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Defying the typical: Prolonged Cholestasis in Children with Hepatitis A – A Case Series

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Abstract:

Background: Hepatitis A virus (HAV) is a common cause of viral liver inflammation in children, usually resolving on its own without complications. However, in rare cases, it can lead to prolonged cholestasis, which creates challenges for diagnosis and treatment.

Methods: This case series discusses five pediatric patients who developed prolonged cholestasis after HAV infection. The study examines their symptoms, treatments, and outcomes, focusing on the success of conservative treatment without the use of oral corticosteroids. It highlights the clinical signs and lab results that help recognize this uncommon condition.

Results: Initially, the children showed typical symptoms of acute Hepatitis A, which later progressed to prolonged cholestasis. High levels of bilirubin and alkaline phosphatase but normal liver enzyme activity identified this. Conservative management, including supportive care and ursodeoxycholic acid, helped all patients recover within 2 to 10 weeks. Notably, no corticosteroids were needed, and all patients fully recovered without any relapses.

Conclusion: Prolonged cholestasis can complicate Hepatitis A in children, but recognizing it early and managing it conservatively can lead to full recovery without aggressive treatments. This series underscores the importance of monitoring such cases carefully and emphasizes preventive measures like vaccination and good sanitation to control HAV spread.

Keywords: Hepatitis A, Children, Cholestasis, Rare Manifestations, Conservative Management.

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Introduction:

Hepatitis A is commonly known for its mild and self-limiting nature, especially in children. However, this article explores an unusual progression of the disease – prolonged cholestasis (1,2). This condition involves a persistent blockage in bile flow, causing symptoms like jaundice and itching for extended periods. Through a detailed review of cases, this study aims to deepen our understanding of how to manage this rare condition in children (3). With cases of atypical Hepatitis A on the rise, early detection and effective treatment strategies are becoming increasingly important. Additionally, the study advocates for preventive measures like vaccination and better hygiene to curb the spread of Hepatitis A(4,5).

Case Summary : Case 1

A 13-year-old prepubertal female arrived with a 20-day history of jaundice. Her symptoms manifested in form of jaundice, dark urine, and pale stools, which followed a week of fever and vomiting. In the initial examination, she was stable but showed signs of pallor, jaundice, and an enlarged liver and spleen. However, she displayed no signs of severe liver complications, like ascites or encephalopathy, which suggested her liver was still functioning well.

Laboratory tests showed high bilirubin levels but normal liver enzyme and clotting profiles. Tests confirmed she had Hepatitis A along with a secondary infection of Scrub typhus. Treatment was started using ursodeoxycholic acid (UDCA), antihistamines, and topical creams for itching. By the sixth week, her liver function began improving, though bilirubin levels took longer to normalize.

Table 1: Summary of Liver Function Tests Over Time:

Test	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Total Bilirubin (mg/dl)	**16.53**	**14.34**	**14.4**	**10.8**	**8.9**	**2.6**	1.2
Direct bilirubin (mg/dl)	**8.24**	**7.6**	**7.8**	**7.5**	**4.6**	**1.2**	0.8
Albumin (g/dl)	**3.9**	-	-	-	-	**3.6**	4.2
Total Protein (g/dl)	**7.78**	-	-	-	-	**6.8**	-
A/G Ratio							
AST (U/L)	**130**	-				**43**	
ALT (U/L)	**69**					**36**	
ALP(U/L)	**523**					**320**	
GGT (U/L)	**211**						
PT/INR	**12.70/0.96**				**11.6/0.93**		

Over eight weeks, her symptoms fully resolved, showing that a conservative approach to treatment, including the use of UDCA and supportive care, was effective for managing prolonged cholestasis caused by Hepatitis A.

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Case Summary : Case 2

A 15-year-old girl, excelling academically and current on all her vaccinations, experienced six months of off-and-on fever, body aches, and chills. Over three months, she developed pain in both lower limbs, which made it hard for her to stay physically active. About three weeks before visiting the hospital, she started experiencing whole-body itching that began in her hands, followed by the appearance of jaundice.

