Case 6657

Tyrosinemia type I
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Patient: 5 years, male

Clinical History:
A 5-year-old boy born of consanguineous parents was hospitalized in poor general condition and growth retardation with, hepatosplenomegaly, and rickets.

Imaging Findings:
A 5-year-old boy born of consanguineous parents was hospitalized in poor general condition and growth retardation with, hepatosplenomegaly, and rickets. Laboratory tests showed pronounced symptoms of hepatic dysfunction, rickets, and Fanconi's syndrome (potassium: 2.7 mmol/l, creatinine: 5 mg/l, Calcium: 92 mg/l, Phosphorus: 11 mg/l, alanine aminotransferase: 31 U/l, aspartate aminotransferase: 57 U/l, gama glutamyl transpeptidase: 121 U/l, alkaline phosphatase: 3079 U/l).

An analysis of the urine for organic acid revealed a markedly elevated level of Succinylacetone. The frontal radiograph of the chest demonstrated rachitic changes at the anterior costochondral junctions. There is widening of the anterior costochondral junctions. The radiograph of the lower extremities shows rachitic changes in all metaphyses. There is diffuse osteopenia and widening of the growth plate. The femoral and tibial metaphysis are frayed and cupped. At sonography, the liver was heterogeneous. There were no focal lesions. There was poor corticomedullary differentiation in the Kidney. CT scan shows irregular aspect of contours of the liver.

Discussion:
Tyrosinemia type I or hepatorenal tyrosinemia is an autosomal recessive caused by an enzymatic defect in fumarylacetoacetate hydrolase (FAH) activity, the last enzyme in the degradation of tyrosine. This deficiency leads to an accumulation of maleylacetoacetate and fumarylacetoacetase, which causes cellular damage possibly by acting as alkylating agents or disrupting sulfhydryl metabolism. The cells most affected are the cells of the liver and the kidneys. It is an inherited disorder with autosomal recessive transmission that affects both sexes equally. It is characterized by progressive liver dysfunction with nodular cirrhosis. There are several enzyme deficiencies within the metabolic pathway of tyrosine that can cause hyper tyrosinemia.

Most infants present within the first 2-3 months of life; far fewer infants present later with a chronic form, which frequently manifests initially as rickets and slowly developing hepatic cirrhosis. Two extremes of the clinical phenotype have been described: the “acute” (severe, early onset and death) and “chronic” (delayed onset and slow course) phenotype. The liver is the most severely affected organ in hepatorenal tyrosinemia. Acute hepatic failure is a frequent reason for presentation, and liver failure and hepatocellular carcinoma cause the majority of deaths.

The patients then develop vomiting and diarrhea, which rapidly progress to bloody stool, lethargy, and jaundice. At
this stage, a distinctive cabbagelike odor may be appreciated. At approximately age 1 year, infants with the chronic form may have failure to thrive and delayed walking, which may indicate rickets. The micronodular changes of cirrhosis are seen at a few weeks of age. There is gradual and steady progression to macronodular cirrhosis. Nephromegaly and nephrocalcinosis are frequently seen in patients with hepatorenal tyrosinemia. Though the liver and the kidney are major target organs of hepatorenal tyrosinemia, the peripheral nerves, pancreas, and heart can also be affected. The radiograph of the lower extremities shows rachitic changes in all metaphyses. The sonographic findings of hepatorenal tyrosinemia are nonspecific. The features are those of a generalized disorder of the liver and kidneys that leads to enlargement and abnormal echogenicity of these organs. Variety appearances in computed tomographic (CT) scans. It may look normal, be diffusely hypoattenuating, or shows nodules that are hyperattenuating or hypoattenuating and enhancing or nonenhancing. It has been suggested that low-attenuation nodules may indicate malignancy.

Urinary succinylacetone is the biochemical marker substance, and its presence is diagnostic for tyrosinemia I. Nutritional treatment should be designed to minimize the phenylalanine-tyrosine load to only essential requirements. Direct medical therapy is aimed at the acute hepatic decompensation and coagulopathy from the outset. Replenishment of depleted coagulation factors may be essential to prevent exsanguination.

Complications are hepatic cirrhosis, renal Fanconi syndrome, including renal tubular acidosis type II, rickets secondary to renal tubular acidosis, peripheral neuropathy, abdominal crisis, seizures, hepatoma or hepatocellular carcinoma.

The patients will be screened regularly with measurement of AFP, ultrasound+/- MRI as they are at risk of developing hepatocellular carcinoma.

Differential Diagnosis List: Tyrosinemia type I

Final Diagnosis: Tyrosinemia type I

References:


Description: There is widening of the anterior costochondral junctions Origin:
**Figure 2**

**Description:** widening of the growth plate. metaphysis are frayed and cuped **Origin:**
Description: femoral and tibial metaphysis are frayed and cupped

Origin:
Description: liver was heterogeneous and there were no focal lesions Origin: