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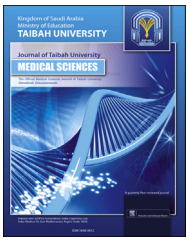

Case Report

Regression of multifocal infantile hepatic hemangioendothliomas after steroid therapy

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الملخص

يعد الورم البطاني الوعائي الكبدي من الأورام النادرة في مرحلة الطفولة. ويعتبر الورم البطاني الوعائي الكبدي للرضع هو الورم الوعائي الأكثر شيوعا في الكبد عند الأطفال حيث يحدث بنسبة ١٢% من جميع أورام الكبد عند الأطفال. نسجل في هذا البحث حالة رضيعة عمرها ٨ أشهر، تم اكتشاف تضخم الكبد لديها عرضيا وعمرها ٤ أشهر. عند الحضور كانت بطنها لينة وطرية. وكان الكبد تحت الحافة الضلعية اليمنى بـ ٨ سم, كما كان الكبد غير مؤلم مع حافة مستديرة وسطح عقدي. لم يكن الطحال محسوسا ولم يتبين وجود أورام أخرى أو استسقاء. اختبار وظائف الكبد كان طبيعيا. أظهرت أشعة الرنين المغناطيسي للكبد وجود عدد من الكتل الدائرية المنتشرة في جميع أنحاء الكبد، مع وجود سمات منخفضة الكثافة في T١ وعالية الكثافة في T٢. بعد الفحص بالمادة الظليلة, كان هناك تعزيز للمادة الظليلة على شكل حواف طرفية سميكة، وأظهرت مرحلة الوريد البابي المتأخرة تعبئة مركزية بالمادة الظليلة. كان الوريد البابي والكبدي طبيعيين. وكانت النتائج التي توصلنا إليها متوافقة مع تشخيص الورم البطاني الوعائي الكبدي متعدد البؤر للرضع. تم البدء بالعلاج بالكورتيزون عن طريق الفم لمدة أسبوعين ومن ثم تم تخفيض الجرعة بشكل تدريجي على مدى ٤ أشهر. أوضحت المتابعة بأشعة الرنين المغناطيسي وجود نقص في عدد وحجم الكتل الكبدية. كما أظهرت المتابعة بالأشعة الصوتية للكبد بعد ٢٤ شهرا من العلاج وجود بقايا لكتلة وحيدة صغيرة في الفص الكبدي الأيسر بقياس ١,٢ x١سم. تم الاستنتاج من هذه الحالة, أن العلاج بالكورتيزون كان ناجحا وكافيا لعلاج الورم البطاني الوعائي الكبير المتعدد البؤر دون الحاجة لعلاجات متقدمة أخرى بما فيها زراعة الكبد.

الكلمات المفتاحية: ورم بطاني وعائي؛ أورام الكبد؛ أورام كبدية وعائية

Abstract

Hepatic hemangioendotheliomas are rare childhood tumors. Infantile hepatic hemangioendothelioma (IHHE) is the most common vascular tumor of the liver in children accounting for 12% of all childhood hepatic tumors. We report an 8-month-old female infant presented at the age of 4 months with incidental hepatomegaly. On presentation her abdomen was soft and lax. The liver was at 8 cm below the right costal margin, not tender with rounded edge and nodular surface. The spleen was not felt and there were no other masses and no ascites. Her liver functions tests were normal. MRI of the liver showed numerous rounded lesions in all the hepatic segments with characteristic of low signal intensity at T1 and high intensity at T2. Post contrast, the lesions showed a peripheral thick rim of enhancement and in the delayed porto-venous phase showed central filling with contrast. The portal and hepatic veins were patent. Our findings were compatible with the diagnosis of multifocal infantile hemangioendothelioma of the liver. Oral prednisone was started for 2 weeks then was tapered over 4 months. A follow up MRI confirmed the decrease in the number and the size of hepatic lesions. A follow-up liver US 24 months after treatment showed residual solitary small lesion in left hepatic lobe measuring 1.2 × 1.0 cm. The authors report that steroid therapy was effective in the treatment of massive multifocal HHE without a need for other advanced therapies including liver transplantation.

