Scientific Research Publishing

Open Journal of Gastroenterology, 2022, 12, 37-43
https://www.scirp.org/journal/ojgas
ISSN Online: 2163-9469
ISSN Print: 2163-9450

Acute Syphilitic Hepatitis in the Early Secondary Phase: A Case Report and Literature Review

Paul Ngock[1,2*], Jacques Mauillon[1], Larry Tangie[2], Antonin Ndjitoyap[2], Célestin Danwang[3], Firmin Ankouane[2]

[1]Department of Gastroenterology and Hepatology, Jacques Monod Hospital, Montivilliers, France
[2]Internal Medicine Department, Faculty of Medicine and Biomedical Sciences, Yaounde, Cameroon
[3]Epidemiology and Biostatistics Unit, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium
Email: ngockdime@yahoo.fr, jacques.mauillon@ch-havre.fr, celestin.danwang@uclouvain.be, ngeklatan@yahoo.com, tonindam3@yahoo.fr, ankouanefirmin@yahoo.fr

How to cite this paper: Ngock, P., Mauillon, J., Tangie, L., Ndjitoyap, A., Danwang, C. and Ankouane, F. (2022) Acute Syphilitic Hepatitis in the Early Secondary Phase: A Case Report and Literature Review. *Open Journal of Gastroenterology*, **12**, 37-43.
https://doi.org/10.4236/ojgas.2022.123004

Received: January 8, 2022
Accepted: March 8, 2022
Published: March 11, 2022

Abstract

Background: The incidence of syphilis is clearly increasing. It is a source of visceral damage, particularly in the secondary phase. Acute syphilitic hepatitis is a rare clinical entity classically described but under-diagnosed because of its non-specific presentation. **Case Presentation:** We report the case of a 25-year-old French woman, without comorbidity, sexually active, having unprotected sex with only one partner. She was admitted to our unit for jaundice and a disturbed liver function test preceded 3 weeks earlier by a rash. The patient did not consume alcohol and did not report the introduction of a new medication. A skin rash compatible with syphilitic roseola and generalized adenopathy were found. The liver workup showed alanine aminotransferase (ALT) at 1984 U/L, aspartate aminotransferase (AST) at 1377 U/L, total bilirubin at 221 µmol/L, alkaline phosphatase activity (APL) at 419 U/L, gamma glutamyl transferase activity (GGT) at 229 U/L and a prothrombin concentration at 73%. The search for the most common etiologies of acute hepatitis was negative. Syphilitic serology was positive with a Treponema Pallidum Hemagglutinations Assay (TPHA) titration of 5120 IU and Veneral Disease Research Laboratory (VDRL) of 64 IU. Abdominal ultrasound revealed only homogeneous hepatomegaly and splenomegaly with no focal lesions. Other sexually transmitted infections (STI) were negative and her partner had positive syphilis serology. After a single dose of Benzathine benzylpenicillin, the clinical signs regressed after one week and the hepatic balance tended to normalize 20 days later. **Conclusion:** This highlights the need for a

high index of suspicion for syphilitic hepatitis in sexually active patients presenting with acute hepatitis associated with a cutaneous rash.

Keywords

Acute Hepatitis, Rash, Syphilis

1. Introduction

Syphilis is STI caused by the spirochete Treponema pallidum. It is a non-immunizing and highly contagious condition with an estimated incidence of 6.3 million in subjects aged 15 to 49 years in 2016 [1]. Syphilis is classified into 2 phases: early syphilis (primary, secondary, and early latent of less than 1 year) and late syphilis (late latent of more than 1 year and tertiary) [2]. Syphilitic chancre may go undetected and untreated; there may be systemic dissemination of spirochetes.

Nicknamed "the great simulator", syphilis can mimic several clinical presentations and can cause visceral damage, particularly to the liver [3]. Hepatic involvement usually occurs in the early phase and is underdiagnosed because of the nonspecific clinical presentation [4]. Acute syphilitic hepatitis is classically described in the literature but remains exceptional. Due to the resurgence of syphilis, we will see an increase in the incidence of acute syphilitic hepatitis. We report here a case of acute syphilitic hepatitis revealed by a disturbance of the liver balance associated with a skin rash.

