International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 04 Issue 07 July 2024

Page No: 618-624

DOI: https://doi.org/10.47191/ijpbms/v4-i7-05, Impact Factor: 7.792

Successful Steroid Therapy in a Child with Suspected Autoimmune Hepatitis

Primadita Syahbani[1], Rendi Aji Prihaningtyas[2], Bagus Setyoboedi[3], Sjamsul Arief[4]

[1,2,3,4] Department of Child Health, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

ABSTRACT

Introduction: Autoimmune Hepatitis (AIH) is an unexplained cause of chronic and progressive liver inflammation. The incidence of AIH is about 4.82/per 100,000 people in Korea, but based on global research the incidence is increasing and it should be taken more seriously. Laboratory and imaging tests were performed which led to the diagnosis of AIH but to diagnose AIH is difficult. Steroid therapy is an option for this patient by considering the side effects that are well-monitored. A favourable outcome was shown and this report is expected to highlight the importance of early diagnosis and treatment in AIH cases.

Case presentation: A 6-year-old, 5-month-old girl presented to Dr. Soetomo General Academic Hospital, Surabaya with jaundice for 2 weeks. She had been unable to walk for the past 1 month due to pain in both legs, nausea and vomiting, anorexia, right-sided abdominal pain, and an enlarged abdomen. She has had a history of fever for the past 1 month. Laboratory parameters showed cholestasis, abnormal liver function test (aspartate aminotransferase (AST) 1406 U/L, alanine aminotransferase (ALT) 1392 U/L, and prolonged coagulation factor), and positive antinuclear antibody (ANA) test (79.10 AU/mL). Hepatitis markers were negative. Liver biopsy and autoantibodies examination (LKM and SMA) was not done due to limited facilities. Hepatitis, cholecystitis, and ascites were noted on abdominal ultrasonography. Ascites and cholecystitis were seen on an abdominal CT scan. Steroid therapy was administered and there was improvement in clinical condition and laboratory results following two weeks duration of treatment.

Conclusion: This case report illustrates that steroid treatment for a child with AIH results in a good improvement and provides achievement of treatment goals following existing guidelines. The use of steroid therapy in suspected cases of AIH, without further diagnostic modalities, may be of value in the prevention of further liver damage, especially in healthcare settings with limited resources.

KEYWORDS: Autoimmune hepatitis; child; steroid

ARTICLE DETAILS

Published On:
18 July 2024

Available on:
https://ijpbms.com/

INTRODUCTION

A condition called autoimmune hepatitis (AIH) is associated with an unclear cause of chronic and progressive liver inflammation.[1] AIH is classified as the category of paediatric autoimmune diseases of the liver, which also includes de novo AIH following liver transplantation and autoimmune sclerosing cholangitis (ASC). Two types of autoimmune hepatitis are recognized.[2] Characteristic of type 1 is the existence of anti-smooth muscle antibodies (ASMA) with or without anti-nuclear antibodies (ANA). Meanwhile, type 2 autoimmune hepatitis is characterized by positive anti-liver/anti-kidney microsome (anti-LMK) type 1 antibodies or anti-liver cytosol (anti-LC) type 1 antibodies.[1]

Based on Korea's data, AIH case prevalence from 2009 to 2013 was 4.82/100,000 persons which showed the age-adjusted prevalence rate.[3] Meanwhile, in the United States, the estimated prevalence of AIH is 31.2/100,000 with more women than men. Both data are comparable when the data in the United States are compared with the reported prevalence of AIH in Europe.[4] Global research shows that the incidence and prevalence of AIH have significantly risen and vary substantially across global locations.[5]

The prevalence of AIH in Indonesia is difficult to know for sure, but the increase in other countries is an issue that AIH

should be taken more seriously. AIH is a disease with broad clinical features and is among the most frequent aetiology of acute liver failure (ALF).[6] Therefore, an appropriate treatment for AIH cases in Indonesia is to diagnose early and distinguish it from other forms of chronic hepatitis because AIH responds to immunosuppressive therapy.[7] When awareness of AIH is high, treatment can be done early as well. In this case report, immunosuppressive treatment was given to a child with a suspected diagnosis of AIH who had non-specific symptoms with prednisone and had a good outcome.

