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Case report

Repeated TACE in HCC after Fontan surgery and situs viscerum inversus: A case report ☆

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ABSTRACT

We describe the case of a 32-year-old man who developed a liver neoplasm due to previous Fontan surgery (FS) for a single ventricle anomaly and situs viscerum inversus. He was admitted to our hospital for suspected hepatocellular carcinoma during an Ultrasound (US) follow up. Computed tomography (CT) showed features of chronic liver disease and 7 cm hepatic nodule with arterial enhancement. Laboratory analyses documented preserved liver function and increased levels of alpha-fetoprotein. Trans-arterial-chemoembolization (TACE) was performed obtaining complete necrosis at 4 weeks of follow up and significant reduction of alpha-fetoprotein. The patient is currently in follow-up, being evaluated for further treatments and/or combined liver-heart transplantation. TACE is a therapeutic option for the treatment of patients with unresectable hepatocellular carcinoma (HCC) and with severe heart disease, like those submitted to FS and with also other vascular abnormalities like those correlated to situs viscerum inversus.

Abbreviation: bpm, beats per minute; ceCT, Contrast Enhanced CT; CM, Contrast Medium; CT, Computed Tomography, EDVi, End- Diastolic Volume index, EF, Ejection Fraction; FALD, Fontan-associated liver disease; HR, Heart Rate; IVC-PA, Inferior Vena Cava-Pulmonary Artery; MRI, Magnetic Resonance Imaging; SI, Situs inversus; SMA, Superior Mesenteric Artery; TACE, trans-arterial-chemoembolization; US, Ultrasound.

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Introduction

The Fontan procedure gives patients with congenital heart defects a survival advantage, with survival rates of almost 80% at 20 years [1]. The number of Fontan procedures performed worldwide is increasing. It is currently the most common cardiac surgery for patients with any type of single ventricle, with approximately 1,000 surgical procedures performed annually in the USA [2].

The term Fontan-associated liver disease (FALD) is used to describe the spectrum of functional and structural alterations of the liver in this setting, including progressive fibrosis, complications related to portal hypertension, liver failure, and the development of regenerative and neoplastic nodules [3].

Situs inversus (SI) is a congenital anomaly that causes specular positioning of the thoracic and abdominal organs. The incidence of SI is approximately one in 100,000 [4]. Because the organs and vessels are not perfectly symmetrical in SI, recognizing the anatomy of the organ vessels is difficult, leading to difficulties in diagnosis and treatment.

We present the case of a 31-year-old patient undergoing Fontan surgery, with IS and multifocal HCC on cardiogenic cirrhosis treated with repeated TACE.

Case report

The patient's clinical history began at birth when he underwent Blalock Taussing Shunt surgery (1989) and subsequent Fontan surgery (1991) for congenital heart disease (single ventricle).

In September 2017, the patient underwent abdominal US which documented asplenia with right-sided stomach, symmetrical transverse liver with nodular margins characterized by markedly inhomogeneous ecostructure, gallbladder in right paramedian site with regular walls and alithiasis and Inferior vena cava to the left of the abdominal aorta.

Periodic follow-up with Magnetic Resonance Imaging (MRI) of the heart documenting Inferior Vena Cava-Pulmonary Artery (IVC-AP) conduit with stable moderate caliber reduction and partially calcific parietal sleeve thickening. Functionally single ventricular chamber of lower limit size (End- Diastolic Volume index - EDVi 69 ml/m^2) with preserved global systolic function (Ejection Fraction - EF 58%). In addition, the examination documented multiple hepatic nodules.

Therefore, the patient underwent CT of abdomen with contrast medium (CM) documenting common hepatic artery originating from the superior mesenteric artery (SMA).

There was an expansile lesion with lobulated margins located at VII segment measuring 67 × 63 mm in close proximity to the inferior vena cava (compressed but patent) (Fig. 1). Additional smaller nodules with the same characteristics were present at segments V, VI and VIII.

The lesion described at the VII segment showed progressive growth in the subsequent follow up with progressive increasing of AFP value up to 619.8 IU/mL.

Contrast enhanced CT (ceCT) also depicted the anomalous origin of a branch of hepatic artery from SMA and another branch from celiac trunk (Fig. 2).

In relation to the high surgical risk and the presence of multiple nodules the patient underwent an intrarterial chemoembolization procedure. The decision was taken in a multidisciplinary team.

Pre-procedure electrocardiogram documented sinus rhythm at HR of 90 bpm, morphology compatible with dextrocardia, impaired intra-ventricular conduction as left bundle branch block.

