy.**	**Bacteria are completely absent in all forms of detection.**

Therapeutic Approach	**Antibiotic therapy as the ultimate intervention (benzathine penicillin G). Total ban on immunosuppressants.**	**Rigorous immunosuppression consisting of corticosteroid therapy and chronic immune-modifying drugs (azathioprine, mycophenolate).**

Table 2. Summarises data collected from following publications [1, 3, 5, 9, 10, 13, 19]

Pathogenesis

Recent studies on syphilis pathogenesis highlight the complex interplay between the host immune response and pathogen immune evasion strategies. When evaluating how syphilitic hepatitis may mimic or even trigger autoimmune liver diseases, three main immunological pathomechanisms are proposed:

Molecular Mimicry: *Treponema pallidum* shares structural homologies with autologous liver antigens. Initially, this similarity allows the spirochete to evade immune surveillance by resembling the host's cells. However, once the host's immune system attacks, the resulting sensitized T-cells and antibodies cross-react with the host's own liver tissue. This incites an autoimmune attack against healthy hepatocytes that persists even after the bacteria have been eradicated by antibiotics. [15, 16]

Manipulation of Regulatory T cells (Tregs): *T. pallidum* utilizes sophisticated evasion mechanisms, including the production of specific virulence factors (such as the TpF1 miniferritin) that actively promote the development of Tregs to suppress effector T-cell activation and establish a persistent, latent infection. When the infection is rapidly cleared by targeted therapy, the sudden shift in the immune milieu, particularly in individuals with underlying genetic predispositions affecting Treg function, leads to a profound breakdown in tolerance. This unleashes autonomous, self-destructive immune brigades against the liver parenchyma. [15]

Bystander Activation: The localized inflammatory response and hepatocyte damage caused by the initial syphilitic infection lead to the release of previously sequestered liver autoantigens. This pro-inflammatory environment provides co-stimulatory signals that trigger the bystander activation of nearby, potentially autoreactive lymphocytes, further compounding the progression from an infectious hepatitis to a permanent autoimmune disorder. [15]

Treponema pallidum induces a polyclonal B-cell activation leading to nonspecific proliferation of these cells, causing a hyperproduction of immunoglobulins, especially antibodies of the IgM class. This phenomenon causes the transient secretion of various autoantibodies, which are not necessarily pathogenic but represent the effect of a specific immunological process. It has been proven that T. pallidum infection may induce serological findings such as antinuclear antibodies (ANA), rheumatoid factor (RF) and

anticardiolipin antibodies, which are typically associated with autoimmune diseases. [16, 17]
The second, much more specific mechanism is cross-reactivity. Structural similarity of epitopes causes this cross-reactivity to be registered by laboratory systems as a false-positive AMA result.
The study from 2001 showed false positive reactions for IgM anti-M2 ELISA in sera from patients with syphilis, hepatitis A and rheumatoid arthritis. The authors of the study showed a return to a negative AMA titer after recovery from hepatitis A. [17]

Histopathology

The liver biopsy in syphilitic hepatitis although being non specific, often shows mixed lymphoplasmacytic and granulocytic portal or lobular inflammation with variable bile duct injury, cholestasis, hepatocellular necrosis and/or associated noncaseating granulomas. However in some cases vasculotropic and epitheliotropic patterns of inflammation may be seen. [13, 14]
Extensive research analyzing the histological patterns of hepatic syphilis has debunked existing myths, showing that in this field there is no existence of a single pattern, which would easily define for the examiner a clear picture of a spirochete in the liver. It has been pointed out that syphilitic hepatitis oscillates its profile from microscopes around so-called masquerade forms, extracting their main clinical subspecies:
Bile Duct Injury Pattern: It consistently presents built changes in the form of an unrestrained outburst of reactivity within small ducts compressed under a mass of massive blockages (edema around the portal triad) and lobules falling deeply into shocks with cholestasis (biliary settlement dysfunction). The images perfectly mimic the indicators of PBC. [12, 18]
Acute Hepatitis Pattern: Shows a highly established architectural chaos of cells on the surface intertwined in inflammatory eruptions of spotty vessel blurring between fragments of isolated hepatocyte nests and silently accompanying coagulative necrosis. It clones the perfect conditions cast by acute types of hepatitis or the phase of entering the gates of AIH. [18]
Autoimmune Hepatitis-like Pattern: Undeniably creates the highest risk of misdiagnosis. It may mimic AIH by bringing into view tissues damaged by inflammation at the border of tissue lobules, joined with condensations by a tightly formed lymphocytic inflammatory conglomerate, creating a very close structure to interface hepatitis. However, the key difference is that syphilitic hepatitis has very few plasma cells, whereas finding an abundance of plasma cells is essential for diagnosing true AIH [18, 19]
Fibroinflammatory Mass Lesions (Gumma): Characterizing the structure through uncontrolled eruptions of fibrosing and mixing clouds of lymphoplasmacyte particles, arranged in circles with a closed necrotizing wound at the base centrally in the middle of a purulent formation, which for advanced digital resonance radiologies immediately throws an oncological suspicion of a nodular conglomerate mass (detected in MRCP scans). [18]
Identification of Treponema spirochetes in the histopathological samples is performed by using Warthin-Starry stain or immunohistochemistry but false negative results have been reported. According to the research, traditional silver staining methods (such as the Warthin-Starry stain) are often difficult to interpret due to heavy background staining and demonstrate a relatively low sensitivity of approximately 41%. In direct comparison, the use of targeted immunohistochemistry (IHC) with monoclonal antibodies against *Treponema pallidum* shows a significantly higher sensitivity of 71% and improved