CASE PRESENTATION

A 6-year-old and 5-month-old girl came to Dr. Soetomo General Academic Hospital with a chief complaint of a yellowish body 2 weeks ago. She was also unable to walk because of the pain in both legs for the last 1 month. She complained of nausea and vomiting, and difficulty eating and drinking. Complaints were also accompanied by right-sided abdominal pain and an enlarged abdomen. She has had a history of fever for the last 1 month. The faeces were pale and the urine was brownish like tea. In the previous hospital, she was treated supportively and was admitted into paediatric intensive care unit for several days, but his complaints of jaundice and abdominal pain had not improved. There was no previous history of similar illness. There was no history of previous surgery. There are no similar complaints in the family. There was no tuberculosis contact. She has a history of consuming instant noodles frequently.

She is the first child, born spontaneously, and full term with a birth weight of 3400 grams. She was born immediately crying, with no history of cyanosis, and no jaundice. His weight gain was adequate and there was no extreme weight loss. His immunization history was complete and development was in line with the child's age. She was breastfed until 5 months of age and continued with formula feeding. His general condition appeared moderately ill. Consciousness was composed of mentis with a body weight of 18 kg, body height of 120 cm, and upper arm circumference of 17 cm. His nutritional status was normal. Physical examination revealed sclera icteric and hepatomegaly.

Laboratory testing revealed a rise in total bilirubin 13.85 mg/dL and direct bilirubin 12.42 mg/dL, abnormality of liver enzyme, including Aspartate Aminotransferase (AST) 1406 U/L, and Alanine Aminotransferase (ALT) 1392 U/L, Gamma-glutamyl transferase (GGT) 404 U/L, and prolonged coagulation factor (Plasma Prothrombin Time (PPT) 25.9 seconds and Activated Partial Thromboplastin Time (APTT) 49.4 seconds). A blood routine examination revealed haemoglobin 13,7 g/dL, leucocyte 25.090 10^3/µL, and thrombocyte 488 10^3/µL. The patient also had an additional Anti-Nuclear Antibody (ANA) test for autoimmunity markers and was found to be high, at 79.10 AU/mL. Anti-ds-DNA was 1.87 IU/mL, Complement C3 141,21 mg/dL, and complement C4 19.3 mg/dL. Hepatitis markers consist of HbsAg, IgG Anti HAV, IgM Anti HAV are negative. The serum electrolyte measurement revealed sodium 139 mmol/l, potassium 3.6 mmol/l, chloride 108 mmol/l, and calcium 8.3 mg/dl. In this case, liver biopsy, SMA and LKM examination were not performed due to limited facilities.

Abdominal ultrasonography showed increased hepatic echo parenchymal intensity with no visible dilation of IHBD and EHBD, the gall bladder wall appeared thickened, and there was free fluid echo intensity in the abdominal cavum. Abdominal ultrasound revealed hepatitis, cholecystitis, and ascites (Figure 1).

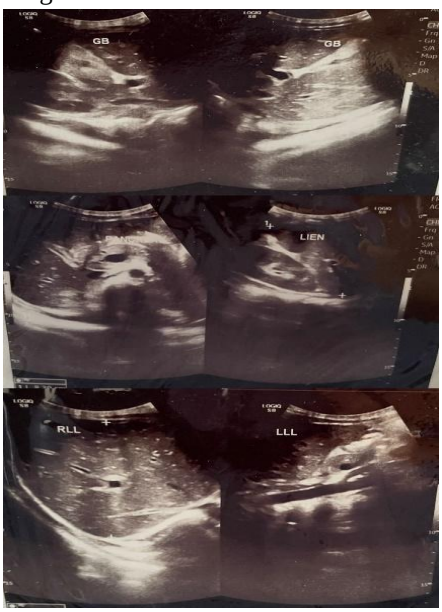

Figure 1. Abdominal ultrasound showed hepatitis, cholecystitis, and ascites

In addition, the abdominal CT scan examination showed omental cake with ascites, normal size liver without dilatation of EHBD and IHBD, thickened gallbladder wall, meteorism with faecal accumulation, and no enlarged lymph nodes of the

aorta, lien, and pancreas within normal limits. An abdominal CT scan revealed peritoneal tuberculosis with minimal ascites, cholecystitis, and meteorism with an accumulation of faecal material (Figure 2).