2. Case Presentation

This is a 25-year-old female patient of French origin, with no comorbidity, admitted to our unit for jaundice and a disturbed liver function test preceded 3 weeks earlier by a non-pruritic skin rash and progressive asthenia. She declared having unprotected sexual intercourse with 1 partner for 4 years. The patient did not consume alcohol, she did not report the introduction of a new medication or risk factors for parenteral transmission of acute hepatitis. She did not report any recent influenza-like illness, no ocular complaints, no oral, anal or vaginal ulceration.

On physical examination, the body mass index of the patient was 21.6 kg/m^2; she presented with mucocutaneous jaundice and was apyretic. The rash was papular, with spaces of healthy skin, localized on the trunk, back, arms and thighs, sparing the face, palms and soles (**Figure 1**). There was also painless mobile occipital, cervical, retro-auricular, left axillary and left inguinal adenopathies varying between 1 - 2 cm in diameter. The abdomen was soft with splenomegaly with little tenderness and painless hepatomegaly with a foamy lower border. There was no asterixis, no stellate angioma and no collateral venous circulation. Cardiovascular and pulmonary examinations were normal. The oral cavity and

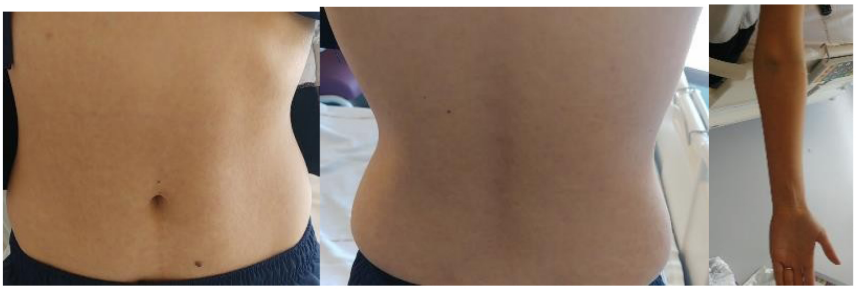

Figure 1. Papular lesions of the thoracic, abdominal and upper limbs.

dander were unremarkable. The examination of the urogenital system did not reveal any lesion.

Complementary laboratory investigations showed a normal haemogram and a normal C-reactive protein (CRP). The hepatic workup was disturbed with cytolysis predominantly on ALT at more than 50 times the upper value of normal (N); ALT: 1984 U/L (N < 35), AST 1377 U/L (N < 35). Prothrombin concentration was 73% with factor V at 90%. ALP was 419 U/L or 4 N and GGT 229 U/L or 5 N with a total bilirubin of 221 µmol/L (N < 15) with a predominantly conjugated bilirubin. Blood proteins were measured at 72 g/L, albumin at 36 g/L, and a normal weight determination of immunoglobulins A, G, and M. The following serological markers were negative: hepatitis A virus antibody IgM, HBsAg, anti-HBc antibody IgM, anti-HBs antibody, hepatitis C virus antibody, hepatitis E virus antibody IgM, human immunodeficiency virus antibody, anti-tularemia antibody and herpes simplex virus antibody. Anti-parvovirus IgM antibody was nonsignificant. PCR of cytomegalovirus and Ebstein Barr virus were negative. The autoimmune work-up was normal, in particular the search for anti-mitochondria type 2, anti-smooth muscle, anti-liver kidney microsome 1, anti-sp100, anti-PML, anti-gp210, anti-liver cytosol 1, anti-soluble liver antigen, anti-Ro52 and anti-carbonic anhydrase antibodies. Abdominal ultrasound revealed a gallbladder without calculi, thin bile ducts, homogeneous hepatomegaly and splenomegaly without focal lesions (**Figure 2**).