During TACE the superior mesenteric artery and the celiac trunk were selectively catheterized. The abnormal origin of

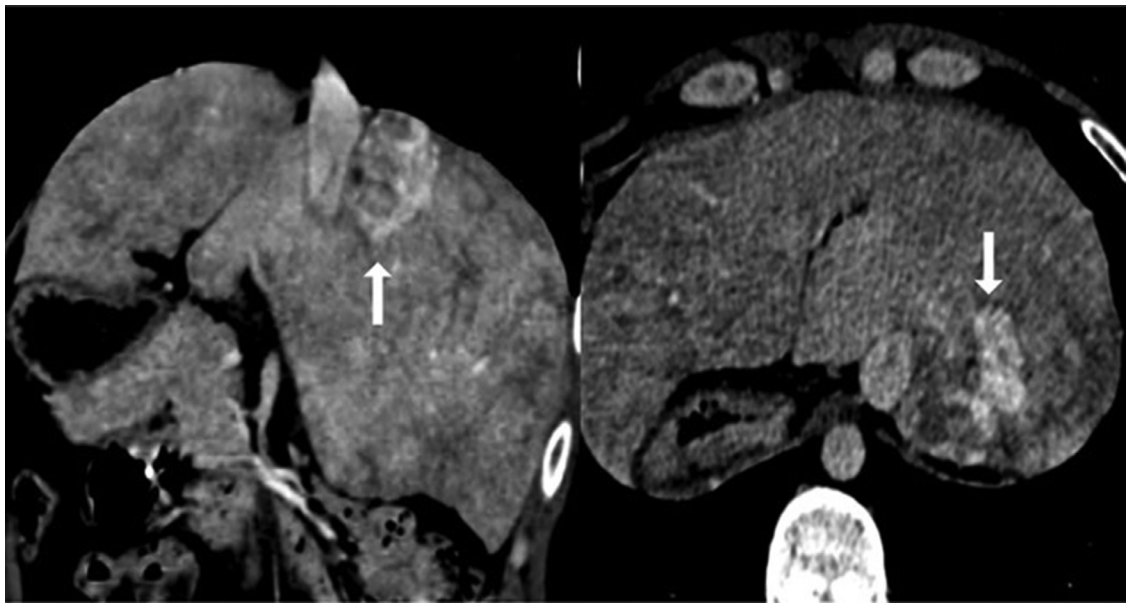

Fig. 1 – CT scan shows symmetrical transverse liver with an expansile lesion with lobulated margins located at VII segment measuring 67 x 63 mm in close proximity to the inferior vena cava (arrow).

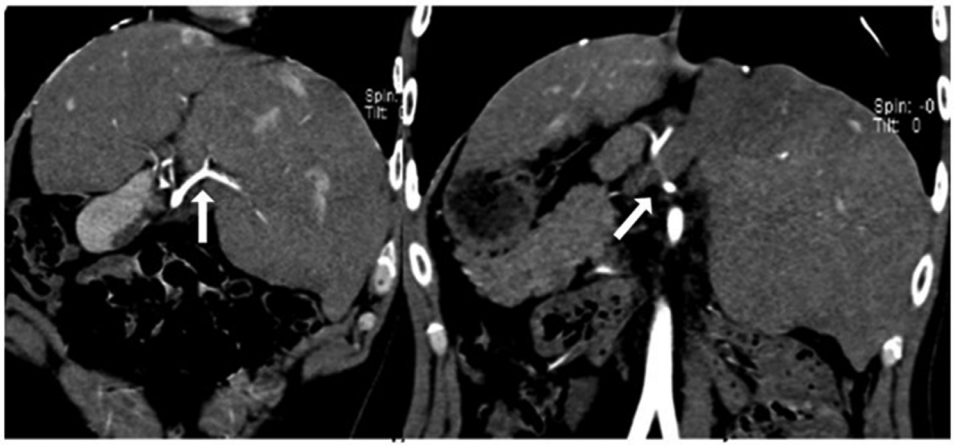

Fig. 2 – ceCT shows anomalous origin of a branch of hepatic artery from SMA (right) and another branch from celiac trunk (left).

