TEACHING FILE

GRAND ROUNDS

Ira Shah

WHEN TO STOP PENICILLAMINE IN WILSON'S DISEASE?

Case: A 5 years old boy was diagnosed as Wilson's disease at the age of 4½ years in view of hepatitis with jaundice, increased copper content in liver (132 µg/gm) and elevated urine copper (643). His ophthalmological evaluation revealed no KF ring. He was started on Penicillamine which he had received for past 6 months. He was referred for further management. On examination, he had hepatomegaly. Other systems were normal. A repeat urinary copper was 105.4 in 24 hours. There were still no KF rings.

How long this child should be continued on penicillamine?

Expert's opinion: The mainstay of therapy for Wilson's disease is pharmacologic treatment with chelating agents along with dietary modification. Pharmacologic treatment can be divided into two phases: the initial phase, when toxic copper levels are brought under control, and maintenance therapy. Generally, penicillamine (25mg/kg/day in 2 dosages) is the first treatment used. This binds with copper and leads to excretion of copper in the urine. Zinc usually in the form of a zinc acetate, may be used to maintain stable copper levels in the body. Zinc stimulates metallothionein, a protein in gut cells that binds copper and prevents their absorption and transport to the liver. If zinc and penicillamine are given together, the interval between zinc and penicillamine should be at least 4 hrs. Zinc is the optimal drug for maintenance therapy and for the treatment for the presymptomatic patient.

Since this child now has decreasing urine copper and no KF ring, maintenance therapy may be required in this child now.

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INDIRECT HYPERBILIRUBINEMIA

Case: A 3 years old boy presented with persistent indirect jaundice since 1 month of life. At 4 months of age he was detected to have involuntary movements with developmental delay. MRI brain showed hypomyellination with hyper intensities in globus pallidus. He was investigated for indirect hyperbilirubinemia.

- G6PD – Normal
- Thyroid function tests – Normal
- Osmotic fragility – Normal
- Pyruvate kinase levels – Normal
- RBC membrane defect – Not detected
- Reticulocyte count – Normal

At 3 years, bilirubin = 12.4 mg/dl (11.4 mg/dl – indirect).

What is the cause of indirect hyperbilirubinemia?

Expert's opinion: This child had kernicterus due to indirect hyperbilirubinemia. Since jaundice is still persisting it is unlikely to be due to ABO incompatibility or Rh incompatibility. Since all other causes of indirect hyperbilirubinemia have been ruled out, the most likely cause is Criggler Najjar syndrome (CNS). This syndrome is divided into types I and II and is inherited in an autosomal recessive manner. Intense jaundice appears in the first days of life and persists thereafter. Type 1 is characterised by a serum bilirubin usually above 345 µmol/l (310–755) (whereas the reference range for total bilirubin is 2–14 µmol/l). No UDP glucuronosyltransferase 1-A1 (UGT) expression can be detected in the liver tissue. Hence, there is no response to treatment with phenobarbitone. Liver transplant is the treatment of choice for type 1 CNS. Before transplantation the serum bilirubin level of CNS type 1 patients should be kept below 350 micromol/l with daily phototherapy. (1) If patients get kernicterus or have neurological impairment, then the neurological outcome is not good. In type-2, bilirubin is between 6 to 20 mg/dl and kernicterus is rare. UGT is reduced and treatment with phenobarbitone is effective. Although no simple, widely available clinical test is available to confirm the diagnosis of Crigler-Najjar syndrome, unconjugated hyperbilirubinemia in the presence of normal liver function test findings is characteristic of the disease. Diagnosis can be established by gene analysis or by liver biopsy demonstrating enzyme transferase activity.

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TUBERCULOUS PERITONITIS WITH PLEURAL EFFUSION

Case: A 12 years old girl presented with fever and abdominal distension. There was no contact with TB. She was detected to have left sided pleural effusion with ascites. Chest X-Ray showed left pleural effusion with hilar adenopathy. USG abdomen showed mild hepatosplenomegaly with moderate ascites. Mantoux test was negative. Hemoglobin was 10.3 gm/dl, white cell count was 5100/cumm (88% polymorphs, 12% lymphocytes), ESR was 60 mm at end of 1 hour. Ascitic tap showed 4.8 gm percent proteins, 480 cells (2% polymorphs, 98% lymphocytes) and ADA-151 µ/L. ANA, dsDNA was negative. Child was started on 4 drugs ATT with steroids. Steroids were stopped after 2 months and ATT was stopped after 9 months. At that time Chest X-Ray was normal. She had gained 7 kg in the same tim.

Is tuberculous peritonitis associated commonly with pleural effusion?

Expert's opinion: Tuberculous peritonitis results from hematogenous spread or contagious spread by reactivation of latent foci from an abdominal focus or mesenteric lymph node. It is an uncommon presentation of tuberculosis (TB) especially in children without any other debilitating disease such as cirrhosis, diabetes and chronic renal failure on continuous ambulatory peritoneal dialysis. Chest radiographs are abnormal in 50-75 percent of patients with tuberculous peritonitis and commonly associated with pleural effusion. (1-4) Ascites causing a marked increase in abdominal pressure and the fluid might move into the thoracic cavity with an unknown mechanism, and the removal of ascites might be needed to prevent this phenomenon. (5) Thus co-existing pleural effusion in patients with tuberculous peritonitis is not uncommon.

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From: Medical Sciences Department, Pediatric Oncall, Mumbai.

Address for Correspondence Dr Ira Shah, 1/B Saguna, 271, B St Francis Road, Vile Parle (W), Mumbai 400056.

BOOK REVIEW

Dr. Anupam Sibal's book titled " Is Your Child Ready To Face The World?" is an inspirational compilation of important values that we need to teach our children. It instills in us the importance of imbibing these values ourselves before teaching them to our children. It emphasizes the need to be humble, compassionate, forgiving, honest, grateful, and most importantly being the change that we would like to see in others. Dr. Sibal through his experiences as paediatrician and father, masters the art of conveying each virtue to his son. This book teaches us lessons for life. A must read for all individuals wishing to make a change in today's world.

- Dr. Noella Pereira, D.N.B., D.C.H.
Assistant Professor,
B. J. Wadia Hospital for Children, Mumbai.