Keywords: Hemangioendothelioma; Liver masses vascular hepatic tumors

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Introduction

Hepatic tumors in children are relatively rare, accounting for 1–4% of all pediatric solid tumors. Infantile hepatic hemangioendothelioma (IHHE) is the most common vascular tumor of the liver in children accounting for 12% of all childhood hepatic tumors. The clinical course depends on tumor size, its growth characteristics, localization, and complications. The most feared complications are cardiac failure and consumptive coagulopathy with thrombocytopenia (Kasabach–Merritt syndrome); therapeutic options for IHHE include both medical and interventional modalities. Medical therapy includes treatment with corticosteroids and interferon-alpha (INF-α), whereas interventional modalities include embolization and ligation of the hepatic artery, resectional surgery, and liver transplantation,[1] we report an infantile massive hemangioendotheliomas of the liver that developed in an 8 months old female which was responded to steroid therapy, and without a need for other advanced therapeutic options including liver transplantation.

Case report

An 8-month-old female infant was born with birth weight of 3.2 kg, the pregnancy was uneventful, and she was found to have pyloric stenosis and underwent pyloroplasty. At the age of 4 months, hepatomegaly was detected during a well baby clinic visit. She was investigated and referred from a secondary hospital to our tertiary hospital, as a case of extensive hepatic multifocal hemangiomas for possible liver transplantation. Physical examination on presentation showed a heart rate of 110/minute, blood pressure of 100/60 mmHg, vital signs were within normal, no skin lesions no pigmentations, and not jaundiced. There was a soft systolic murmur at the left lower sternal border 2/6 in the with normal capillary refill time. The chest was clear with no abnormal respiratory sounds. The abdomen was soft and lax. The liver was 8 cm below the right costal margin, not tender with rounded edge and nodular surface. The spleen was not felt and there were no masses and no ascites. Skin was free with no cutaneous lesions, Musculoskeletal and Neurological examination was normal.

Laboratory investigations showed, WBCs 10.2×10^9/L ($N = 5.5–16.5$), Hgb 13.5 g/dl ($N = 10–15$), platelets 305×10^9/L ($N = 124–512$), Billirubin 5.2 μmol/L ($N = 4–21$), ALT 31 U/L ($N = 17–49$), AST 39 U/L ($N = 8–38$), GGT 42 U/L ($N = 5–55$), Albumin 31 g/L ($N = 34–50$), PT 11.5 s ($N = 9.6–12.6$), PTT 27 s ($N = 25.3–33.8$), INR 0.9 ($N = 0.8–1.2$), Alpha fetoprotein 97.08 ng/ml ($N = 1.09–8.04$ ng/ml), TSH 4.8 ml U/L ($N = 0.35–4.9$), FT4 21 pmol/L ($N = 12.9–21.3$).

US abdominal showed an enlarged liver of 12.4 cm in craniocaudal diameter with multiple variable sized hypo echoic focal lesions in both the right and left lobes. The largest lesion measuring 3.6 × 3 cm. The portal vein was patent and the hepatic vein was dilated. CT scan with contrast, showed hypodense lesions pre contrast that became hyperdense after the injection of the contrast with peripheral enhancement post contrast and in delayed phase showing progressive filling (Figure 1). MRI of the liver showed numerous rounded lesions in all the hepatic segments with characteristic low signal intensity at T1 and high intensity at T2. Post contrast, the lesions showed a peripheral thick rim of enhancement and in the delayed porto-venous phase showed central filling with contrast. The portal and hepatic veins were patent. Echocardiogram showed normal structure and function of the heart indicating no compromised cardiovascular function. A brain CT scan, chest X-ray, skeletal survey, and ophthalmology examination were all normal excluding extra hepatic involvement, and make the possibility of associated syndrome is unlikely. The findings were compatible with the diagnosis of multifocal infantile hemangioendothelioma of the liver. Review of the literature, the authors did not find any correlation between IHHE and pyloric stenosis, and we believe that the correlation between IHHE and the occurrence of pyloric stenosis in our patient is coincidental.

The patient was started on oral prednisone 2 mg/kg/day for 2 weeks, and then increased to 4 mg/kg/day for 2 weeks after which she was tapered off the medication then tapered over 4 months. Follow up 4 and 8 months later showed gradual regression in the liver size. The liver function tests remained normal and the alpha-fetoprotein became 22.14. MRI confirmed the decrease in the number and the size of hepatic lesions (Figure 2). A follow up US of the liver 24 months after treatment showed mild hepatomegaly with residual solitary small lesion in left hepatic lobe measures 1.2 × 1.0 cm (Figure 3).