During her checkup, the girl's vital signs were stable, but her skin and eyes were clearly jaundiced. Her liver was tender to the touch and notably enlarged, measuring about 16 cm. There were no signs of severe liver dysfunction, such as fluid accumulation or neurological issues.

Laboratory tests confirmed she had Hepatitis A with high anti-HAV IgM levels (4.02) and additional infections of Scrub typhus and Typhoid fever. Tests ruled out other liver infections like Hepatitis B and C. Imaging studies found no obstructions in her bile ducts, indicating that her symptoms stemmed from cholestatic hepatitis A.

Treatment and Recovery:

She was treated with Azithromycin for Scrub typhus, ursodeoxycholic acid (UDCA), and supportive measures such as itch relief and liver support. Her bilirubin levels steadily dropped, and her liver function improved over 42 -50 days.

Table 2: Liver Function Test Trends:

Test	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Total Bilirubin (mg/dl)	**6.83**	**7.41**	**6.57**	**7.07**	**6.6**	**3.54**	1.8
Direct bilirubin (mg/dl)	**3.55**	**3.87**	**3.22**	**3.52**	**3.4**	**1.55**	0.9
Albumin (g/dl)	**3.67**	**4.00**	**4.00**	**3.9**	**3.5**	**-**	4.0
Total Protein (g/dl)	**8.05**	**8.22**	**8.64**	**8.62**	**-**	**-**	-
A/G Ratio	**0.84**	**074**	**0.86**	**8.62**	**-**	**-**	**-**
AST (U/L)	**113**	**111**	**128**	**164**	**-**	**-**	**-**
ALT (U/L)	**80**	**73**	**91**	**209**	**-**	**-**	**-**
ALP(U/L)	**646**	**677**	**656**	**437**	**-**	**-**	**-**
GGT (U/L)	**248**	**247**	**215**	**197**	**-**	**-**	**-**
PT/INR	**-**	**11.6/0.87**	**11.7/0.88**	**11.9/0.88**	**-**	**-**	**10.4/0.80**

By the end of the treatment period, her symptoms had resolved completely, highlighting the effectiveness of a conservative management approach for complex cases involving multiple infections.

Case Summary : Case 3

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A 14-year-old adolescent male came to the hospital with a 10-day history of jaundice and four days of fever. His symptoms included dark-colored urine, itching, black-colored stools, loss of appetite, and increased sleepiness. During the examination, he was found to have a fever, noticeable jaundice, and a non-tender but significantly enlarged liver (15 cm). There were no signs of spleen enlargement, fluid buildup, or other serious complications.

Diagnostic Findings:

Initial lab tests revealed abnormal liver function, prompting further investigation. Imaging studies ruled out any issues with the gallbladder or bile ducts. Blood tests confirmed an acute Hepatitis A infection. Further testing ruled out autoimmune hepatitis and other liver disorders, with no evidence of Kayser-Fleischer rings, which are associated with Wilson's disease.

Table 3: Summary of Liver Function Tests:

Test	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Total Bilirubin (mg/dl)	**25.4**	**20.51**	**20.71**	**19.47**	**11.62**	**9.61**	4.75
Direct bilirubin (mg/dl)	**12.8**	**10.46**	**9.62**	**9.23**	**7.43**	**4.53**	1.92
Albumin (g/dl)	**4.18**	**3.93**	**4.20**	**3.81**	**4.02**	**3.84**	4.33
Total Protein (g/dl)	**7.99**	**7.37**	**7.11**	**7.53**	**-**	**7.61**	7.81
A/G Ratio	**1.10**	**1.14**	**1.18**	**1.14**	**1.15**	**1.02**	**1.24**
AST (U/L)	**57**	**51**	**50**	**51**	**35**	**34**	**41**
ALT (U/L)	**110**	**58**	**48**	**52**	**35**	**27**	**37**
ALP(U/L)	**299**	**278**	**284**	**274**	**275**	**232**	**183**
GGT (U/L)	**26**	**18**	**19**	**18**	**18**	**16**	**18**
PT/INR	**15.3/1.17**	**14.10/1.07**	**-**	**-**	**13.2/1.1**	**-**	**-**

