



Case Report

A 10 Years Old Girl with Isolated Hepatitis (Fulminant Liver Failure) was Incidentally Found to Have B-Cell Leukemia Evident in Liver Histopathology

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Citation: Hejji Z, Abouhazima K, Rahman HA, Al Masri W, Ilaria R (2023) A 10 Years Old Girl with Isolated Hepatitis (Fulminant Liver Failure) was Incidentally Found to Have B-Cell Leukemia Evident in Liver Histopathology. Arch Pediatr 8: 296. DOI: 10.29011/2575-825X.100296

Received Date: 26 October 2023; **Accepted Date:** 1 November; **Published Date:** 6 November 2023

Abstract

A young girl who was previously healthy with no evidence of systemic illness but rather sudden onset of abdominal pain, jaundice and fever was evaluated as hepatitis for investigation and management. Main differential was viral hepatitis among others, as the most common reasons of acute liver failure. However, the initial investigations ruled out infectious sources, drug induced causes of the disease, and chronic liver diseases. Thus, as hepatitis with impending liver failure of unknown source, liver biopsy was performed. Surprisingly, results were persistent with leukemia. This child was an extraordinary case that presented as liver case initially, however ended up being a systemic illness, malignancy, causing secondary liver failure. Upon reviewing records, all children either manifested early on or later with hepatitis, have other signs of malignancy which were evident with initial presentation to consider malignancy as a source.

Keywords: Liver Failure; Liver Histopathology; Hepatitis

Introduction

Hepatitis and acute liver failure are manifestations that can happen solely or in combination with other systemic diseases. Usually, having other manifestations can guide us and work us as a clue to the differential in mind when approaching any patient. Acute liver failure used to be a rare phenomenon in pediatric which is becoming more common specially after COVID-pandemic, and its life threatening that can occur suddenly especially in previously healthy otherwise kids. It is considered to happen when liver fails to function to the threat leading to severe dysfunction within a short period of time. It involves coagulopathy, and can progress to hepatic encephalopathy or even metabolic disruptions. Most common cause and usually has good prognosis is infections

specially hepatitis A or E. Other include: autoimmune, drug induced (acetaminophen), toxins, metabolic or even rare genetic conditions such as GALD/LARS1. Manifestations usually come as jaundice, with abdominal pain and nausea and vomiting which can manifest with worsening mental status if was severe requiring support with N-acetylcysteine infusion as anti-oxidant or even ICU support care until recovery. However, after the era of COVID- pandemic, many acute liver failure whether resolved or worsened leading to urgent liver transplant remained a mystery with unknown cause. An interesting relation of leukemia cases developing acute liver failure secondary to disease progression/metastasis or secondary to chemotherapy are well known and studied.

However, having a leukemia case manifesting as solely acute liver failure with no other leukemia markers or signs was very interesting to encounter. As its well known in literature,

leukemia is a type of cancer affecting bone marrow and blood cells. It's usually not associated with acute liver failure, but rarely can manifest as mentioned above. Case of leukemia can be missed as leukemic infiltrates spread in liver instead of BM and that's why a case presentation of a young girl who was diagnosed as leukemia by liver biopsy when undergoing liver failure work up. Thus, these two distinct medical conditions can coincide in rare occasions and its essential for every healthcare providers to keep in mind when unknown cause of liver failure is encountered even when full blown picture is not manifested.

Case of K. A

A 10 years old girl, previously healthy, Middle Eastern, resident in Qatar. Presented to emergency center, with three durations of abdominal pain, which was severe, diffused with no radiation, and was associated with vomiting, fever and vertigo. Child otherwise denied recent travel history, sick contact, drug ingestion or any medical/surgical background or bleeding tendency. Bedside Exam, with stable vital signs and GCS 15/15, was only remarkable for jaundice and diffused abdominal tenderness. Child was managed as acute hepatitis pending full work up. Blood investigations were evident for impending liver failure, and full blood investigations were sent to rule out acute and chronic causes of liver disease. Child was admitted initially to intensive care unit for one night observation for hepatic encephalopathy risk, which did not occur. Managed with Nacetylcysteine infusion for 48hrs, and vitamin k. Once stable, Child was then managed in the floor. Child remained well and stable, however liver enzymes were not trending down significantly.

Hyperbilirubinemia and persistent neutropenia. With some improvement noted, liver biopsy was done and patient was sent home for follow up. Returned back in almost 48hrs with fever, pancytopenia picture and maculopapular rash. At that time, biopsy results were highly suggestive of leukemia and patient was transferred to oncology floor for diagnosis and management. Currently following chemotherapy protocol as per Sidra Medicine Institute.

Blood investigations with graph trends

Infectious causes of Hepatitis ruled out which included: A,B,C, D, E--NEG

Resp/GI pcr-- Neg Blood virology (CMV, HSV, EBV)

Alpha -1 antitrypsin-Normal Covid IgG ab -- >2080

Plasma Amino acids- high cysteine ? related to liver failure

Toxicology: negative for aspirin and acetaminophen

Wilson Work up: negative

Autoimmune hepatitis work up-Normal

Complete blood count and peripheral smear was unremarkable.