Discussion

IHHE is the most common vascular tumor of the liver in childhood and the third most common hepatic tumor in infants and children. It resents most commonly before the age of 6 months and is more predominant in females.[1] Two histological subtypes of IHHE are recognized; Type I, is the commonest and consist of vascular channels lined by a single layer of plump endothelial cells separated by fibrous tissue. Type II, composed of multiple layer of larger more pleomorphic endothelial cells with hyper chromatic nuclei forming poorly defined vascular spaces. The later type behaves more aggressively and can metastasize.[2] IHHE can

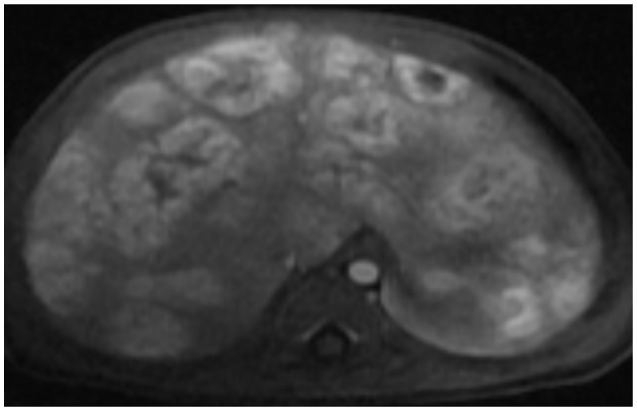

Figure 1: MRI images at presentation: numerous rounded lesions all over the hepatic segments with characteristic and high signal intensity (hyperintense) at T2-weighted image.

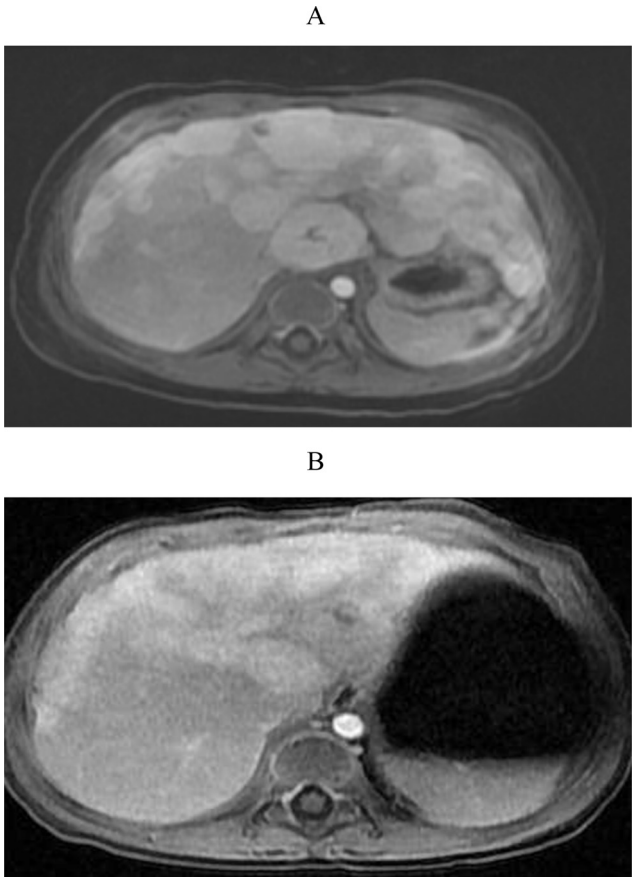

Figure 2: MRI of the liver 4 months (A) and at 8 months (B) post discontinuation of steroid therapy.

present in variable presentation depending on its size and location ranging from being asymptomatic to life threatening such as high output cardiac failure, abdominal compartment syndrome, hepatic failure, hypothyroidism, multi organ failure and Kasabach–Merritt Syndrome (hemangioma, thrombocytopenia, and coagulopathy).[3] The findings in our patient did not fit with the criteria for Kasabach–Merritt Syndrome.

