

Undifferentiated Embryonic Liver Sarcoma with Situs Inversus Totalis, Polysplenia, and Patent Ductus Venosus

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Abstract

Situs inversus totalis in the pediatric population is a rare laterality defect characterized by a complete mirror-image reversal of the normal anatomy. The association with hepatic malignancies has been rarely described in the literature. Because of the complex anatomy, multidisciplinary approach and adequate pre-operative planning are crucial in order to understand the hepatic anatomy.

Keywords: Embryonic liver sarcoma; Hepatic tumor; Situs inversus totalis; Polysplenia; Patent ductus venosus

Abbreviations: CT: Computed Tomography; I-IMP: N-isopropyl-p-[¹²³I]-iodoamphetamine; IV: Intravenous; IVC: Inferior Vena Cava; MR: Magnetic Resonance; MRI: Magnetic Resonance Imaging; PDV: Patent Ductus Venosus; UELS: Undifferentiated Embryonic Liver Sarcoma; US: Ultrasound; VDC: Vincristine, Doxorubicin, and Cyclophosphamide

Introduction

Situs inversus totalis in pediatric patients is an uncommon entity, and its association with hepatic tumors is an even rarer finding. In the English medical literature, to date, 4 patients with situs inversus have been found to have hepatocellular carcinoma and 1 with hepatoblastoma [1,2]. However there are no reported cases of undifferentiated embryonal liver sarcoma with situs inversus totalis reported in the literature. Polysplenia syndrome is regularly associated with levo-isomerism, and its occurrence with situs inversus totalis is exceedingly rare. Patent ductus venosus is also a rare entity. Its incidence with hepatic tumors has been previously reported in many cases, yet the majority were benign, and there have been no documented cases of sarcomas in patients with a patent ductus venosus [3]. We describe a rare association of situs inversus totalis with polysplenia, patent ductus venosus, and malignant hepatic embryonal sarcoma.

Case Report

A previously healthy 12 year-old boy presented with a four-month history of jaundice and abdominal distention. The patient denied any fever, weight loss, or change in bowel habits. Upon presentation, the patient was jaundiced, had an oral temperature of 37°C, and his oxygen saturation was 99% on room air. He had a heart rate of 75 beats/min, a blood pressure of 110/70 mmHg, and a respiratory rate of 18 per minute. Examination of the abdomen revealed hepatomegaly and mild left lower quadrant tenderness. Contrast-enhanced CT examination of the chest, abdomen, and pelvis showed a left-sided liver containing a 16 × 11.8 cm heterogeneously enhancing, non-vascular hepatic mass with cystic component in segments II, III, and IV (right-sided left lobe). There was no invasion of the major vascular structures in the porta hepatis. Multiple spleens were noted in the right side of the upper abdomen, compatible with polysplenia. The stomach was noted on the left side, the cecum on the right side, and the superior mesenteric vein to the left of the superior mesenteric artery as a complete mirror image of the abdominal viscera (Figure 1). In the chest, the heart apex was right-

sided, compatible with dextrocardia (Figure 1). There was a complete mirror image of the cardiac chambers, right-sided thoracic arch, and a left-sided pulmonary trunk: a typical description of situs inversus with dextrocardia. The left-sided right lung consisted of 3 lobes and the