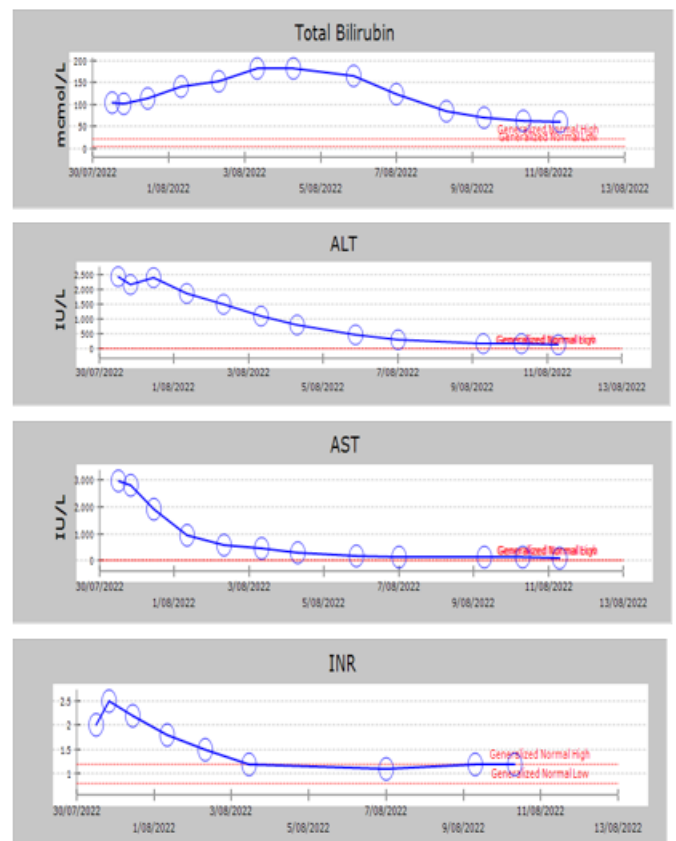
Inflammatory markers (CRP/ESR) were: negative

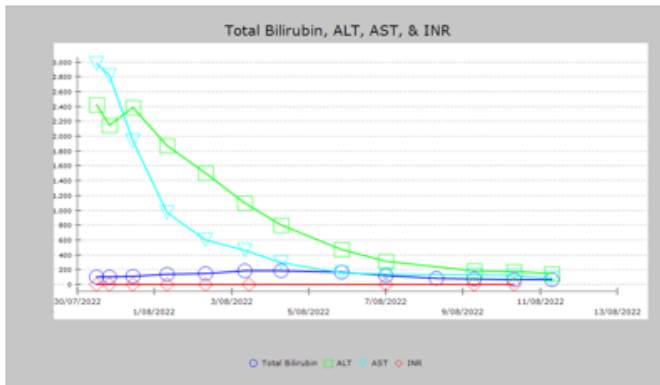
Child spiked fever 2 days after discharge after liver biopsy, and work up showed pancytopenia picture (hgb 10, platelets 140, and neutropenia of 0.2) with elevated ferritin and LDH level. LDH >1200

Ferritin 1737

Negative infectious work up again, including blood, urine cultures.

Lymphocyte subset was sent, showed low NK cells and borderline low B cells





Imaging

US abdomen: echogenic normal sized liver with no focal lesions.

Histopathology

Liver biopsy

Portal atypical B-cell blastoid TdT positive B lymphoid infiltrate, which was confirmed by bone marrow biopsy. Child is currently being treated with chemotherapy as per COG protocol, and showing good response. Liver enzymes were normalized, and now transaminases noted due to multifactorial reasons.

Methods

Using Pubmed to search the database for articles that could have presented case reports related to our case. Key words included: ALF AND Leukemia AND pediatric, acute liver failure AND Leukemia AND pediatric

Discussion

It is interesting to find that our case is very unique for its presentation as accidental finding of leukemia noted in liver biopsy was the first to happen in literature. Literature reviewed and case reports mentioned and studies of children showed evidence of malignancy with high suspicion given the other red flags/risk factors involvement in the cases noted, in form of lymphadenopathy, hepatosplenomegaly, and coagulopathy features with pancytopenia pictures. However, this case did not have any systemic manifestations rather solely liver dysfunction picture and was diagnosed by liver biopsy as part of acute liver failure of unknown diagnosis work up. All cases reported are in adults and had presentations which were suggestive of malignancy in addition to raised liver enzymes/hyperbilirubinemia, and in pediatric almost 3 case reports with similar fashion. Recent case report in Arrowhead Regional Medical Center, Colton, USA, in 2023 reported a young adult, 18 years of age who presented with jaundice and transaminases with axillary LAD, family history positive for leukemia, with blasts cell evident in blood smear [1-

8]. A 7 years old boy, reported as a case of ALL who also presented with history of transaminases which got worse over weeks, and was diagnosed with flow cytometry.

Child also had hepatosplenomegaly and Inguinal lymphadenopathy [6]. Another case report of a 15 years old adolescent child in Department of Hematology, Third Hospital of Hebei Medical University, Shijiazhuang in China, who presented with history of fatigue, with jaundice and pancytopenia with LAD as well, and noticed atypical cells in peripheral smear which expedite the need for bone marrow aspirate and flow cytometry that confirmed the diagnosis of ALL [4].

Conclusion

As well as hepatitis becoming a major and common presentation seen in children within the last few years, it was never being associated with malignancy as sole presenter. Rather children will have evidence of systemic illness involvements and other suggestive indicators are present. This case indeed was incidental finding, and can be a key to emphasize the nature that malignancy can occur in any shape. With growing number of hepatitis and malignancy, children can present interchangeably and broadening the differential and working the child up for rarer causes can be undertaken if needed.

Notes on patient consent

Informed consent: taken from parents as the child is a minor.

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