TEACHING FILE

GRAND ROUNDS

Ira Shah

PARADOXICAL ADENOPATHY IN A CHILD WITH TUBERCULOSIS

Case: A 13½ years old girl suffering from tuberculosis (TB) presented with clinical deterioration. She was diagnosed as having tuberculous mediastinal adenopathy 7 months ago and was started on antituberculous therapy (ATT) [2 months of Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) followed by continuation phase of HR]. However after 3 months of ATT, she developed cervical adenopathy for which a fine needle aspiration was done that did not grow any acid fast bacillus and child was continued on same ATT. After 5 months of ATT and no improvement in cervical adenopathy, child underwent an excision of the cervical gland and histopathology was suggestive of tuberculous abscess. On examination, her weight was 36 kg, height was 152 cm. She had midline suprasternal healing ulcer and other systems were normal. Child was thus continued on HR and total 9 months of ATT was given. She had a weight gain of 4 kg in the same period and was asymptomatic post treatment completion.

Were steroids indicated in this child?

Expert's opinion: This child has a paradoxical reaction. Paradoxical reaction (PR) in tuberculosis is defined as the clinical or radiological worsening of pre-existing tuberculous lesion or development of new lesion in a patient who initially improves with anti-tuberculosis therapy in the absence of disease relapse. Paradoxical reactions are usually self-limiting. Sometimes corticosteroids are used for relieving paradoxical reaction and anti-tuberculous therapy (ATT) is continued. The rationale behind the use of adjuvant steroids lies in reducing the harmful effects of inflammation as the ATT kill the organisms. However, advantage of steroid for lymph node tuberculosis is unclear. In contrast to patients with intracranial upgrading reactions, most patients with lymph node TB who have a paradoxical reaction recover without developing severe sequelae. In addition, the simpler intervention of aspiration of pus is associated with fewer unwanted side effects than is steroid therapy. The use of aspiration has been reported to be a successful therapeutic intervention for suppurative post- bacille Calmette-Guérin adenitis, and similarly aspiration or excision is useful for the treatment of a paradoxical reaction in a patient with lymph node TB.

DOI No.: 10.7199/ped.oncall.2015.59

ELEVATED SERUM BILE ACIDS IN A CHILD WITH LIVER DISEASE

Case: A 2½ years old girl presented with generalized itching since 8 months of age. There was no history of jaundice. Her milestones were appropriate for age. On examination, weight was 9.4 kg, height was 81 cms, and she had dry excoriated skin with 9 cms hepatomegaly. Other systems were normal. Investigations showed bilirubin 1.6 mg/dl, SGOT - 41 IU/L, SGPT – 62 IU/L, GGTP – 20, total proteins 6.7 gm/dl, albumin 3.2 gm/dl, alkaline phosphatase 894 IU/L, prothrombin time 11.1 sec, partial thromboplastin time 31.7 sec, cholesterol = 190 mg/dl and serum bile acids of 152.4 µmol/L (Normal = 0 - 10 µmol/L). Ultrasound abdomen showed mild hepatosplenomegaly with gall bladder sludge. Liver biopsy showed piecemeal necrosis with early cirrhosis and no bile stasis or bile duct proliferation. She was started on cholestyramine, diphenhydaramine, ursodeoxycholic acid to which she had mild relief.

How to interpret serum bile acids?

Expert's opinion: Bile acids are the main by-product of cholesterol metabolism in the liver and play a major role in maintaining bile flow. Many enzymes are involved in the conversion of cholesterol into bile acids. (1) Diseases associated with inborn error of bile acid metabolism lead to formation of atypical bile acids that may be toxic and cause decrease in bile flow or cholestasis whereas those with defects in bile acid transporters such as the progressive familial intrahepatic cholestasis (PFIC) may interfere with the transport processes of bile components. (1) Thus in patients with bile acid synthesis defect, the serum or urine primary bile acids will be normal whereas in patients with PFIC and other causes of neonatal cholestasis, it will be elevated. However, in these patients, there should be conjugated hyperbilirubinemia. In familial hypercholanemia, there is elevated serum bile acid concentrations, itching, and fat malabsorption and biochemical markers of liver injury are normal. (2) Thus in this child, with minimally elevated serum bilirubin, normal GGTP, itching, liver disease on histology, the elevated serum bile acids would suggest transport defect such as PFIC and not a bile acid synthetic defect.

