Pediatric Oncall Journal
DOI: https://doi.org/10.7199/ped.oncall.2026.91

TEACHING FILES (GRAND ROUNDS)

PROGRESSIVE THROMBOCYTOPENIA IN A CHILD WITH WILSON'S DISEASE

Sheryl Chettiar, Suhani Jain, Vishrutha Poojari, Shivangi Tetarbe, Ira Shah.
Department of Pediatric Gastroenterology and Hepatology, B J Wadia Hospital for Children, Mumbai, Maharashtra, INDIA.

ARTICLE HISTORY
Received 05 Aug, 2025
Accepted 04 Mar, 2026

KEYWORDS
Wilson's Disease, Penicillamine, Thrombocytopenia.

Clinical Problem

An 8-year 7-month-old female suffering from Wilson's disease since February 2025 presented in June 2025 with fever and abdominal distention for 4 days, diarrhea for 2 days, lethargy and decreased urine output for 1 day. She was on penicillamine (20 mg/kg/day) since February 2025. She had a urinary tract infection with urine culture positive for Enterococcus faecalis in April 2025 for which she had been hospitalised and given IV antibiotics (details of treatment not available). Her immunizations were up to date. On examination in June 2025, weight was 25 kg (25th percentile, according to Indian Academy of Pediatrics (IAP) and height was 121 cms (10th percentile, IAP). She was afebrile, with heart rate 88/min, respiratory rate 24/min, blood pressure 112/64 mmHg. Abdominal examination revealed hepatosplenomegaly with ascites. Systemic examination was normal. Laboratory investigations are as shown in Table 1.

Table 1: Laboratory investigations

	Feb 2025	April 2025	Day 1 of hospitalisation in June 2025	Day 2 of Hospitalisation (in PICU)	Day 4 of Hospitalisation	Day 9 of hospitalisation	Day 11 of Hospitalisation	Day 13 of Hospitalisation	Day 15 of Hospitalisation
Hemoglobin (g/dl)	6.9	9.6	8.4	8.8		9.2	9.0	8.9	8.6
White cell count (cells/cumm)	3960	4210	8660	1470		2980	3090	2890	2290
Neutrophil (%)	65.8	61.4	76.3	68		41.5	55.3	39.6	41
Lymphocyte (%)	27.3	33.9	16.7	25		46.25	35.8	48.4	46
Platelet count (cells/cumm)	64000	58000	46000	64000		63000	62000	58000	48000
Reticulocyte count (%)	1.9								
Sodium (mmol/L)	135	131	132	135	134	138	135	134	137
Potassium (mmol/L)	3.8	2.9	3.8	3.7	4.6	4.7	4.2	5.2	4.6
BUN/Creatinine	9/0.41	7/0.22	31/0.97	25/0.51	-/0.32			-/0.3	
PT/INR	25.7/2.34	28.½.48	25.3/2.15		19.5/1.65	2.6/1.91	19.8/1.66	20.9/1.75	16.4/1.36
Bilirubin(Total) (mg/dl)	4.5	4.2	2.3					2.5	
Bilirubin (Direct) (mg/dl)	3.9	3.6	1.7					0.9	
Serum glutamic oxaloacetic transaminase (SGOT) (U/L)	200	134	87			105		101	
Serum glutamic pyruvic transaminase (SGPT)(U/L)	75	48	59			56		51	
Serum gamma glutamyl transferase (GGT)(U/L)	68		56					54	
Serum alkaline phosphatase (ALP) (U/L)	397	457	4.5			449		458	
Total Protein (gm/dl)	6.2	6.1	5.2			6.8		6	
Serum albumin (gm/dl)	2.6	2.1	1.8		1.9	3.1		2.7	
Ammonia	86		168	85			144	147	
C Reactive Protein	18.7	20	73		24.5		5.2	4.1	

Address for Correspondance: Sheryl Vincent, Chettiar, Vasant Galaxy, Mars-C-Wing, Flat No: 402, Bangur Nagar, Goregaon (W), Mumbai.
Email: sherylchettiar12@gmail.com

Ultrasound (USG) abdomen showed a cirrhotic liver, splenomegaly with multiple splenic collaterals, moderate ascites, and collapsed, edematous bowel loops. Ascitic tap was done under random donor platelet (RDP) transfusion with 330 mL of fluid drained. Ascitic fluid analysis revealed protein: 0.5 g/dL, sugar: 163 mg/dL, red blood cells (RBCs):

1000 cells/mm³, white blood cells (WBCs) 3072 cells/mm³ with 73% neutrophils. She was started on IV cefotaxime. The following day, she had altered sensorium, and sodium benzoate, rifaximin, and lactulose were added. She also received 1 unit of fresh frozen plasma (FFP). Oral penicillamine (20 mg/kg/day) and zinc (75 mg/day) were continued. Due to re-accumulation of ascites, a repeat paracentesis was performed on hospital day 4, draining 1350 mL of ascitic fluid. Analysis showed: protein: 0.4 g/dL, sugar: 106 mg/dL, WBCs: 151 cells/mm³ with 39% neutrophils and no RBCs, She was given intravenous albumin at 1 g/kg for volume replacement. In view of portal hypertension, carvedilol was initiated. She was given IV cefotaxime for 14 days and then discharged. NCCT thorax in May 2024 showed almost complete regression of the previously seen right paratracheal mass with subtle foci of fibroatelectatic changes.

