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Adult diffuse hepatic hemangiomatosis associated with focal segmental glomerulosclerosis

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Introduction

Diffuse hepatic hemangiomatosis (DHH) is an extremely rare disease in adults characterized by the replacement of the liver parenchyma by diffuse angiomatous lesions. The etiology and natural history of DHH are not completely understood because of the rarity of the condition. The association with conditions like hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease), systemic hemangiomatosis, and the possible role of drugs (metoclopramide and oral contraceptives) was described previously [1]. We report a patient with adult DHH having splenic involvement which was associated with focal segmental glomerulosclerosis.

Case report

A 31-year-old male was admitted with bilateral pedal edema for 3 months. His past medical history was unremarkable and he had no addictions or high-risk behavior. Examination showed high blood pressure and hepatosplenomegaly. His blood counts were normal and blood biochemistries were normal except for hypoalbuminemia and mild renal failure. He had nephrotic range proteinuria (24-h urine protein–5.185 g). Ultrasonography of the abdomen showed enlarged liver and spleen with multiple ill-defined heterogeneous lesions. Contrast-enhanced computed tomography of the abdomen showed multiple hypodense lesions in the liver of varying sizes with peripheral enhancement and complete filling in the delayed phase. Multiple low attenuation nodules in the spleen with enhancement in the arterial phase and filling in the venous phase were present (Fig. 1A, B). Magnetic resonance imaging of the abdomen showed multiple lesions in the liver and spleen which were T1 hypointense and hyperintense in T2 (Fig. 1C, D), diffusion-weighted, and apparent diffusion coefficient images. Histopathology of the ultrasound-guided liver biopsy from the lesion showed anastomosing vascular spaces lined by endothelial cells which were CD34 positive (vascular endothelial marker) without cellular atypia (Fig. 1E, F). Radiological and histopathological findings were suggestive of hemangioma. Renal biopsy revealed focal segmental glomerulosclerosis (FSGS) (Fig. 1G, H). C3 and C4 levels were normal. HIV, hepatitis B, and hepatitis C serologies were negative. Antinuclear antibody was negative. Exome sequencing revealed no mutations responsible for monogenic forms of FSGS. He was diagnosed to have diffuse hepatic hemangiomatosis with paraneoplastic FSGS. The usual causes of FSGS were ruled out (including maladaptive, virus, genetic, drugs, and immune) by appropriate tests. He was managed with dietary salt restriction, Ramipril, and steroids which was tapered slowly. He was referred to a hepatobiliary surgeon for the management of diffuse hepatic hemangiomatosis and was advised conservative management with follow-up imaging and liver function tests.

Discussion

Diffuse hepatic hemangiomatosis (DHH) is an extremely rare disease and to date, there are only eighteen cases of adult DHH reported in the literature with pathological evidence [2]. Most of the reported cases were females with a female to male ratio of 2.4:1 [2]. DHH was

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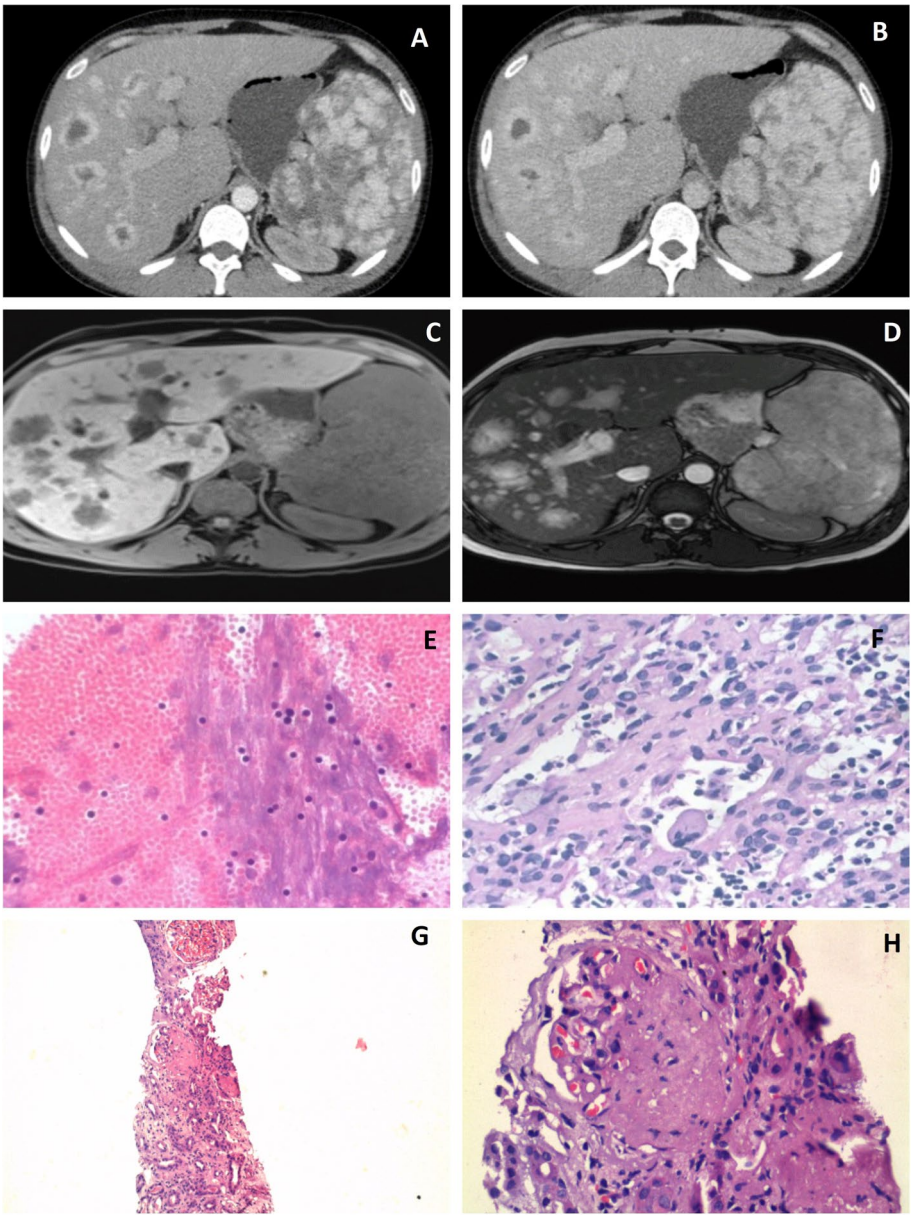