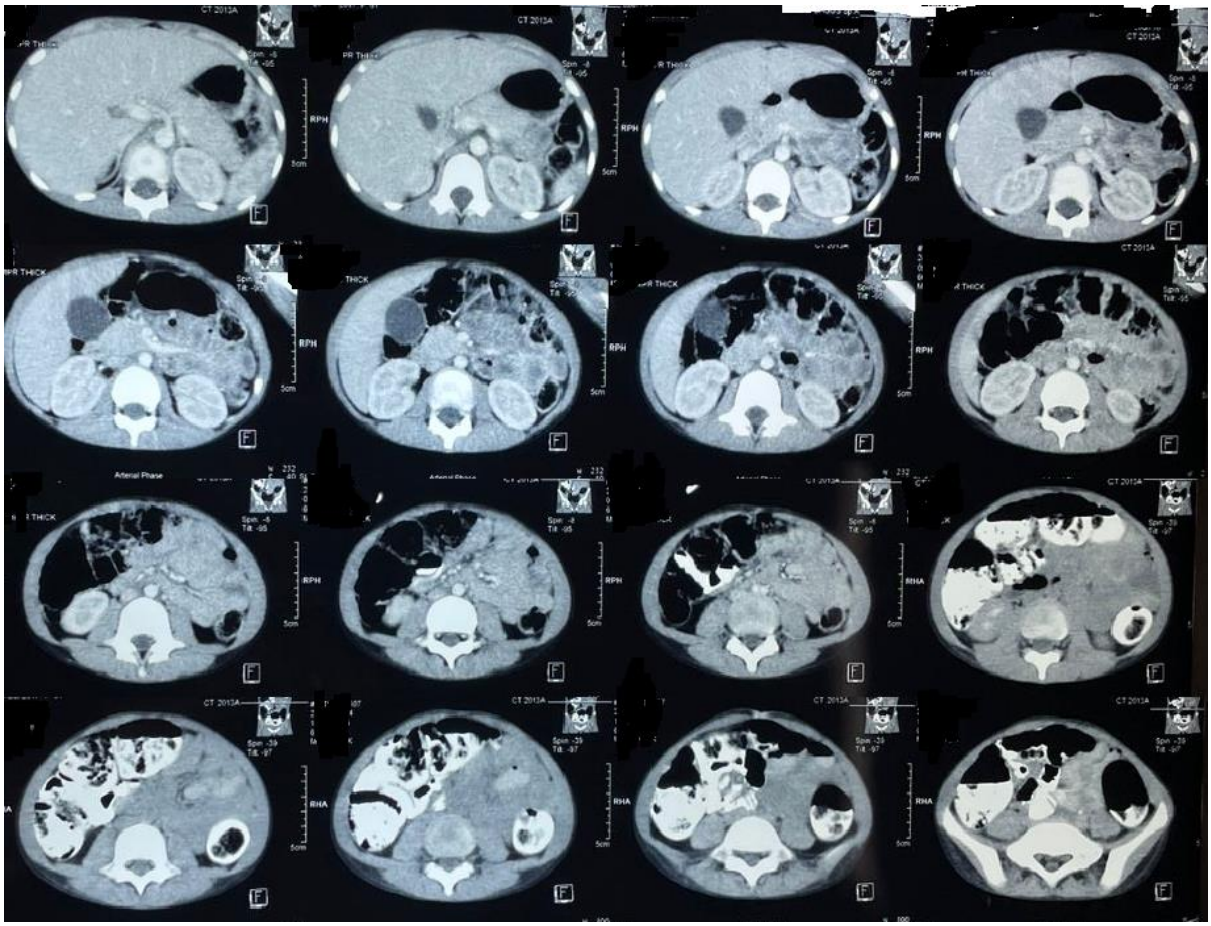

Figure 2. An abdominal CT scan revealed peritoneal tuberculosis with minimal ascites and cholecystitis

The tuberculosis workup was negative. Mantoux test was 0 mm. Echocardiography revealed normal. Differential diagnosis of hepatitis is already ruled out by no previous history of hepatitis symptoms of jaundice and others, other than that, no family history of having the same complaints similar to the patient. Besides, viral hepatitis markers are negative. Metabolic disorder like haemolytic disease is ruled out due to no history of spontaneous bleeding in this patient and no other chronic condition or medical history in this patient.

Based on the clinical complaints of jaundice and increase of serum bilirubin with dominance of direct bilirubin, the patient was in cholestasis state. At this stage of the disease, therapy should be given to reduce the damaging effects of cholestasis and AIH. In this case, the patient received steroid therapy consisting of prednisone at a daily dose of 2 mg/kg BW for two weeks, followed by a weekly tapering-off. Then, the patient was re-evaluated after the 2nd week of treatment. She no longer complained of abdominal pain. There was no sclera icteric; she gained 2 kg of weight, could eat more, and could walk (Figure 3). The abdominal circumference was smaller, the stool was getting darker, and the urine was turned clear yellow.