Syphilitic serology, which had been requested at the time of the rash and generalized adenopathies, was positive with a TPHA titration of 5120 units and VDRL of 64 units. The diagnosis of acute syphilitic hepatitis in the early secondary phase was retained with the following arguments: the disturbance of the hepatic balance associated with a skin rash compatible with syphilitic roseola after the dermatologist's examination, generalized adenopathies and syphilitic serology suggestive of progressive treponematosis. On further questioning, no ulceration related to a syphilitic chancre was found. Other STI were absent, the partner had positive syphilitic serology and admitted having had an extramarital relationship. Benzathine Benzylpenicillin treatment at a single dose of 2.4 million IU intramuscularly was performed without clinical signs of a Jarisch-Herxheimer reaction. The clinical course was marked by regression of the rash and adenopathy after one week. Biologically, cytolysis and cholestasis regressed after 20 days of treatment before normalizing.

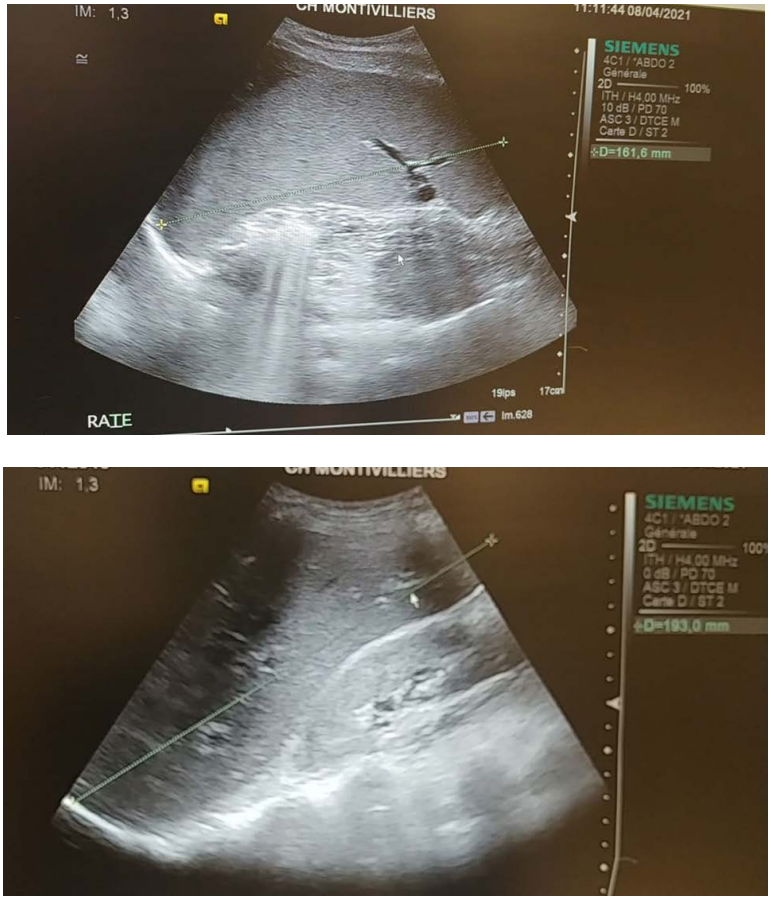

Figure 2. Homogeneous hepatomegaly and splenomegaly without focal lesions.

3. Discussion

Although excluded from the list of notifiable diseases in France in July 2000 because of the low number of new cases, syphilis has been steadily increasing for several years with a worldwide incidence in people aged 15 - 45 years of 6.3 million in 2016 [1] [5]. Syphilis is described according to 2 periods: an early contagious period including the primary, secondary and early latent phases and the late non-contagious period divided into late latent and tertiary phases [2] [6]. The secondary phase appears within 2 to 10 weeks after the syphilitic chancre and is characterized by visceral damage, particularly to the liver. Our patient presented with a skin rash compatible syphilitic roseola 3 weeks prior to altered liver function tests. This classifies our patient in the early secondary phase of syphilis.