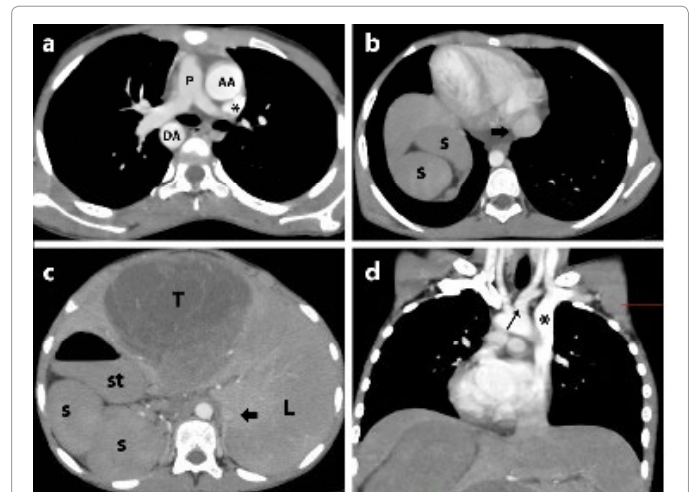


Figure 1 (a, b and c): Axial contrast-enhanced CT examination at the level of the upper chest, lower chest and upper abdomen respectively, showing a conciliation of findings compatible with situs inversus totalis with dextrocardia. Note the left-sided superior vena cava (asterisk) and inferior vena cava (large arrow), the right-sided descending thoracic aorta (DA), and the ascending aorta (AA) coursing to the left of the pulmonary trunk (P). Multiple spleens (S) and the stomach (St) are located in the right side of the upper abdomen. **(d)** Coronal CT image showing the left-sided superior vena cava (asterisk) and brachiocephalic trunk (oblique arrow). The left-sided liver (L) contains a large multiseptated hepatic tumor (T) occupying most of the segments II, III and IV with cystic and heterogeneously enhancing soft tissue components.

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right-sided left lung consisted of 2 lobes. Incisional biopsy of the liver mass revealed hepatic embryonal sarcoma.

Patient underwent five cycles of adjuvant chemotherapy with Vincristine, Doxorubicin, and Cyclophosphamide (VDC). A repeat CT scan showed regression in size and extent of the previously described mass, measuring 11 × 9 cm. He underwent cholecystectomy, and partial hepatectomy of segments II, III, and IV which contained the hepatic mass. Intraoperatively, the portal vein was identified coursing on the peripheral aspect of the liver in an unusual location, consistent with a patent ductus venosus. The patient was transferred to the paediatric intensive care unit for close observation. He was extubated the following day and transferred to the paediatric oncology unit, for further observation. He was then discharged home in a stable condition after four days of uneventful hospital stay. He received post-operative chemotherapy upon his return to Syria.

The pathologic examination of the hepatic lesion showed residual undifferentiated embryonal sarcoma, with extensive necrosis, hemorrhage, and granulation tissue (10% viable tumor, 90% necrosis) (Figure 2). Necrotic tumor was present at surgical margins, with a 1mm viable tumor-free margin. The gall bladder specimen revealed no pathologic abnormalities.

Discussion

Situs inversus totalis occurs around 1 in every 10,000 live births, with a male to female ratio of 3:2, and no racial predilection [4]. It is a laterality defect characterized by a complete mirror-image reversal of the normal anatomy, and it also indicates dextrocardia i.e. complete reversal of the heart chamber with the aorta arching to the right [4]. Classically, polysplenia syndrome is usually accompanied with levo-isomerism i.e. when the heart, lungs, and liver are symmetrically arranged in the midline with bilateral left-sidedness, while there are multiple accessory spleens [5]. Interestingly, however, our patient presented with situs inversus totalis and polysplenia, an extremely rare combination with only a few reported cases [5].

When indicated, liver resection in patients with situs inversus totalis is usually associated with a technical challenge because of the unusual anatomy and the possible associated vascular abnormalities. Therefore, computed tomography (CT) with oral and IV contrast, ultrasound (US), and barium studies are crucial as part of the pre-operative assessment of patients with situs inversus totalis, in order to completely understand the anatomy prior to surgical interventions [6].

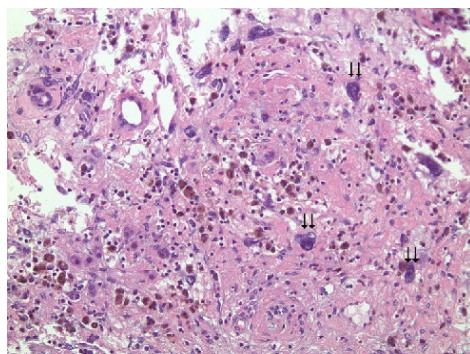


Figure 2: High-magnification pathology image of the surgical specimen showing residual sarcoma cells (double arrow), hemosiderin-containing cells (oblique arrows) and the pink collagen medium throughout the slide.

Although situs inversus has been widely considered not to be premalignant, recently some authors postulate that alterations in gene expression may increase the susceptibility of cancer, thus promoting carcinogenesis via upregulation of pro-inflammatory factors [7]. To the best of our knowledge, many cases of malignant tumors have been reported in patients with situs inversus totalis in the English medical literature, of which only 5 were hepatic in origin (4 cases of hepatocellular carcinoma and 1 case of hepatoblastoma [1,2]). However, no cases of undifferentiated embryonic liver sarcomas have been reported in patients with situs inversus.

