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Brief Report

Hepatocellular carcinoma in the adult Fontan patient

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Abstract In this study, we describe the case of a 36-year-old woman who was diagnosed with hepatocellular carcinoma on a background of Fontan procedure for tricuspid atresia. She had worsening heart failure in the months before presentation, and early investigations noted derangement in liver enzymes and hepatomegaly. Liver biopsy confirmed a hepatocellular carcinoma. Hepatocellular carcinoma is a rare but recognised consequence of cardiac cirrhosis in Fontan patients.

Keywords: Fontan; hepatocellular; cirrhosis; screening

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The initial Fontan procedure was performed in 1968 and represents a palliative approach to single ventricle circulation. As early Fontan patients have aged, emphasis has shifted to the long-term complications secondary to the procedure, particularly Fontan-associated liver disease.

Over the past 45 years, the body of knowledge has grown rapidly regarding Fontan-associated liver disease. These complications include fibrosis, cirrhosis, protein-losing enteropathy, hypovitaminosis D, immune deficiencies, renal disease, and lower extremity venous varicosities. There are rare reports of hepatocellular carcinoma.[1,2]

We report the case of a 36-year-old woman diagnosed with hepatocellular carcinoma on a background of advanced heart failure and a Fontan circulation.

Presentation

Our patient, E.B., was born with tricuspid atresia and underwent a classic Fontan at seven years of age, with revision to a non-fenestrated extracardiac conduit at 18 years of age. An epicardial dual-chamber pacemaker was placed for atrial tachyarrhythmia with four revisions by the time of current presentation.

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Her condition deteriorated in the months before presentation, with worsening lower limb oedema, ascites, and fatigue. She had also developed derangement of liver enzymes consistent with hepatic congestion. Her most recent abdominal ultrasound, three years earlier, noted a heterogeneous liver with a focal hypoechoic region in the right lobe. Despite apparent worsening heart failure, she had actually lost five pounds since her last admission.

On presentation, she was noted to be cachectic and hypoxic with saturations of 87% on room air. Jugular venous distension was present to the angle of the jaw with peripheral oedema to mid-calf bilaterally. The abdomen was firm, with a palpable liver to two fingerbreadths above the pelvic brim, and no jaundice.

Investigations

E.B.'s initial investigations were notable for increased venous congestion on her chest X-ray, a therapeutic international normalised ratio, and deranged liver enzymes. Pro-B natriuretic peptide was 1478. She was admitted under the cardiology service with a tentative diagnosis of decompensated heart failure and commenced on intravenous diuretic medications.

Her transthoracic echocardiogram noted her Fontan anatomy, with a Glenn Shunt and Fontan pathway that had non-obstructed, non-turbulent flow. Her left ventricle size and ejection fraction were normal.

Given her rapid decline, the decision was made to begin evaluation for heart transplant. The hepatology team was engaged because of persistent derangement in liver enzymes and hepatomegaly on ultrasound. They recommended transjugular liver biopsy, and histopathology results were positive for poorly differentiated hepatocellular carcinoma.

Plan

The presence of this malignancy posed a contraindication to heart transplant, and the case was instead reviewed by the oncology and palliative care services. The oncology service's opinion was that she would be unlikely to tolerate or benefit from systemic chemotherapy, and they recommended a palliative approach. Following extensive discussion with the family, the decision was made to proceed with home hospice; she was discharged home and died 10 days later.

Discussion

The increased risk of hepatocellular carcinoma in a cirrhotic milieu is well established, but little was known of its incidence in cardiac cirrhosis until the 1990s. This was likely attributable to poor survival in advanced heart disease, which pre-empted the development of cirrhosis. The progress in surgical and medical management of congenital heart disease in the 1960s and 1970s has increased survival among these patients, but these improvements also unmasked the threat associated with subclinical organ damage.

The proposed mechanism is transmission of increased central venous pressures of right-sided heart failure directly to the liver, leading to sinusoidal dilatation and eventually fibrosis.