Figure 3. Improvement of jaundice after treatment

After 5 days of treatment, laboratory evaluation showed a decrease in total bilirubin 4.32 mg/dL, direct bilirubin 3.66 mg/dl, AST 49 U/L, and ALT 135 U/L, GGT 153.6 U/L, Alkaline phosphatase 160 U/L, and Albumin 5,22 g/dL. Following 14 days of treatment, laboratory evaluation showed a decrease in total bilirubin to 0.87 mg/dL, direct bilirubin to 0.76 mg/dL, AST 34 U/L, and ALT 49 U/L (Figure 4). After completion of treatment, a normal liver function test was obtained, with AST 36 U/L, ALT 33 U/L,

GGT 35.2 U/L, Alkaline phosphatase 218 U/L, and ANA test turned negative with a value of 12.2 AU/mL (Figure 5).

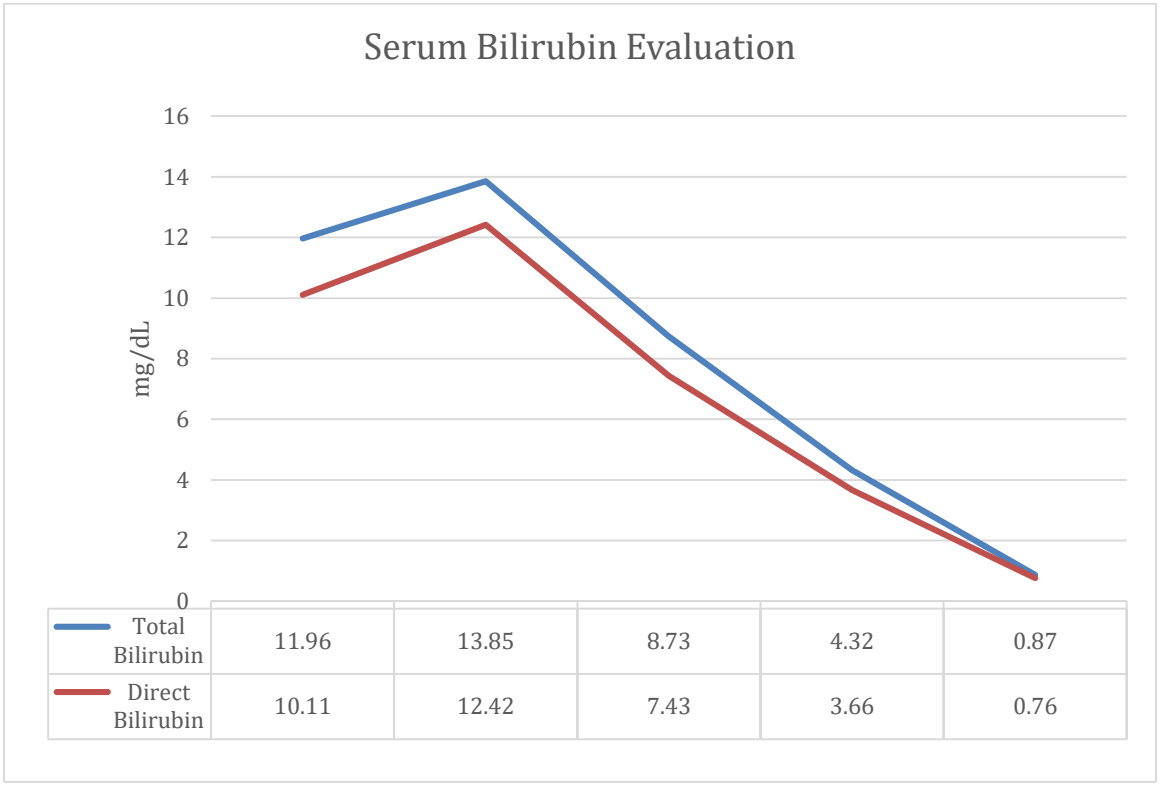

Figure 4. Serum Bilirubin Evaluation after treatment

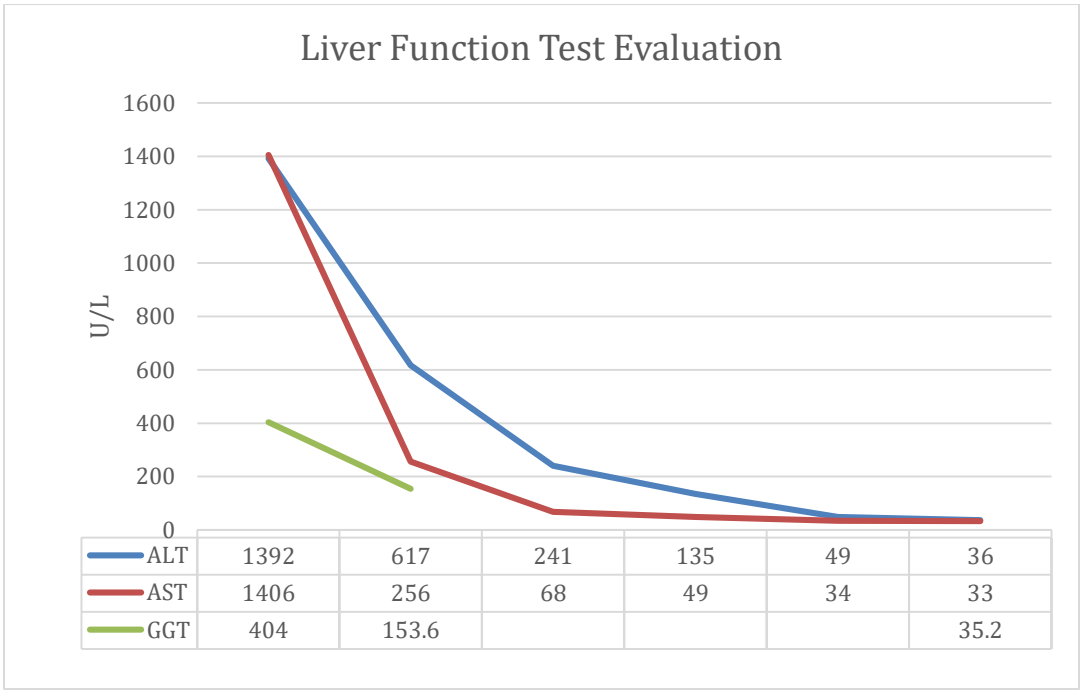

Figure 5. Liver Function Test Evaluation after treatment

DISCUSSION

Based on anamnesis data, the patient is a 6-year-old female with complaints of jaundice for 2 weeks. Epidemiologically, AIH patients are more dominated by women, such as in a study conducted in a hospital in Jordan, 75% of AIH patients were female with an average age of 9.84 ± 4.13 years.[8] A global meta-analysis also showed that most AIH patients in adulthood are female.[5] A population study showed a predominance of female patients with AIH, and based on these data, women have risk factors for AIH.[9] In this case, the patient is a 6-year-old female, so the patient has risk factors for AIH. Another risk factor for AIH is a viral infection, but to confirm infection, special tests are needed

which take time, and not all medical facilities may be able to perform them.[10]