Question – How to determine whether worsening cytopenia in a child on penicillamine is due to the drug or due to worsening portal hypertension and hypersplenism?

Discussion:

Wilson's disease (WD) is an autosomal recessive disease which results from mutations in the ATP7B gene which impairs the body's ability to eliminate excess copper through bile. As a result, copper builds up to toxic levels, particularly in the liver and other organs. Liver dysfunction is the earliest clinical manifestation, while neurological symptoms often emerge as the disease progresses.[1] Liver disease can manifest in a wide spectrum,ranging from asymptomatic, with only biochemical abnormalities to advanced cirrhosis with complications.[2] Patients can present with isolated splenomegaly as a result of subclinical cirrhosis accompanied by portal hypertension.[2] Other presentations include hemolysis, neurologic disease and psychiatric symptoms.[2]

Penicillamine, the first line treatment for WD, acts as a copper chelator, effectively lowering copper levels by excreting it through urine. It stimulates the production of copper-binding metallothionein proteins in the liver, which helps diminish copper toxicity.[1] Therapy is required lifelong but is often difficult due to frequent dosing and significant side effects.[1] Serious side effects requiring discontinuation occur in 20–30% of cases.[1] Early reactions (within 1–3 weeks) include fever, cutaneous eruptions, lymphadenopathy, neutropenia or thrombocytopenia, and proteinuria. Later effects may involve nephrotoxicity, lupus-like syndrome, fragile skin, Goodpasture syndrome, etc.[1]

The patient had been on Penicillamine for 5 months at a dose of 20 mg/kg/day and presented with thrombocytopenia, with a platelet count of 46,000 cells/cumm. Following RDP transfusion, there was only a marginal increase in platelet count followed by a persistent decrease throughout admission. The underlying cause of this thrombocytopenia remained uncertain, whether it was Penicillamine-induced or secondary to splenomegaly.

D-penicillamine is known to significantly reduce the platelet production rate through bone marrow suppression, presenting as a decline in cell lines.[3] However , another cause of decreased platelets can be an enlarged spleen as it enhances the filtration and breakdown of red blood cells, white blood cells and platelets.[4] Thrombocytopenia in chronic liver disease (CLD) is caused by multiple factors, including reduced platelet production, splenic pooling, and increased destruction.[4] An enlarged spleen from portal hypertension leads to platelet sequestration (hypersplenism). Platelet destruction is increased by factors such as shear stress, infections, fibrinolysis, autoimmune responses and elevated antiplatelet antibodies.[4] To differentiate between these causes, seeing the bone marrow response with a reticulocyte count is empirical. Reticulocytosis can be seen when there is hemolytic anemia with splenomegaly.[4]

For our patient, the retic count was 1.9%. This was suggestive that thrombocytopenia in our patient is caused directly as a side-effect of Penicillamine.

If thrombocytopenia, leukopenia, or anemia develops during treatment with penicillamine, the medication should be discontinued and other chelating agents should be used. Trientine tetrahydrochloride can be used as an alternative. It is known for it’s effectiveness and is a well-tolerated form of therapy with twice-daily dosing.[5]

Compliance with ethical standards

Funding: None

Conflict of Interest: None

References:

1 Peng AJ, Chen L, Li Y, Fang JJ, Zhou D, Feng P. Penicillamine for Wilson's disease. Cochrane Database Syst Rev. 2017 Sep 1;2017(9):CD009739.

2 European Association for the Study of the Liver. EASL-ERN Clinical Practice Guidelines on Wilson's disease. J Hepatol. 2025 Feb 22:S0168-8278(24)02706-5. doi: 10.1016/j.jhep.2024.11.007. Epub ahead of print.

3 Thomas D, Gallus AS, Brooks PM, Tampi R, Geddes R, Hill W. Thrombokinetics in patients with rheumatoid arthritis treated with D-penicillamine. Ann Rheum Dis. 1984 Jun;43(3):402-406.

4 Mitchell O, Feldman DM, Diakow M, Sigal SH. The pathophysiology of thrombocytopenia in chronic liver disease. Hepat Med. 2016 Apr 15;8:39-50.

5 Kamlin COF, M Jenkins T, L Heise J, S Amin N. Trientine Tetrahydrochloride, From Bench to Bedside: A Narrative Review. Drugs. 2024 Dec;84(12):1509-1518.