The earliest reviews of survival and complications among Fontan patients have no record of liver abnormalities,[3] and the first report of cirrhosis was published in 1983.[4] Given that the Fontan procedure only became widespread in the 1970s, this is unsurprising. The first record of a Fontan-associated hepatocellular carcinoma was in 1991,[1] with no additional mention in the literature until 2005;[2,3] one of the 2005 papers reviews the clinical and pathological features of nine patients on autopsy, who had undergone a Fontan procedure. Of the nine patients, four had cirrhosis and one had hepatocellular carcinoma. There is a positive correlation between time from Fontan and severity of disease, and that patient with hepatocellular carcinoma had the longest postoperative survival, of 18 years.

Optimal screening strategies for Fontan patients with liver disease are uncertain: American Association for the Study of Liver Disease guidelines for hepatocellular carcinoma screening do not reference cardiac cirrhosis; however, they deem the threshold incidence of hepatocellular carcinoma in "other" causes of cirrhosis for efficacy of surveillance to be 1.5% per year.[5] Given that the risk of hepatocellular carcinoma in Fontan patients is estimated to be 1.5–5% per year,[6] it seems appropriate to screen.

Screening for hepatopathy should be undertaken on an annual basis and should include transaminases, and non-invasive abdominal imaging must be performed every two years, including liver elastography or liver MRI with elastography depending on the expertise of the institution.[7] HCC-specific screening should take place every 6–12 months, including platelet count, alpha-fetoprotein, and liver ultrasound. With regard to time of screening initiation, recommendations in the literature vary from 5 to 11 years after Fontan completion. It is also reasonable to screen for the effects of portal hypertension in those with severe cirrhosis. Risk stratification with the MELD XI score[8] and the VAST score[6] remain valuable tools in the evaluation of these complex patients.

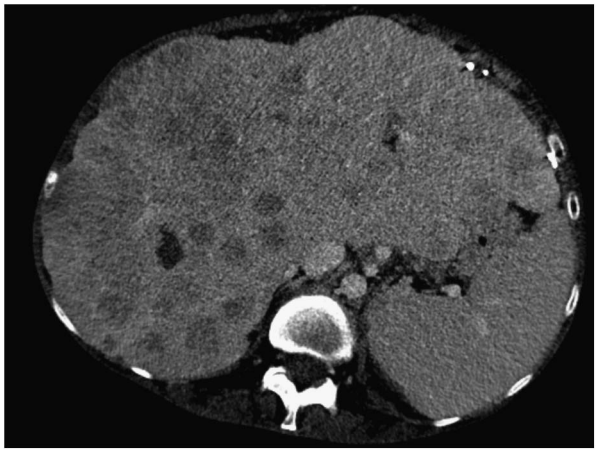

Figure 1.
CT imaging of liver metastasis.

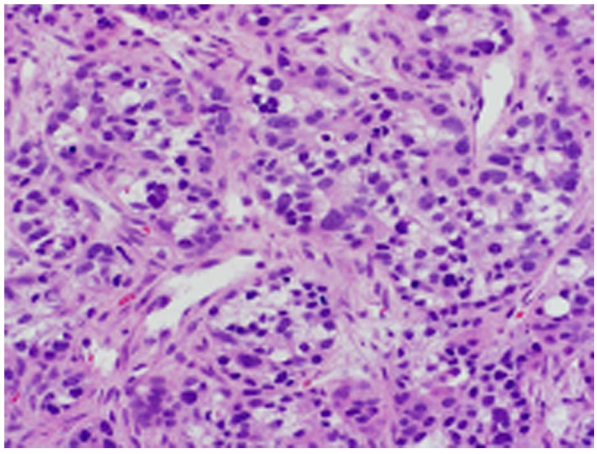

Figure 2.
Biopsy sample showing hepatocellular carcinoma.

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Patients and families who are considering a Fontan completion should be counselled regarding well-understood, long-term consequences of the palliation, including Fontan-associated liver disease. Elder et al[9] argue that delaying Fontan completion may be a reasonable approach.

It is known that adult congenital heart disease patients are disproportionately likely to die while on the transplant waiting list. This case lends further weight to the concept that complex adult congenital heart disease patients should be evaluated serially for transplant candidacy. Fontan conversion continues to be an option; however, it only remains appropriate for selected candidates. Further study is needed to appropriately determine indications for liver transplant, timing of cardiac transplant, and the most appropriate modality to assess hepatic functional capacity (Figs 1 and 2).

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