Liver involvement in syphilis was first described in 1585 by Paracelsus and reported in 1917 [7]. Liver involvement can occur at any stage of syphilis and is found in 90% of cases during the early phase [4]. Liver involvement in syphilis is rare (less than 1% of cases) [8].

The clinical presentation during acute hepatitis of syphilitic origin is diverse and non-specific [4] [9]. In a systematic review of 2018, finding the clinical data of 97 patients, skin involvement during syphilitic hepatitis was the most com-

mon presentation in 78% of cases and then followed hepatomegaly and jaundice respectively in 54% and 35% [4]. The skin rash is most often bilateral generalized macular or papular, nonpruritic, measuring 5 to 10 mm in diameter, localized to the trunk and proximal extremities. Generalized adenopathy, arthralgia and myalgia may also be present. Untreated acute syphilitic hepatitis may progress to severe forms. Cases of fulminant syphilitic hepatitis have been reported in the literature. In the first case, a liver transplant was performed [10] and in the other case, in the absence of a transplant, the evolution was towards death despite appropriate medical treatment [11]. This patient however presented with a non-severe acute syphilitic hepatitis with a prothrombin concentration of 73% and the absence of any neurological involvement and thus no indication for liver transplantation.

Syphilitic hepatitis is thought to be secondary to systemic dissemination of spirochetes from the primary lesions, followed by portal invasion leading to a peri-portal inflammatory response [12]. In our case, the patient met the diagnostic criteria for acute syphilitic hepatitis proposed in 2004 by Mullick, which include: a disturbed liver function test, exclusion of other causes of acute hepatitis, progressive positive syphilitic serology associated with a clinical presentation consistent with secondary syphilis, and clinical and biological improvement after appropriate antibiotic treatment [9].

During acute syphilitic hepatitis, the liver workup is disturbed with a constant and predominant elevation of ALP and GGT activity; there is a moderate elevation of bilirubin and cytolysis [4] [8] [9] [13]. In this observation, the liver workup profile was unusual with cytolysis greater than 50 N and bilirubin greater than 200 µmol/L with no other concomitant etiology found. Liver biopsy is not essential for the diagnosis of acute syphilitic hepatitis [13]. It may be indicated if there are other possible etiologies for liver involvement. When the liver biopsy is performed, the histological study reveals nonspecific lesions including an inflammatory infiltrate in the portal or periportal region associated with foci of intralobular necrosis [4] [14]. Isolated granulomatous and giganto-cellular hepatitis lesions have been described in tertiary syphilis but remain rare [15]. In more than half of the cases, Treponema pallidum spirochetes can be found either by immunohistochemistry or by Wharthin-Starry staining [4].

Treatment of acute syphilitic hepatitis, as in all early syphilis, is based on a single dose of Benzylpenicillin (2.4 million units) administered intramuscularly [16]. The time to normalization of liver function abnormalities in syphilitic disease is unknown. In our case, the rash and adenopathy regressed after one week. Cytolysis and cholestasis regressed after 20 days of treatment.

4. Conclusion

Liver involvement in syphilis is non-specific. This case report documents the need for a high index of suspicion for syphilitic hepatitis in sexually active patients presenting with acute hepatitis associated with a cutaneous rash. The first-

line treatment remains Benzathine Benzylpenicillin in single dose with a favorable clinical and biological evolution.

Acknowledgements

We thank all the staff of the Department of Gastroenterology and Hepatology of the Havre Jacques Monod hospital group.

Ethics Approval and Consent to Participate

Consent for publication was obtained from the patient.

Consent for Publication

All authors approved the final version of the manuscript and agree for publication.

Availability of Data and Material

All materials are available in the manuscript.

Conflicts of Interest

We declare no competing interests.