In autoimmune diseases, diet is one of the risk factors included in the group of environmental factors, followed by some genetic factors that also influence it.[11] Similar to AIH, environmental factors also act as predisposing factors and increase the risk of AIH.[12] A study on industrial food additives found that they can disrupt human epithelial barrier function. Additionally, the immune response will be triggered via various pathways, such as molecular mimicry between dietary ingredients and self-antigens or the interaction of specific chemical products with self-molecules to produce new antigenic molecules.[13,14]

The patient complained of persistent jaundice for approximately 2 weeks. In addition, complaints were also accompanied by complaints of abdominal pain specifically on the right side, nausea and vomiting, and dark-coloured urine, where these complaints indicate the presence of acute hepatitis conditions with various causes, including AIH.[15] Based on an Arab study, initial presentation of AIH are jaundice, fatigue, pruritus, and abdominal pain, with jaundice as the most common early symptom of acute AIH at around 96% of the patients.[16] Similarly, in a severe acute AIH study, where the symptoms commonly found were fatigue, jaundice, and anorexia.[17] Jaundice and abdominal pain are also recognized in this patient. Other symptoms that the patient had previously felt were fever that had disappeared and pain in the legs for 1 month. Rheumatologic complaints such as joint pain are commonly found in liver disease, including AIH. When AIH is compared to rheumatologic disorders there will be distinct features, but there may be a lack of clear distinction between them and the patient's rheumatologic symptoms may cover up the existence of underlying liver disease. However, several things can distinguish AIH from other autoimmune diseases, the presence of certain autoantibodies that are more specific to AIH, such as anti-smooth muscle in type 1 AIH or anti-LKM1 and anti-LC1 in type 2 AIH, as well as the rise of liver enzymes.[18]