Radiological evaluation seems to be the standard initial approach for the diagnosis. Non invasive procedures such as US, CT, and MRI performed by an experienced radiologist are adequate for both diagnosis and follow up.[3] The diagnosis in our patient was obtained by US of the liver that showed a characteristic well defined hypo echoic lesions and confirmed blood shunting. However, confirmation of diagnosis was by MRI of the liver which shows a characteristic low signal intensity at T1 and high intensity at T2. Post contrast the lesions showed a peripheral thick rim of enhancement and in the delayed porto-venous phase showed central filling with contrast. In general, MRI remains the radiologic test of choice in diagnosing infantile hepatic masses.

Angiography should be reserved for patients with symptomatic shunt in whom endovascular therapy is anticipated. Liver biopsy is rarely indicated in IHHE in those with atypical radiological signs, and in case of refractory medical therapy. It should be carried out cautiously and under vision only if patient is above one year of age.[4] Liver biopsy was not indicated in our patient.

IHHE can significantly affect the liver to the extent of advanced hepatic failure, a situation that may require a decision for urgent liver transplantation. Medical and supportive treatment is rewarding in the majority of patients. The therapeutic modality of IHHE treatment in the literature concluded that, if the hepatic tumor is focal or multifocal and is asymptomatic and with no other complication then the management is to observe until spontaneous resolution occurs. In case the tumor is massive but asymptomatic then the first line of treatment is the use of steroids treatment.[5,6] Patients with the Kasabach–Merritt Syndrome may show some response to interferon therapy (anti-angiogenic agent). The serum vascular endothelial growth factor level is a reliable indicator of efficacy with this treatment.[3] In advanced IHHE, shunting of blood in the liver could be

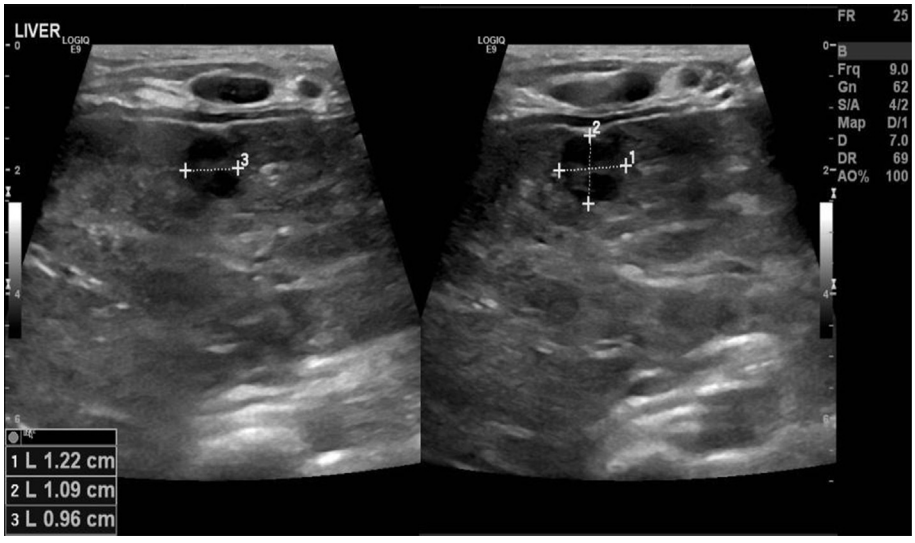

Figure 3: Abdominal US 24 months after discontinuation of treatment showing residual solitary small lesion in left hepatic lobe measuring about 1.2 cm × 1.0 cm.

complicated by congestive heart failure. Ligation of the hepatic artery to reduce the hepatic blood flow could be indicated.[6] The interventional occlusion of tumor feeding vessels with flexible coils is safe and feasible method in the treatment of symptomatic IHHE with sever shunt and cardiac failure, with lesser risk of hepatic necrosis and bleeding when compared with other surgical interventions.[7] Liver transplantation is the last choice in case of diffuse IHHE with rapid deterioration and signs of hepatic failure with many reports of successful transplantation of massive IHHE.[2]

In our case report, our patient was referred to our tertiary hospital for possible liver transplant. We treated the patient with Prednisolone and periodic reassessment clinically and radiologically showed significant improvement, indicating that medical treatment was rewarding and without a need for liver transplantation.

We conclude that medical treatment should be given ample of time in order to show response before liver transplantation is considered.

Conflict of interest

The authors declare no conflict of interest.

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