specificity, as it markedly reduces background artifacts. For this reason, the immunohistochemical method is considered more effective and precise than classic silver staining for detecting spirochetes in tissue biopsies of patients with secondary syphilis. [13, 20]

Conclusion

In conclusion, syphilitic hepatitis is a disease that is difficult to diagnose. It can mimic autoimmune liver diseases such as primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) through serological cross-reactivity and molecular mimicry. Because direct histological identification of *Treponema pallidum* may be unsuccessful, often due to rapid spirochete phagocytosis by Kupffer cells, clinicians must maintain a high index of suspicion, especially in high-risk populations. Diagnosis is based on established clinical criteria: abnormal liver enzymes, positive syphilis serology, the strict exclusion of alternative causes, and the complete resolution of liver abnormalities following targeted antibiotic therapy. Distinguishing transient, pathogen-induced liver damage from a true autoimmune disease is very important clinically. The incorrect administration of immunosuppressive therapy for a presumed autoimmune condition can lead to serious consequences, such as fulminant systemic infection and severe neurological damage like syphilitic retinitis. Furthermore, practitioners must remain vigilant during patient follow-up, as the initial infection can occasionally serve as a genuine environmental trigger that irreversibly breaks immune tolerance, leading to true AIH. Ultimately, timely recognition and treatment with appropriate antibiotics not only resolve the acute hepatic injury but also prevent the potentially catastrophic progression of this great imitator.

Author Contributions

Conceptualization: Artur Merc, Milena Mordarska, Joanna Paluchowska, Łukasz Szymański

Methodology: Alicja Piwowarczyk, Jan Łozowski, Natalia Gołąbek, Alicja Kodura, Artur Merc

Software: Not applicable

Check: Julia Białas, Przemysław Piątek, Milena Mordarska, Łukasz Szymański, Joanna Paluchowska

Formal analysis: Artur Merc, Alicja Kodura, Jan Łozowski, Natalia Gołąbek, Alicja Piwowarczyk, Przemysław Piątek, Julia Białas

Investigation: Łukasz Szymański, Milena Mordarska, Joanna Paluchowska, Natalia Gołąbek, Artur Merc, Alicja Kodura, Jan Łozowski, Alicja Piwowarczyk

Resources: Przemysław Piątek, Julia Białas, Artur Merc, Jan Łozowski, Alicja Kodura, Milena Mordarska, Łukasz Szymański

Data curation: Joanna Paluchowska, Natalia Gołąbek, Alicja Piwowarczyk, Przemysław Piątek, Julia Białas, Milena Mordarska, Jan Łozowski, Artur Merc

Writing - rough preparation: Artur Merc, Jan Łozowski, Alicja Kodura, Natalia Gołąbek,

Joanna Paluchowska, Julia Białas, Przemysław Piątek, Milena Mordarska, Alicja Piwowarczyk, Łukasz Szymański
Writing - review and editing: Natalia Gołąbek, Artur Merc, Jan Łozowski, Milena Mordarska, Alicja Kodura, Joanna Paluchowska
Visualization: Łukasz Szymański, Julia Białas, Przemysław Piątek, Natalia Gołąbek, Alicja Piwowarczyk, Joanna Paluchowska
Supervision: Przemysław Piątek, Alicja Kodura, Jan Łozowski, Milena Mordarska, Alicja Piwowarczyk
Project administration: Artur Merc, Łukasz Szymański, Julia Białas

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