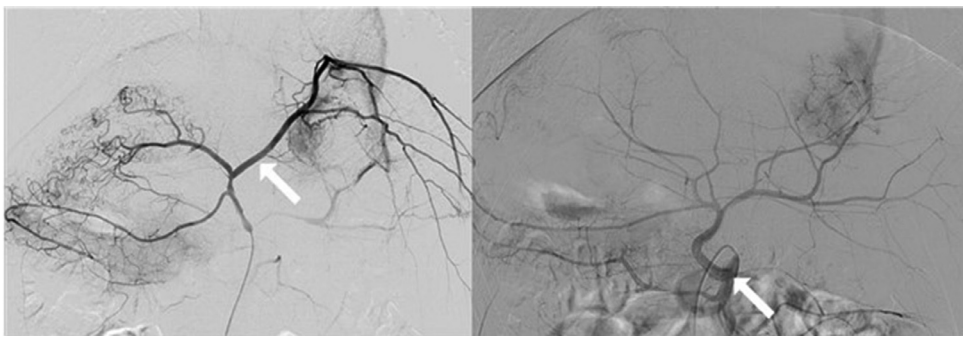

Fig. 3 – On the left, DSA shows a branch from the celiac trunk vascularizing the right liver (arrow). On the right, DSA shows abnormal origin of the common hepatic artery from the SMA (arrow).

the common hepatic artery from the SMA and the presence of a branch partially vascularizing the right liver from the celiac trunk were noted (Fig. 3).

Arteriographic examination confirmed the presence of inverse anatomical situation (situs viscerum inversus) and a voluminous area of focal heteroplasic neoangiogenesis in the seventh hepatic segment, mainly supplied by the arterial branch coming from the SMA and partially by the one coming from the celiac trunk (Fig. 4). From the latter, two other suspicious areas were also appreciated at the V and VI segment. The vascularity of the remaining liver segments, particularly the left, was markedly irregular due to the known condition of chronic hepatopathy. After superslective catheterization of the branch supplying the lesion to VII segment with a coaxial catheter (2.7 F), chemoembolization was performed. Degradable embolizing particles (Embocepts S DSM 50 μm; PharmaCept GmbH) and a total of 50 mg doxorubicin hydrochloride were administered. To complete the procedure, vessel closure with the same embolizing particles was performed.

Fluoroscopic and radiographic control showed optimal distribution of the mixture of doxorubicin, iodinate contrast medium and embolization material in the vascularized part of the lesion. Further treatment of the part of the lesion supplied by the arterial branch from the celiac trunk was not performed in relation to the patient's body mass and the amount of drug administered.

The patient underwent ceCT of abdomen one month after the procedure, that documented the known HCC lesion at segment VII with a large central area of necrotic appearance and the reduction of the peripheral vascular component with dimensions of 54 × 51 mm compared to 67 × 63 mm before treatment. An area of neoangiogenesis remained, a finding compatible with partial response to the TACE procedure according to m-RECIST criteria.

Therefore, the patient underwent a new TACE procedure for HCC of the VIIs after 40 days.

The arterial branch originating from the celiac trunk and a branch originating from the left diaphragmatic artery, hypertrophic due to vascularization of the lesion at the VII segment were catheterized. Subsequently, a branch vascularizing the right sections of the liver, originated from the SMA, was catheterized. Arteriographic examination confirmed the presence of a residual heteroplastic neoangiogenesis in the seventh hepatic segment (Fig. 5).

After superselective catheterization of the branch supplying the residual lesion with a coaxial coater (2.7 F), further chemoebolization was performed with the same resorbable embolising particles (Embocepts S DSM 50 μm; PharmaCept

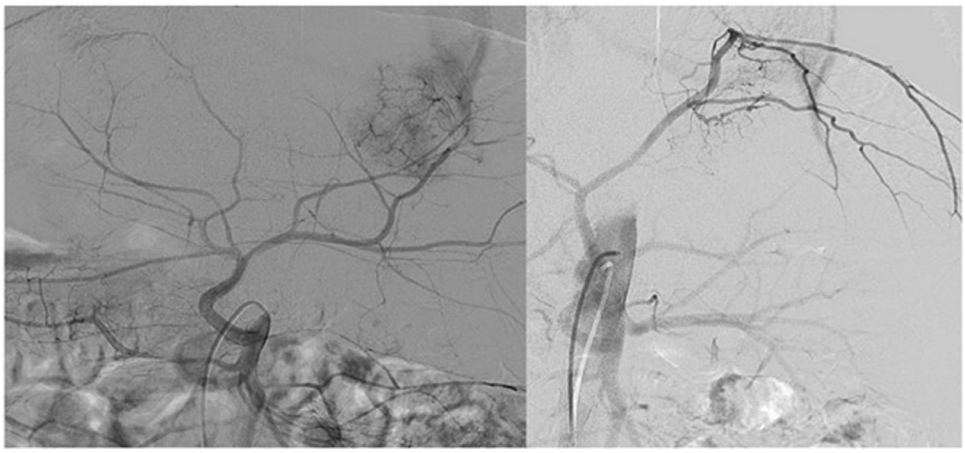

Fig. 4 – DSA shows a voluminous area of focal neoplastic vascularization in the seventh hepatic segment, mainly supplied by the arterial branch coming from the SMA (left) and partially by that coming from the celiac trunk (right).