References

[1] Rowley, J., Vander Hoorn, S., Korenromp, E., Low, N., Unemo, M., Abu-Raddad, L.J., *et al*. (2019) Clhamydia, Gonorrhoea, Trichomonasis and Syphilis: Global Prevalence and Incidence Estimates, 2016. *Bulletin of the World Health Organization*, **97**, 548-562. https://doi.org/10.2471/BLT.18.228486

[2] Dupin, N. (2016) Syphilis. *Journal of Internal Medicine*, No. 11, 735-742. https://doi.org/10.1016/j.revmed.2016.05.010

[3] Suzuki, I., Orfanidis, N., Moleski, S., Katz, L.C. and Kastenberg, D. (2009) The "Great Imitator" Presents with Abnormal Liver Enzymes. *The Medicine Forum*, **11**, 17. https://doi.org/10.29046/TMF.011.1.015

[4] Huang, J., Lin, S., Wan, B. and Zhu, Y. (2018) A Systematic Literature Review of Syphilitic Hepatitis in Adults. *Journal of Clinical and Translational Hepatology*, **6**, 306-309. https://doi.org/10.14218/JCTH.2018.00003

[5] Couturier, E., Dupin, N., Janier, M., Halioua, B., Yazdanpanam, Y., Mertz, J.-P., *et al*. (2001) Resurgence of Syphilis in France 2000-2001. *BEH*, **35**-**36**, 168-169.

[6] Arando, L.M. and Otero, G.L. (2019) Syphilis. *Enfermedades Infecciosas y Microbiología Clínica*, **37**, 398-404. https://doi.org/10.1016/j.eimce.2019.03.007

[7] Wile, U.J. and Karshner, R.G. (1917) Icterus Gravis Syphiliticus. *JAMA*, **68**, 1311-1314. https://doi.org/10.1001/jama.1917.04270050013005

[8] Lee, M., Wang, C., Dorer, R. and Fergusson, L. (2013) A Great Masquerader: Acute Syphilitic Hepatitis. *Digestive Diseases and Sciences*, **58**, 923-925. https://doi.org/10.1007/s10620-012-2322-1

[9] Mullick, C.J., Liappis, A.P., Benator, D.A., Roberts, A.D., Parenti, D.M. and Simon, G.L. (2004) Syphilitic Hepatitis in HIV-Infected Patients: A Report of 7 Cases and Review of the Literature. *Clinical Infectious Diseases*, **39**, 100-105.

https://doi.org/10.1086/425501

[10] Lo, J.O., Harrisson, R.A. and Hunter, A.J. (2007) Syphilitic Hepatitis Resulting in Fulminant Hepatic Require Liver Transplantation. *Journal of Infection*, **54**, e115-e117. https://doi.org/10.1016/j.jinf.2006.07.005

[11] Affonso da Costa, A.B., Fornazari, B., da Silva, F.P.M., Frandoloso, G.A. and Breda, G.L. (2018) Fulminant Hepatitis in a Patient with Secondary Syphilis. *International Journal of STD & AIDS*, **29**, 1348-1350. https://doi.org/10.1177/0956462418785257

[12] Sell, S. and Norris, S.J. (1983) Biology, Pathology and Immunology. *International Journal of Experimental Pathology*, **24**, 203-276.

[13] Honrubia-Lopez, R., Rueda-Garcia, J.L., Burgos-Garcia, A., Fernadez-Martos, R. and Mora-Sanz, P. (2018) Acute Hepatitis as a Manifestation of Secondary Syphilis. *Gastroenterology & Hepatology*, **41**, 505-506. https://doi.org/10.1016/j.gastre.2018.08.005

[14] Rampal, P., Veynes, B., Agrati, D., Saint-Paul, M.C., Rampal, A., Francois, E., *et al*. (1986) Hepatic Involvement in Syphilis. *Annals of Gastroenterology and Hepatology*, **22**, 77-81.

[15] Carrère, C., Rey, P., Toussaint, P., De Wilde, S. and Casassus-Builhe, D. (2003) Resurgence of Syphilis and Rediscovery of an Ancient Cause of Hepatitis: Clinical and Biological Gastroenterology. 656-657.

[16] Workowki, K.A. and Bolan, G.A. (2015) Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. *MMWR*, **64**, 1-137.