The physical examination supported the patient's complaint by revealing the icteric sclera and hepatomegaly. Patients with systemic autoimmunity often have asymptomatic hepatomegaly and elevated liver enzymes.[19] Clinical jaundice and hepatomegaly are also common in other hepatic disorders. Autoimmune hepatitis is a medical condition characterized by immune-mediated hepatocyte injury linked to the lysis of liver cells, which leads to fibrosis, liver failure, and inflammation. Autoantibodies will produce an antibody that plays a role in producing hepatitis conditions with positive ANA test results. Thus, the clinical course of AIH is similar to other hepatitis cases and lacks pathognomonic clinical symptoms.[12]

The first laboratory examination showed an increase in total bilirubin to 11.96 mg/dL, and a very high increase in liver enzymes AST and ALT 1406 and 1392, respectively. After stabilization of the general condition, bilirubin and liver enzymes decreased but still exceeded normal limits. In AIH patients, the hepatitis process that occurs causes a decrease in hepatic excretory and synthesis functions, which is described by an increase in serum bilirubin, a decrease in albumin, and an extension of the international normalized ratio (INR).[20] Serum transaminase elevation (AST, ALT) occurs frequently and may indicate the severity of the disease and the prognosis at presentation.[1] However, if only based on bilirubin and markers of hepatic function (AST and ALT) alone cannot support the suspicion of an autoimmune diagnosis. Hence, an autoantibody examination, one of which is an antinuclear antibody (ANA) test, is often needed to confirm the diagnosis of autoimmune diseases. This is because, in AIH, a positive ANA test result can be classified as type 1 AIH and is found in 60-70% of patients with AIH.[10] The patient also had an ANA test and the results were elevated. Unfortunately, due to limited facilities, the anti-smooth muscle, anti-LKM1, and anti-LC1 tests could not be performed.

The patient had an abdominal ultrasound examination and was found to have hepatitis, cholecystitis, and ascites. CT scan of the abdomen showed peritoneal tuberculosis, cholecystitis, and meteorismus. In general, AIH does not have specific characteristics on ultrasound examination, but there may be inflammatory signs such as enlarged perihepatic lymph nodes.[21] These features can also be found in other disease states such as hepatitis.[22] Thus, in the event of AIH, liver cirrhosis and its related complications can be found using ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI).[21]

In the anamnesis, complaints of jaundice for 2 weeks were obtained followed by abdominal pain, nausea and vomiting, and dark urine. Complaints of jaundice were obtained following a physical examination where there was icteric sclera. In addition, the presence of hepatomegaly also supports complaints of right abdominal pain. The patient also complained of leg pain and fever a few months earlier. The supporting examination showed an increase in bilirubin, markers of hepatic function, and elevated ANA test results. Based on these data, the patient was suspected of having autoimmune hepatitis, where based on a review of risk factors, several factors were favourable, such as female gender and the habit of eating instant food. The diagnosis of AIH can be established by histology results obtained from hepatic biopsy. Besides, hepatic biopsy may provide information on patient prognosis, management, and screening.[23] However, hepatic biopsy is an invasive diagnostic tool and in this patient was not performed because the family refused. Other than that, due to limited resources, serological markers facilities for SMA and LKM examinations are not available.

An idiopathic condition called autoimmune hepatitis is defined by immune-mediated hepatocyte injury that results in the breakdown of liver cells, resulting in inflammation, liver failure, and fibrosis. It is usually linked to autoantibodies. The pathophysiology of AIH is also thought

to involve deficits and defects in immune cells, including CD4+ T cells, regulatory T cells, CD8+ T cells, natural killer cells, B cells, plasma cells, and monocytes are also implicated.[12] AIH pathogenesis also includes disruption of the regulatory and effector immunity composition of leukocytes in the intrahepatic population and peripheral blood varies in the immunoregulatory systems. Immunosuppressive medication targets the inflammatory leukocytes in AIH cases.

According to the pathophysiology of AIH, there is hepatic damage caused by an inflammatory process mediated by the patient's immune system. If nothing is done about this inflammatory process, it will lead to hepatic fibrosis and eventually acute liver failure (ALF) which AIH is one of the common cause.[6] The patient also had autoimmune symptoms such as joint pain, which reinforced the suspicion of an autoimmune process. Based on the American Association for the Study of Liver Diseases guideline, first-line treatment of AIH is prednisone or prednisolone with or without azathioprine.[23] The first-line treatment also is meant to prevent disease progression and enhance the regression of fibrosis at the lowest risk of drug-induced complications. In this case, the patient is a suspected AIH case, in an effort to reduce symptoms and complications, steroid administration may be an option, especially in settings with limited facilities.