Management and Outcome:

The patient was treated conservatively with supportive care and close monitoring of his liver function. Over the next eight weeks, his liver function tests showed significant improvement, and his bilirubin levels returned to nearly normal. Continued follow-ups in the outpatient department confirmed a complete recovery without any indications of autoimmune hepatitis or other complications.

Case Summary: Case 4

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A 16-year-old adolescent male came to the hospital with a two-week history of fever, abdominal pain, and vomiting. These symptoms had not improved despite prior symptomatic treatment. A week later, he developed intense itching all over his body and noticeable jaundice, prompting an evaluation for Acute Infective Hepatitis.

Diagnostic Findings:

Test	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Total Bilirubin (mg/dl)	**14.57**	**17.19**	**11.88**	**-**	**-**	**1.8**	0.8
Direct bilirubin (mg/dl)	**12.78**	**8.12**	**6.53**	**-**	**-**	**0.9**	0.6
Albumin (g/dl)	**3.07**	**3.53**	**4.03**	**-**	**-**	**4.0**	3.8
Total Protein (g/dl)	**5.96**	**8.17**	**7.11**	**-**	**-**	**-**	-
A/G Ratio	**1.06**	**1.31**	**1.31**	**-**	**-**	**-**	**-**
AST (U/L)	**79**	**156**	**104**	**-**	**-**	**-**	**-**
ALT (U/L)	**220**	**183**	**129**	**-**	**-**	**-**	**-**
ALP(U/L)	**420**	**306**	**298**	**-**	**-**	**-**	**-**
GGT (U/L)	**78**	**157**	**94**	**-**	**-**	**-**	**-**
PT/INR	**11.2/1.65**	**-**	**13/0.98**	**-**	**-**	**-**	**10.4/0.80**

Initial tests showed elevated bilirubin levels and liver enzymes, indicating a cholestatic pattern of hepatitis. Bloodwork confirmed an acute Hepatitis A infection with a high anti-HAV IgM titer (2.0). Imaging studies, including an abdominal ultrasound, ruled out blockages or obstructions in the bile ducts, supporting the diagnosis of cholestatic Hepatitis A.

Management and Outcome:

The patient was treated with supportive care, focusing on maintaining proper nutrition and managing symptoms. Over the next nine weeks, his bilirubin levels gradually returned to normal, and his symptoms resolved completely. This case highlighted how a conservative approach to treatment can effectively manage even more severe presentations of Hepatitis A.

Case Summary: Case 5

A 14-year-old girl was admitted to the hospital with a week-long history of fever and vomiting. Her condition worsened over the next day, with discolored urine, slurred speech, and altered mental status. Upon examination, she displayed signs of jaundice and early-stage hepatic encephalopathy (mental confusion caused by liver dysfunction). Her abdomen showed an enlarged, tender liver but no signs of chronic liver failure like fluid accumulation.

Diagnostic Findings:

Laboratory tests revealed fluctuating bilirubin levels and abnormal liver enzyme patterns, consistent with a cholestatic form of hepatitis. Tests confirmed an acute Hepatitis A infection

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with high anti-HAV IgM titers (4.01). Other liver infections, such as Hepatitis B and C, were ruled out. Imaging studies also showed no obstructions in the bile ducts, eliminating mechanical causes of her symptoms.

