

Hepatocellular carcinoma in South Sudan: possible aetiologies, presentation, diagnostic challenges and ways forward

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Hepatocellular carcinoma is one of the common malignancies in both the developed and developing worlds. This is most likely due to its wide variety of causes. The aetiologies vary from one part of the world to another determined by many factors ranging from geography, life style, availability of advanced medical care etc among many others. Though the presentation and diagnosis of hepatocellular carcinoma is straight forward in many developed countries, the reality is different in many resource-constrained regions and countries such as South Sudan which has only one Computer-Tomography machine country wide, lack of most of the non-invasive liver screening tests as well as coupled with lack of medical personnel. However, in spite of these challenges, the authors of this article believe that the diagnosis of hepatocellular carcinoma can be reasonably made considering the clinical presentation of this condition and maximizing the use of available diagnostic tools.

KEY WORDS: *common malignancies, hepatocellular carcinoma, South Sudan*

Introduction

Hepatocellular carcinoma (HCC) is the 5th commonest cancer among adult men and the 7th among women. It is the second most common cause of cancer related deaths in the world [1]. In terms of aetiology, it had been shown that almost 80% of global HCC is related to chronic hepatitis B and C infections [2]. This gets us to question the prevalence and distribution of these two viruses. It is argued that the prevalence of HCC is determined by the geographical distribution of these two viruses and the age of acquisition. For example, in the West, the commonest causes of HCC are alcohol related cirrhosis and hepatitis C (due to intravenous drug injection) which are all related to older age while in the developing world, the commonest cause is Hepatitis B virus which is mainly acquired vertically (thus the importance of age of acquisition) and aflatoxin which are related to early exposure. This is further aggravated by the lack of wide Hep B vaccine coverage in the developing world (Sub Saharan Africa) in the past. However, horizontal transmission of Hepatitis B is also on the rise in the developing world among children due to salivary viral shedding while playing with each other. Also, improper/incomplete sterilization of barbers' shavers is another reason for the horizontal transmission among adults in the developing world. Although this partially explains the high Hep B related HCC in the developing world, alcohol is also seen to be rising as a potential cause of cirrhosis and thus, HCC in this part of the world [5].

In South Sudan, there are no data showing prevalence of HCC or its related risk factors such as hepatitis, alcohol consumption and many others.

Causes of HCC

It is worth noting that 80-90% of HCC present in the background of cirrhosis [3]. So, what are the causes of cirrhosis and which ones are common in South Sudan? It is literally proven that any condition that can lead to cirrhosis of the liver can cause HCC. These conditions include (but not limited to):

- Chronic Hepatitis B and C viruses
- Aflatoxins
- Excessive alcohol consumption
- Moderate alcohol consumption in a background of another liver condition
- NAFLD
- Hemochromatosis
- Wilson's disease
- Right sided heart failure
- Alpha 1 antitrypsin deficiency
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Tyrosinosis

Sube et al. determined the co-infection rate between HIV and Hepatitis B and C among blood donors in Juba Teaching Hospital to be 50% and 18% respectively [4].

Although they pinned this down to the common modes of transmission of these viruses, it is worth mentioning that these are high prevalence among healthy population attending for blood donation. Out of clinical experience in South Sudan, one can tell that the prevalence of Hepatitis B and C viruses is high with the former much common than the later. This is a grey area calling for a country-wide research. This high prevalence could be explained by the lack of vaccination (for Hep B) in the past for children due to the civil war which rendered many parts of the country inaccessible. Not only is that, the avoidance of vaccination in the past by communities due to surrounding myths as well can explain this. Therefore, there is a clear need for urgent studies to determine the prevalence of the possible causes of liver cirrhosis and thus, HCC in South Sudan.