References

1. Yousef IM, Perwaiz S, Lamireau T, Tuchweber B. Urinary bile acid profile in children with inborn errors of bile acid metabolism and chronic cholestasis` screening technique using electrospray tandem mass-spectrometry (ES, MS, MS). Med Sci Monit. 2003` 9: MT21-31
2. Hypercholanemia, Familial` FHCA. Available at website: ww.omim.org, entry, 607748. Accessed on 25th May 2015

DOI No.: 10.7199/ped.oncall.2015.57

RECURRENT TUBERCULOSIS

Case: A 2 years 3 months old boy presented with recurrent tuberculosis since 1 month of age. He was born at term and had meconium aspiration and required neonatal intensive care stay for 6 days. At 1 month of age, he had fever and abdominal distension. Ultrasound abdomen showed multiple splenic, hepatic and omental abscesses that showed acid fast bacilli (AFB) on pus aspiration. He was vaccinated for BCG and neither parents had TB. He was treated with antituberculous therapy (ATT). At 6 months of age, he developed left axillary lymphadenopathy and lymph node biopsy again showed AFB on smear. He received ATT for 1 year. At 13 months of age (after 1 week of completion of ATT), he developed swelling on left tibia and X-Ray was suggestive of osteomyelitis. Pus was aspirated that showed acid fast bacilli but TB culture was negative. He was treated with ATT and Ofloxacin again for 1 year. After 3 months of completion of second course of ATT, he again developed left axillary lymphadenopathy and fine needle aspiration has been done and sent for TB Bactec culture. In view of recurrent tuberculosis, an immunodeficiency is considered and serum immunoglobulins are normal, CD3, CD4 and CD8 are normal and HIV ELISA is negative.

What is the likely cause of recurrent tuberculosis in this child?

Expert Opinion : Mendelian susceptibility to mycobacterial disease (MSMD). It is a rare syndrome conferring predisposition to clinical disease caused by weakly virulent mycobacteria, such as Mycobacterium bovis, Bacille Calmette Guérin (BCG) vaccines and non-tuberculous mycobacteria (NTM). (1) Serious and disseminated infections with BCG and NTM are observed and can involve soft tissue, bone marrow, lungs, skin, bones and lymph nodes. These patients are also prone to systemic non-typhoidal salmonellosis. (2) It occurs due to disorders of the interleukin (IL)-12–interferon (IFN) gamma circuit. Diagnosis is made by laboratory analysis. IFN-gamma, IL-12p40 and IL-12p70 levels can be measured by ELISA, after whole blood activation by BCG, BCG+ IL-12 and BCG+ IFN-gamma. There are 6 genetic mutations identified till date.

BCG vaccination should be avoided in these patients. But this seemingly is a difficult task in keeping with the fact that most children in a country like India that is endemic for tuberculosis are vaccinated soon after birth. Anti-mycobacterial therapy may have to be continued for extended periods with supplementary measures such as drainage of pus, attention to nutrition and growth are important. IFN gamma can also be tried in these patients. Antibiotics should not be discontinued and bone marrow transplantation may be considered in children with complete IFNγR1 or IFNγR2 deficiency, in whom IFNγ treatment is ineffective and mycobacterial infections overwhelming.

References

1) Mendelian susceptibility to mycobacterial diseases. Available at website: orpha.net/consor/cgi-bin/OC_Exp.php_?Lng=ENandExpert=748. Accessed on 22 January 2015.
2) Bustamante J, Picard C, Dupuis SB, Abel L, Casanova JL. Genetic lessons learnt from X-linked Mendelian susceptibility to mycobacterial diseases, Ann NY Acad sci. Dec2011:1246:92-101.

DOI No. : 10.7199/ped.oncall.2015.60

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.