Table 5: Summary of Liver Function Tests:

Test	Day 1	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
Total Bilirubin (mg/dl)	**8.57**	**12.24**	**7.85**	**8.95**	**-**	**1.8**	0.8
Direct bilirubin (mg/dl)	**4.78**	**6.81**	**3.06**	**5.22**	**-**	**0.9**	0.6
Albumin (g/dl)	**3.07**	**3.97**	**2.79**	**3.06**	**-**	**4.0**	3.8
Total Protein (g/dl)	**5.96**	**8.33**	**6.09**	**6.86**	**-**	**-**	-
AST (U/L)	**794**	**112**	**97**	**90**	**-**	**-**	**-**
ALT (U/L)	**2520**	**56**	**407**	**184**	**-**	**-**	**-**
ALP (U/L)	**520**	**179**	**217**	**312**	**-**	**-**	**-**
GGT (U/L)	**63**	**33**	**66**	**42**	**-**	**-**	**-**
PT/INR	**21.20/1.05**	**-**	**13/0.98**	**-**	**-**		**10.4/0.80**

Management and Outcome:

The patient was treated with ursodeoxycholic acid (UDCA) alongside supportive therapies, including fluids and nutritional support.

Her condition gradually improved, with bilirubin levels normalizing and liver function returning to normal within 8–10 weeks. The successful resolution of her symptoms demonstrated the effectiveness of conservative treatment, even in cases complicated by mild encephalopathy.

Discussion:

Research has shown that although Hepatitis A virus (HAV) infection typically resolves on its own, there are documented cases of unusual disease presentations, including extended illness periods and recurring episodes. Our research contributes fresh insights to current knowledge through an examination of young patients who developed sustained cholestasis, an uncommon complication of HAV infection. These pediatric cases showed gradual improvement in liver enzyme levels across multiple weeks, supporting earlier findings that indicate a portion of children infected with HAV may experience non-standard disease progression (6,7)

The occurrence of extended HAV infection is uncommon, with liver function markers usually returning to baseline within half a year of initial infection. When the disease resurfaces, these subsequent episodes tend to be milder and resolve quickly, typically within 21 days (8). Clinical approaches to managing persistent jaundice caused by HAV-related cholestasis vary widely, from basic supportive care to steroid therapy, though the benefits of steroids remain controversial. An instructive example comes from a documented case of a pre-teen patient whose prolonged cholestatic condition failed to respond to initial treatments with

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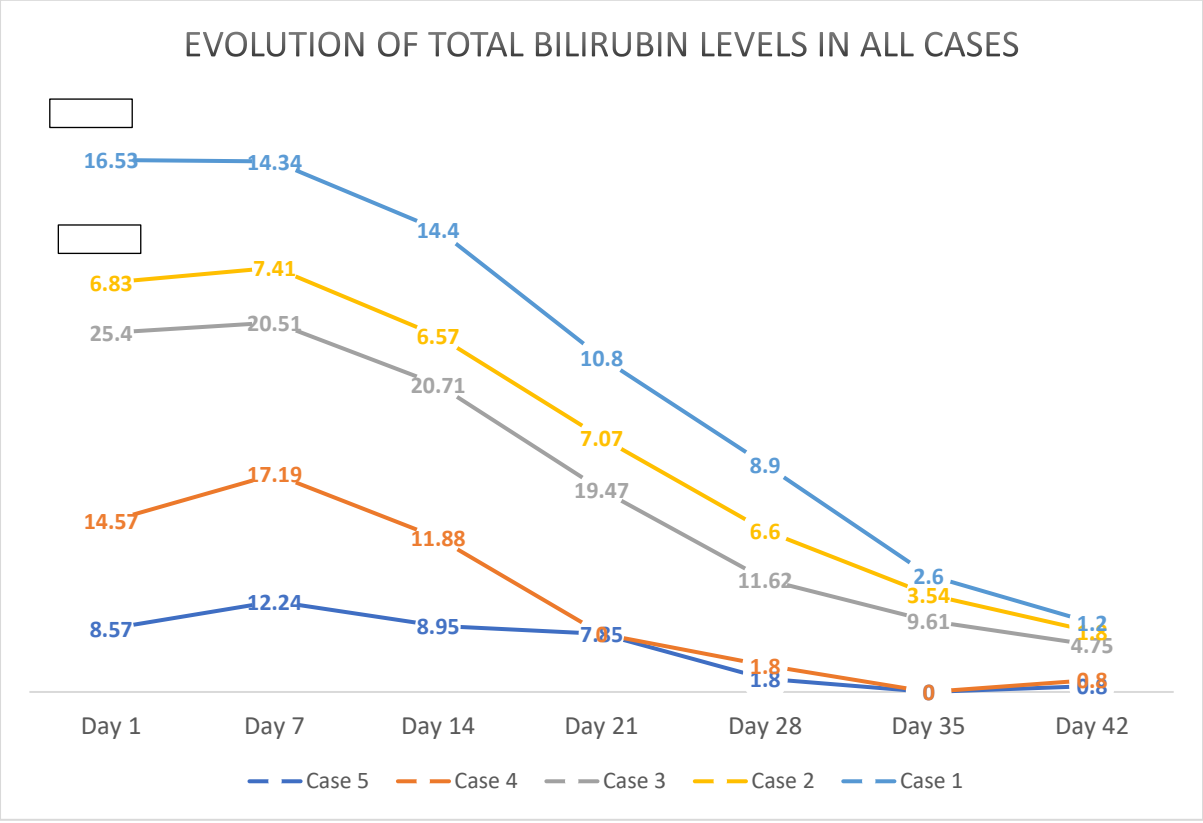
cholestyramine and rifampicin. This patient's persistent itching eventually improved after starting oral prednisolone treatment at week eight of the illness (9,10).