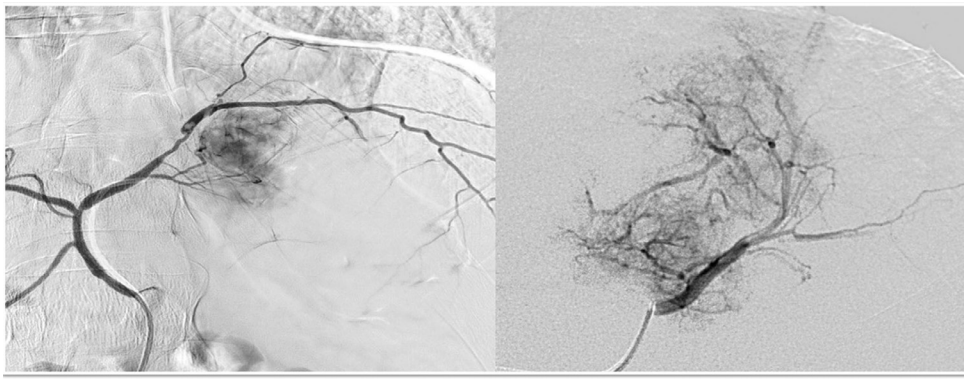

Fig. 5 – Arteriographic examination confirmed the presence of a residual neoplastic vascularization in the seventh hepatic segment vascularized by a branch from the SMA (left) and by a branch originating from the celiac trunk (right).

GmbH, Berlin Germany) and a total of 35 mg Doxorubicin hydrochloride were administered.

Post procedure Cone-Beam CT control showed the optimal distribution of the mixture of doxorubicin, CM and embolization material in the vascularized parts of the lesion (Fig. 6).

At ceCT follow-up one month after treatment, the lesion had a almost complete absence of hypervascular areas with alpha-fetoprotein values close to zero (Fig. 7).

Discussion

The diagnosis of HCC is predominantly based on imaging criteria of arterially- enhancing lesions that demonstrate washout on portal venous and delayed-phase images.

The high prevalence of hypervascular hepatic nodules in patients with FALD makes HCC diagnosis particularly challenging.

Current imaging criteria for HCC are not always reliable in Fontan surgery patients, as non-malignant hepatic nodules may mimic HCC and feature hypervascularity and washout [5].

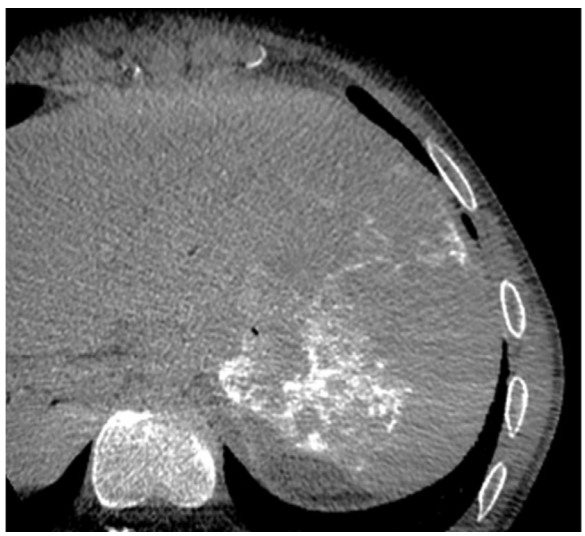

Fig. 6 – Post-DSM-TACE Cone-Beam CT showed the distribution of the mixture of doxorubicin, contrast media and embolization material in the vascularized parts of the lesion.

