Haemolytic anaemia as an initial presentation of Wilson’s disease in paediatric patients

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- ❖ **Objectives and study:** Wilson’s disease is a rare autosomal recessive genetic disorder of copper metabolism, causing copper induced damage to various organs. The clinical presentation is highly diverse. Although hepatic disease is the common presentation in children and adolescents, neurologic, psychiatric, and haematological symptoms do occur. Haemolytic anaemia is a rare clinical manifestation of Wilson’s disease in up to 20 % (1).
- ❖ **Methods:** We report three cases of Wilson’s disease presented with haemolytic anaemia and liver involvement.

❖ **Patient 1**, 8-year-old boy presented with nausea, vomiting, abdominal pain, jaundice, dark urine and pale stools. Physical examination revealed hepatosplenomegaly, normal neurological status and Kayser-Fleischer rings in both eyes. The laboratory tests showed Coomb’s negative haemolytic anaemia, mildly elevated liver enzymes, both conjugated and unconjugated hyperbilirubinemia, hypoalbuminemia with coagulation failure. The diagnosis was genetically confirmed after registering low ceruloplasmin and high urinary copper excretion after penicillamine challenge.

❖ **Patient 2**, 7-year-old girl complained of fatigue, weight loss, abdominal pain, jaundice and dark urine. She had hepatomegaly and Kayser-Fleisher ring in the eyes with no neurological symptoms. Jaundice has reached extreme values of bilirubin up to 1892 µmol/l. Ceruloplasmin was normal, but the penicillamine challenge showed elevated copper in the urine. Genetic analysis confirmed Wilson’s disease.

❖ **Patient 3**, 16-year-old girl presented with jaundice and dark urine. She had hepatosplenomegaly, mild tremor and Kayser-Fleisher ring in the eyes. Ceruloplasmin was low and urinary copper excretion after penicillamine challenge was high. The genetic test showed she has compound heterozygous mutations.

➤ All patients showed Coombs-negative haemolytic anaemia with high reticulocytes rate and liver failure. All of them were tested for viral hepatitis and were negative. They are treated with penicillamine 20 mg/kg and have normal liver function one year later. Patient 3 is being transitioned and followed up by an adult hepatologist.

	Hgb g/l	RBC x 10 ¹²	MCV fl	Retic ‰	Coomb’s test
Patient 1	38	1.07	107	93	Negative (-)
Patient 2	51	1.5	113	65	Negative (-)
Patient 3	68	1.9	109	70	Negative (-)

	Hepatomegaly (under the rib)	Splenomegaly (under the rib)
Patient 1	2 cm	3,5 cm
Patient 2	5 cm	Non palpable
Patient 3	5 cm	3 cm

	Neurological symptoms	Kayser-Fleischer ring
Patient 1	Negative (-)	Positive (+) in both eyes
Patient 2	Negative (-)	Positive (+) in both eyes
Patient 3	Mild tremor	Positive (+) in both eyes

	Mutation
Patient 1	H1069Q/H1069Q
Patient 2	c.1708-1 G>A/c.1708-1 G>A
Patient 3	H1069Q/P1134Pfs

	ASAT IU/l	ALAT IU/l	ALP IU/l	GGT IU/l	Bilirubin µmol/l	Direct bilirubin µmol/l	Protein g/l	Albumin g/l	INR	Ceruloplasmin (N o.2-0.6) g/l	Penicillamine challenge µmol/l
Patient 1	125	16.7	18.6	72.7	213.7	132.7	53	29	3.0	0.18	43.1
Patient 2	122	25	43	315	1892	1483	54	27	2.0	0.34	74.4
Patient 3	79.9	32.8	31	206	778	670.4	60	29	2.43	0.14	45

Patient 1 – Enlarged liver heterogeneous with gallstones

Patient 2: Enlarged hyperechoic liver with gallbladder with sludge

Patient 3 – Enlarged hyperechoic liver, cirrhosis

- ❖ **Conclusion:** Wilson’s disease should be considered in paediatric patients presenting with haemolytic anaemia, liver dysfunction or neurological symptoms of unknown cause. Establishing diagnosis and starting an appropriate treatment can be life-saving.

❖ **Ref:** 1. EASL Clinical Practice Guidelines: Wilson's disease. J Hepatol. 2012 Mar;56(3):671-85.