In examining our patient group, we opted for a minimally interventional approach, avoiding steroid administration. We observed that bilirubin concentrations reached their highest points approximately four weeks into the illness, followed by a steady decrease to normal levels over the subsequent month (11,12). This outcome suggests that cholestatic jaundice in HAV infection may resolve naturally without steroid intervention, thus avoiding potential complications such as disease recurrence associated with steroid use (13).

Below is the line diagram representing all cases: Figure 1

Figure 1:



Limitations:

While our research group analyzed a constrained number of cases, potentially limiting broad generalizations, the findings contribute meaningful observations regarding the diverse presentations and therapeutic approaches in extended cholestasis associated with HAV

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infection. Current medical documentation presents various treatment protocols, spanning from fundamental supportive measures to more complex drug-based interventions. Our investigation, which prioritized non-aggressive therapeutic methods, corresponds with established guidelines while demonstrating the success of measured approaches in particular instances of sustained cholestasis.

The documented outcomes not only validate the existence of unusual prolonged cholestatic manifestations in childhood HAV infections but also support the effectiveness of restrained treatment protocols. These results prompt a critical reassessment of intensive therapeutic interventions, advocating for a thoughtful analysis of risk-benefit ratios when considering steroid administration in comparable clinical scenarios. This careful evaluation of treatment intensity versus potential complications represents a significant contribution to the evolving understanding of managing atypical HAV presentations in pediatric populations

Conclusions:

Our research underscores the critical importance of thorough clinical oversight in cases of pediatric HAV infection presenting with extended jaundice, particularly emphasizing prompt identification and intervention for sustained cholestasis. The documented outcomes demonstrate that attentive monitoring coupled with non-aggressive therapeutic approaches can lead to successful patient recovery. These observations validate the effectiveness of measured intervention strategies when appropriately implemented.

The insights gained from this investigation reinforce the significance of preventative healthcare measures, including immunization programs and enhanced sanitation practices, as primary tools for reducing both the occurrence and complications of HAV infections. Looking ahead, expanded research initiatives should examine extended patient outcomes and optimize treatment protocols, ultimately strengthening community health strategies. This approach would contribute to developing more refined and evidence-based guidelines for managing similar cases in diverse healthcare settings.

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