Fig. 1 Contrast-enhanced computed tomography of the abdomen showing multiple hypodense lesions in the liver of varying sizes with peripheral enhancement and complete filling in the delayed phase. Multiple low attenuation nodules in the spleen with enhancement in the arterial phase and filling in the venous phase (**A**, **B**). Magnetic resonance imaging of the abdomen showing multiple lesions in the liver and spleen which were T1 hypointense and hyperintense in T2 (**C**, **D**). Histopathology from the liver lesion showing anastomosing vascular spaces lined by endothelial cells which were CD34 positive (vascular endothelial marker) without cellular atypia (**E**, **F**). Renal biopsy core with 1/11 glomeruli showing features of focal segmental glomerulosclerosis (**H**, **E** × 10) (**1G**). Glomerulus with segmental sclerosis with adhesion to the capsule (**1H**) (**H**, **E** × 40)

commonly found among middle-aged and elderly people of both sexes. Most of the cases were reported from Asian countries (Korea and Japan) [2]. Splenic involvement was only reported in a Japanese patient with DHH [3].

Extrahepatic lesions in DHH can be seen in the skin, intestine, lungs, spleen, central nervous system, adrenal glands, and bone marrow [4]. Involvement of the spleen can cause thrombocytopenia, anemia, consumptive coagulopathy, Kasabach–Merritt syndrome, and disseminated intravascular coagulopathy [5].

Nephrotic syndrome in patients with solid tumors is usually due to membranous nephropathy but cases of

minimal change disease, FSGS, mesangiocapillary glomerulonephritis, crescentic glomerulonephritis, and amyloidosis have also been reported [6]. Although paraneoplastic syndrome is usually associated with malignancy, there are reports describing paraneoplastic syndromes induced by benign tumors [7]. Benign tumors like carotid body tumor, spinal schwannoma, and adrenal ganglioneuroma were reported previously in association with membranous nephropathy [6]. Minimal change disease and mesangiocapillary glomerulonephritis were also found to be associated with benign tumors [6]. FSGS was previously reported associated with malignant solid tumors of various organs but not with benign tumors [6]. The usual causes of FSGS in our patient were ruled out (including maladaptive, virus, genetic, drugs, and immune) by appropriate tests. The association of FSGS with DHH in the above patient may be secondary to the tumor or by chance.

Conclusions

The case described above is important for the following reasons;

1. This is the 19th patient with DHH and the second case with DHH having splenic involvement in the whole literature.
2. To the best of our knowledge, this kind of association of an extremely rare disease (DHH) with FSGS was not reported previously.

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Human and Animals Rights
No animals were involved in the study.

Author's contributions
MCA—clinical analysis, writing the manuscript, clinical analysis, and critically revised and approved the manuscript. The author read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were by the ethical standards and with the 1964 Helsinki declaration and its later amendments.

Consent for publication
Informed signed written consent was taken from the patient involved.

Competing interests
The author declare no conflict of interest.

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