This patient was given steroid therapy with prednisone at a dose of 2 mg/kg BW/day for 2 weeks which was then tapered off per week, while azathioprine was not given. This treatment follows the AIH first-line treatment algorithm, where patients are given steroid treatment.[23] In order to monitor the condition, laboratory tests will be performed every 2 weeks. Clinical signs such as jaundice, abdominal pain, and myalgia will be monitored as well. Prednisone as steroid might have some adverse effects such as facial rounding, dorsal hump, hirsutism, weight gain, opportunistic infections, and emotional instability.[23] Therefore, to reduce the side effects of prednisone, the dose will be tapered gradually to reach a dose of 20 mg in a day, if after 2 weeks there is biochemical remission. After that, a dose reduction of 2.5-5 mg per 2-4 weeks is done until the patient only takes a dose of 5-10 mg a day to sustain biochemical remission. Then prednisone can be withdrawn and the patient is given azathioprine as a glucocorticoid-sparing-drug. When biochemical remission has been accomplished, patients with AIH should have laboratory examinations every 3-4 months and will be gradually increased to every 4-6 months if biochemical remission extends to 24 months.[23]

Steroids in the form of prednisolone play a role in stimulating remission in AIH and azathioprine plays a role in maintaining remission.[24] Parts of the glucocorticoid class of steroids, such as prednisone, have anti-inflammatory properties that are mediated by T-cell signalling and downregulation of proinflammatory cytokine production.[10],[25] In addition, glucocorticoids also modulate the proliferation of Tregs.[10,26] In one of the theories of AIH pathogenesis, It has been demonstrated that the malfunctioning of regulatory T cells (Tregs) is linked to a loss of tolerance to self-antigens. Tregs have been well studied in AIH and have been shown to play a crucial role in preserving immunological tolerance, according to numerous research.[10,27]

The aim of the treatment in this AIH case was to achieve biochemical remission, which was defined as normal levels of blood transaminase and IgG; in children, remission is also defined by negative or low-titre autoantibodies. After 2 weeks of prednisone therapy, there was satisfactory clinical and laboratory improvement. The complaints of yellow eyes and abdominal pain had disappeared, the stools were not pale, and the bowel movements were yellow. The patient's total bilirubin level and markers of hepatic function also decreased. There were no symptoms of predinson’s side effects. This case report shows that steroid therapy in this paediatric AIH case provided satisfactory results and met the treatment objectives according to the existing guidelines. Without invasive further diagnostics, steroid therapy in suspected AIH cases is expected to prevent further damage, especially in limited health facilities.

CONCLUSION

This case report demonstrates the good outcome of steroid therapy as an effort in a child with suspected AIH and the achievement of treatment goals according to existing guidelines. But, there might be potential misdiagnosis and side effects found in this patient. So, monitoring of treatment must be done alongside with the treatment regimen. Especially in healthcare settings with limited resources, the use of steroid therapy in suspected cases of AIH in limited diagnostic test settings may be of value in preventing further liver damage. Any additional immunosuppressants might be given for long-term treatment.

REFERENCES

I. Linzay CD, Sharma B, Pandit S. Autoimmune Hepatitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jun 20]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK459186/

II. Mieli-Vergani G, Vergani D, Baumann U, Czubkowski P, Debray D, Dezsofi A, et al. Diagnosis and Management of Pediatric Autoimmune Liver Disease: ESPGHAN Hepatology Committee Position Statement. J pediatr gastroenterol nutr. 2018 Feb;66(2):345–60.

III. Kim BH, Choi HY, Ki M, Kim KA, Jang ES, Jeong SH. Population-based prevalence, incidence, and disease burden of autoimmune hepatitis in South Korea. Yu ML, editor. PLoS ONE. 2017 Aug 3;12(8):e0182391.

IV. Tunio NA, Mansoor E, Sheriff MZ, Cooper GS, Sclair SN, Cohen SM. Epidemiology of Autoimmune Hepatitis (AIH) in the United States

Between 2014 and 2019: A Population-based National Study. Journal of Clinical Gastroenterology. 2021 Nov;55(10):903–10.

V. Hahn JW, Yang HR, Moon JS, Chang JY, Lee K, Kim GA, et al. Global incidence and prevalence of autoimmune hepatitis, 1970–2022: a systematic review and meta-analysis. eClinicalMedicine. 2023 Nov;65:102280.

VI. Mercado LA, Gil-Lopez F, Chirila RM, Harnois DM. Autoimmune Hepatitis: A Diagnostic and Therapeutic Overview. Diagnostics. 2024 Feb 9;14(4):382.

