Lifesaving but tiresome treatment for tyrosinemia type 1

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Introduction

- Tyrosinemia Type I (HT1) is a rare autosomal recessive condition caused by a genetic mutation disrupting proper functioning of the fumarylacetoacetate hydrolase (FAH) enzyme, the terminal enzyme in the tyrosine catabolism pathway.

Clinical Presentation

A 23-year-old male with known tyrosinemia type I presents with progressively worsening back, lower extremity, and abdominal pain over the last six months

HPI:

- Progressively worsening back, lower extremity, and abdominal pain over the last six months
- Lost to follow-up to Metabolism/Genetics clinic for the last ten years
- No longer adherent to nitisinone therapy and diet modifications since five to eight years ago due to multiple socioeconomic barriers

Vitals:

- Afebrile with normal heart rate, respiratory rate, blood pressure and oxygen saturation on room air.

Physical Exam:

- Mildly tender on palpation at RUQ abdomen with no guarding or rebound tenderness and mild tenderness in the lumbar and thoracic back.

Labs/Studies:

- Alkaline phosphatase of 356, INR 1.5 with otherwise AST, ALT, Bili WNL.
- CBC and BMP WNL.
- AFP level of 188.
- Amino acid panel (collected after admission): normal tyrosine level of 62, low levels of arginine, isoleucine, leucine, and valine.
- MRI Abdomen with and without contrast with findings of cirrhotic liver morphology, borderline enlarged spleen, collateral vasculature with no ascites, and hepatic segment 8 lesion measuring 2.3cm x 1.4cm in diameter.

Hospital Course and Treatment

- Patient was admitted with genetics consulted with recommendations to restart nitisinone and modify nutrition for low protein/Tyrosine intake.
- Patient given IVFs with glucose to suppress catabolism
- Subsequently discharged on conservative pain regimen and back on nitisinone therapy and education regarding diet modifications.
- Case discussed at multidisciplinary HCC conference with plan to refer to HBP Surgery conference for possible resection and to follow with repeat MRI and possible biopsy.

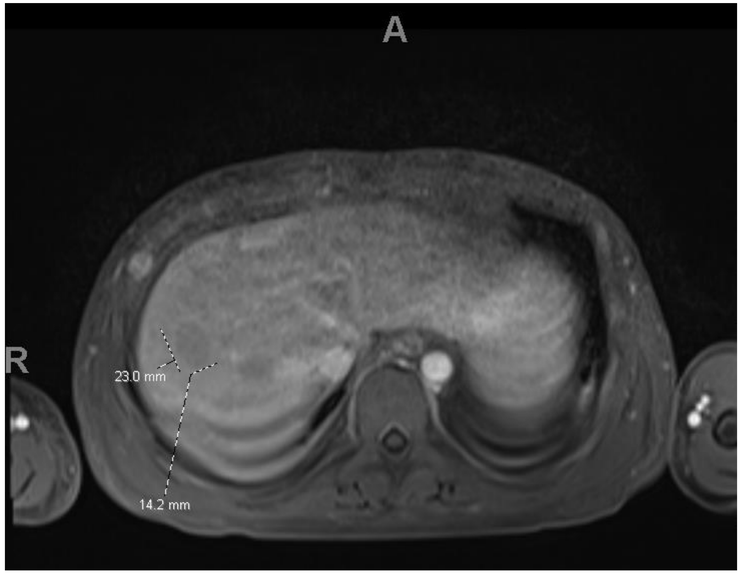

Figure 1.
Image of MRI Abd with and without contrast with findings of nodular liver consistent with cirrhosis, developing portal hypertension, and 2.3 x 1.4cm liver lesion of segment 8 LR 4 concerning for HCC.

Discussion

- The presentation of neurological crises and abdominal pain is common for untreated or non-adherent patients with HT1.
- Hepatocellular carcinoma (HCC) is highly associated with untreated/non-adherent HT1 patients.
- Nitisinone therapy is highly effective for this condition with 4-year survival rates of 94% compared to 29% of diet modification alone when started before 2 months of age.
- Recent evidence is finding increasing non-adherence as the patients grow older into adolescence and adulthood.

Learning Points

- HT1 is a rare genetic disease with effective therapies to prevent progression of cirrhosis requiring OLT and decrease risk of HCC.
- The decreased rate of adherence during adolescence to adulthood phases of life indicate need for awareness during these times to prevent poor outcomes.

References

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