Undifferentiated embryonic liver sarcoma (UELS) is a rare and highly malignant liver cancer formed from primitive mesenchymal cells. Until recently, more than 200 cases of UELS in children and adults have been reported since 1978 when the tumor was first described [8]. It mainly occurs in children between the ages of five and ten years, but can also occur in adulthood. In various series of hepatic tumors in the pediatric population, UELS accounts for around 9% to 13% of all hepatic tumors [9]. Diagnostic tools include US, CT, and magnetic resonance imaging (MRI), followed by biopsy to confirm the diagnosis. The radiologic finding, typically, is a large septated mass with both solid and cystic portions; the tumor has a solid appearance on US, while it has a cystic appearance on CT and MRI [10]. Management of the tumor has been successfully reported by surgical resection and chemotherapy [8].

In our case, a rare association was described between situs inversus totalis and an extremely rare hepatic tumor. In addition, our patient had a patent ductus venosus (PDV), which has not been reported up until this date to be associated with UELS. Children with a PDV may present with liver tumors that develop in response to abnormal perfusion of the liver, but the majority, however, have been reported to be benign. A recent case series by Pupulim et al. reported 8 patients with congenital portosystemic shunts, all presenting with at least 1 benign hepatic nodule (including adenomas, focal nodular hyperplasia, and nodular regenerative hyperplasia) [3]. Whether in the pediatric or adult population, fewer than 20 cases of symptomatic patent ductus venosus have been reported as a whole, and the prevalence of asymptomatic cases is unknown [11]. A patent ductus venosus occurs more commonly in males than females, at a ratio of 3:1 [12]. Some cases have been reported in families, suggesting a genetic predisposition to congenital shunts [11]. It is hypothesized that the congenital shunts arise from a vascular accident between the fourth and eighth week of gestation [13]. The ductus venosus is one of three shunts in the fetal circulation that is essential for adaptation to the intrauterine environment. It travels caudo-cranially, carrying oxygenated blood from the umbilical vein to the heart and bypassing the liver [12]. This fetal shunt begins closure as early as the first minute after birth, and continues its functional closure postnatally till day 18 on average [13]. Its fibrous remnant is the ligamentum venosum of the liver, running in the fissure separating the left and right hepatic lobes, and coursing posteriorly to the inferior vena cava [12]. In some rare instances the ductus venosus remains patent, leading to a side-to-side intrahepatic portosystemic venous shunt, i.e. resulting in an abnormal connection between the left or right branch of the portal vein and either the hepatic vein or the intrahepatic portion of the inferior vena cava [13].

3-Dimensional CT angiography and MR angiography are currently used to confirm a patent ductus venosus and accurately describe its anatomy [13]. Rectal scintigraphy with ¹²³I-IMP is commonly used to quantify the degree of shunting if surgical intervention is considered as the next step in management [12]. A good prognosis relies on early

detection and appropriate management. If incidentally diagnosed before the age of two years, the physician may opt to wait for spontaneous closure of the shunt to occur, whilst ensuring close follow-up to observe for the development of symptoms [13]. Some reports suggest a trial of conservative therapy in asymptomatic patients, such as a protein-free diet and oral lactulose to prevent hyperammonemia, and a galactose-free diet to prevent hypergalactosemia [13]. In symptomatic patients, many options are available for closure of the shunt, depending on the patency of the portal circulation: mainly transcatheter embolization, surgical ligation, or surgical banding [12].

Conclusion

Herein, we have presented the case of a 12 year-old boy with a rare association of undifferentiated embryonic liver sarcoma with situs inversus totalis, polysplenia, and patent ductus venosus. The patient underwent a successful surgical resection of the tumor after a course of neoadjuvant chemotherapy. To the best of our knowledge, this is the first such case to have been reported in the English literature. Clinicians, surgeons, and radiologists should be familiar with such an association in order to accurately diagnose similar future cases and guide the management. In addition, we emphasize that, when operating on patients with situs inversus totalis, precise preoperative anatomical evaluation is necessary.

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