VII. Ansari Q, Sawant V, Kondekar A. Different presentation of autoimmune hepatitis in children: Case series. J Family Med Prim Care. 2023;12(2):406.

VIII. Altamimi E, Al Omari D, Obeidat H, Barham K. Retrospective, single-center analysis of autoimmune hepatitis in Jordanian children: clinical features, treatments, and outcomes. BMC Pediatr. 2024 Feb 8;24(1):102.

IX. Chung Y, Rahim MN, Graham JJ, Zen Y, Heneghan MA. An update on the pharmacological management of autoimmune hepatitis. Expert Opinion on Pharmacotherapy. 2021 Jul 24;22(11):1475–88.

X. Terziroli Beretta-Piccoli B, Mieli-Vergani G, Vergani D. Autoimmmune hepatitis. Cell Mol Immunol. 2022 Feb;19(2):158–76.

XI. De Luca F, Shoenfeld Y. The microbiome in autoimmune diseases. Clinical and Experimental Immunology. 2018 Dec 19;195(1):74–85.

XII. Sirbe C, Simu G, Szabo I, Grama A, Pop TL. Pathogenesis of Autoimmune Hepatitis—Cellular and Molecular Mechanisms. IJMS. 2021 Dec 17;22(24):13578.

XIII. Lerner A, Matthias T. Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease. Autoimmunity Reviews. 2015 Jun;14(6):479–89.

XIV. Mazzucca CB, Raineri D, Cappellano G, Chiocchetti A. How to Tackle the Relationship between Autoimmune Diseases and Diet: Well Begun Is Half-Done. Nutrients. 2021 Nov 5;13(11):3956.

XV. Schaefer TJ, John S. Acute Hepatitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jun 20]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK551570/

XVI. Aljumah AA, Al-Ashgar H, Fallatah H, Albenmousa A. Acute onset autoimmune hepatitis: Clinical presentation and treatment outcomes. Annals of Hepatology. 2019 May;18(3):439–44.

XVII. Zheng L, Liu Y, Shang Y, Han Z, Han Y. Clinical characteristics and treatment outcomes of acute severe autoimmune hepatitis. BMC Gastroenterol. 2021 Dec;21(1):93.

XVIII. Fernandes B. Rheumatologic manifestations of hepatic diseases. aog [Internet]. 2019 [cited 2024 Jun 21]; Available from: http://www.annalsgastro.gr/files/journals/1/earlyview/2019/ev-05-2019-10-AG4472-0386.pdf

XIX. Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD. Liver involvement in patients with systemic autoimmune diseases. Maedica (Bucur). 2013 Sep;8(4):394–7.

XX. Biewenga M, Inderson A, Tushuizen ME, Crobach ASLP, Van Hoek B. Early Predictors of Short-Term Prognosis in Acute and Acute Severe Autoimmune Hepatitis. Liver Transpl. 2020 Dec;26(12):1573–81.

XXI. Dong Y, Potthoff A, Klinger C, Barreiros AP, Pietrawski D, Dietrich CF. Ultrasound findings in autoimmune hepatitis. WJG. 2018 Apr 21;24(15):1583–90.

XXII. Schreiber-Dietrich D, Pohl M, Zentrum der Kinderheilkunde Abteilung für Kindergastroenterologie und Mukoviszidose, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany, Cui XW, Innere Medizin 2, Caritas Krankenhaus Bad Mergentheim, Bad Mergentheim, Germany, Braden B, et al. Perihepatic lymphadenectomy in children with chronic viral hepatitis. J Ultrason. 2015 Jul 20;61:137–50.

XXIII. Mack CL, Adams D, Assis DN, Kerkar N, Manns MP, Mayo MJ, 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 Aug;72(2):671–722.

XXIV. Lohse AW, Sebode M, Jørgensen MH, Ytting H, Karlsen TH, Kelly D, et al. Second-line and third-line therapy for autoimmune hepatitis: A position statement from the European Reference Network on Hepatological Diseases and the International Autoimmune Hepatitis Group. Journal of Hepatology. 2020 Dec;73(6):1496–506.

XXV. Ramamoorthy S, Cidlowski JA. Corticosteroids. Rheumatic Disease Clinics of North America. 2016 Feb;42(1):15–31.

XXVI. Libert C, Dejager L. How Steroids Steer T Cells. Cell Reports. 2014 May;7(4):938–9.

XXVII. Longhi MS, Mieli-Vergani G, Vergani D. Regulatory T cells in autoimmune hepatitis: an updated overview. Journal of Autoimmunity. 2021 May;119:102619.