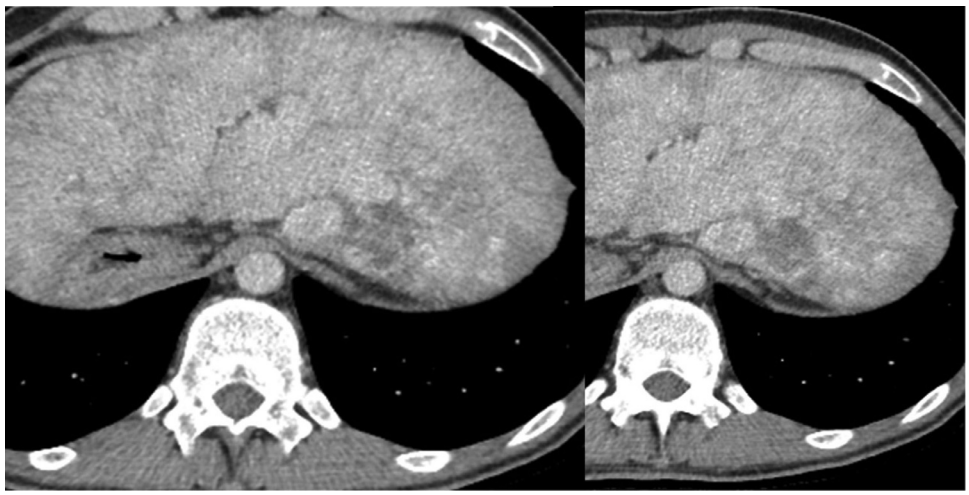

Fig. 7 – CT follow-up one month after treatment shows complete absence of focal high vascularized areas.

The reverse is also true, as the arterial enhancement of HCC may be obscured in the presence of cardiac failure and intrahepatic vascular shunts [6].

Serum alpha-fetoprotein is a valuable complementary tool in the diagnosis of HCC.

Biopsy is reserved for diagnosis of indeterminate lesions. There is an increased risk of bleeding following liver biopsy due to elevated central venous pressure and the increased use of oral anticoagulants in this population. There is also a small but appreciable risk of biopsy tract seeding in association with biopsy of tumor nodules (2.7%) [7].

In our case HCC diagnosis was exclusively based on non-invasive criteria. There were multiple liver nodules but only one of these showed the characteristic imaging features of HCC and an increase in size at follow-up associated with increased serum alphafetoprotein levels.

There is limited evidence as to the optimum treatment strategy for HCC complicating FALD.

Fontan haemodynamics features unique anatomical and functional abnormalities that should be considered when tailoring treatment.

Surgery seems to be safe, including laparoscopic resection, but specialized anaesthesia and perioperative management are crucial in this fragile patient population.

Bleeding risk is also a concern given the frequent use of antithrombotic therapy and the fact of elevated central venous pressure.

Radiofrequency and microwave ablation can be of limited applicability due to the presence of pacemaker or other cardiac devices [8,9].

Experience with liver or combined (heart and liver) transplantation is anecdotic, and no consensus exists on their indication.

TACE and sorafenib are usually selected as the first choice of treatment for multiple (≥4) unresectable HCC in adult patients.

Although no cardiotoxicity was reported with Sorafenib, close monitoring is advisable considering that cardiac function can be easily compromized.

In this case, in relation to the presence of multiple suspicious lesions and the presence of anatomical vascular variants, the patient was a candidate for TACE.

There are no reports of TACE in SI. In our view the following points were important for the success of the procedure: extensive study of the preoperative anatomy, correct preparation of the room with possible reversed position of the operators and the table; and operation with care to avoid misidentification of the anatomy.

The most important anatomical factors for TACE in this case were inverted liver anatomy and vascular anatomical abnormalities with multiple afferent branches to the lesion from SMA, celiac trunk and diaphragm.

Despite this technical difficulty, the repeated TACE was effective for HCC.

In addition, the interventional oncology procedure made it possible to detect and confirm the presence of areas of neovascularisation, further confirmation of HCC.

The presence of situs viscerum inversum and vascular anatomical variants did not prevent super-selective catheterization and precise identification of all the tumor supplying branches.

Portosystemic, extrahepatic and right-to-left cardiac shunts are frequent and may increase the risk of adverse events of TACE and radioembolization, as shown by the case of retinal artery embolism reported in literature [10].

Thus, since there is no fixed anatomical type, accurate understanding of the anatomy of organs and blood vessels before treatment is essential for success.

In this case no sistemic embolization or postembolization syndrome occurred and the patient was discharged pain free, and tumor markers were significantly decreased confirming that TACE offers in these patients a therapeutic option for unresectable HCC to improve survival.

There are cases in the literature of TACE in Fontan surgery [11] but there have been no reports of TACE in SI in Fontan cases, the detailed organ and vascular anatomy of SI obtained from this case is important. This case will serve as a reference for successful treatment in future cases.

Patient consent

Written consents must be obtained from the patient before procedural activities.

Declaration of Competing Interest

Corresponding authors declare no conflict of interest for all the other authors.

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