Clinical presentation

Depending on the cause of HCC, patients can present slightly differently. However, keeping in mind that 80-90% of HCC occur in cirrhotic patients, then presentation mimics that of cirrhosis and could be in form of cachexia, jaundice, rapid ascites (due to portal vein thrombosis given that HCC like any other cancer is a pro thrombotic condition), pruritus (due to ductal compression), finger clubbing, right upper quadrant pain, variceal bleeding (hematemesis and/or melaena) etc. On the other hand, HCC can be an incidental finding on an US scan of an abdomen done for unrelated complains. This is rare though.

Investigating HCC

For every jaundice or liver mass (on examination) of unknown cause, it is always worth performing the routine investigations plus the Non Invasive Liver Screening. The routine tests include: FBCs, Urea and Electrolytes, LFTs and coagulation. These could offer a hint on the possible aetiology or performance status. For example, raised MCV (alcohol?), very high WCC (Leukaemia? Infection?), thrombocytopenia (alcohol? portal hypertension?), raised urea and creatinine (hepatorenal syndrome?), very high GGT (HCC?, Alcohol?), deranged coagulation (failing liver? DIC?), very high AST and ALT (Ischaemic liver? Paracetamol overdose?), low platelets and high INR (reconsider liver biopsy?)

Non-Invasive Liver Screening Tests (NILS) include:

- Liver auto antibodies: AMA, Gastric parietal cell, LKM antibody and Smooth muscle antibody.
- Immunoglobulin G, A and M: Looking for autoimmune hepatitis
- 24 hr urinary copper and serum ceruloplasmin: In those under 40 yrs looking for Wilson's disease
- Alpha 1 antitrypsin level: Looking for a low level
- Alpha fetoprotein: When there is a mass on imaging

- Hepatitis B and C. Can cause both acute and chronic liver disease though acute presentation is rare in C.
- Hepatitis A, CMV, EBV and Adenovirus: For acute jaundice only. They don't cause chronic liver problems. In South Sudan, most people are immune to these.
- Serum ferritin level: If high (supported with clinical features), think of HFE gene
- Serum lipids: If you are thinking of NAFLD
- US abdomen: Liver, spleen, gall bladder, CBD, ascites, PV, HV, head of pancreas, etc. On finding a low attenuating hepatic lesion on US, there should be a high index of suspicion for a HCC and thus, an alpha fetoprotein and CT chest, abdomen (liver) and pelvis should be requested to clearly define the liver lesion(s) and establish any metastases. However, a definite diagnosis of an HCC is histological. Tissue is usually obtained by an US guided liver biopsy which is safer than a blind intervention. [6]

Diagnostic challenges in South Sudan

South Sudan has very limited tests to investigate HCC and its possible cause(s) beside hepatitis serology, ultrasound and a CT (only found in one private facility). There is an absence of all the other relevant tests and only two pathologists in the country (when thinking of biopsy). Some private facilities can perform the AFP titres as well. This is the reality at the time of writing and publishing this article. These limited resources make it hard (but not impossible) to reasonably diagnose HCC and determine a possible cause. A strong clinical sense (supported by detailed history and examination) with a maximum use of the available limited resources should allow this to happen though undoubtedly, we shall be missing out some aetiologies for HCC. So, the authors of this article are saying, US, AFP, LFTs, viral hepatitis serology and a good clinical approach should pick up most of the HCC cases and determine their viral causes.

Treatment modalities

Definitive curative treatments for HCC are either hepatic resection or liver transplantation. This entirely depends on the size, number and spread (metastasis) of the cancer. This is outside the scope of this article. However, it is worth mentioning that all patients with a HCC (non metastatic) be referred to specialist care (non-existent in South Sudan) immediately as some of them could benefit from interventions such as Radiofrequency ablation (RFA), Trans-arterial Chemoembolization (TACE), resection or transplant.

For those with clear metastatic disease, it is worth

offering specialist option as well for palliative purposes. All these treatment options are currently missing in South Sudan and therefore, it is worth to critically think and maximally involve patients in deciding the balance between the costs of foreign travelling and medical care/ outcome expected to that of remaining at home and spending quality time with family.

Conclusions and ways forward

From the review of articles and the possible causes and prevalence of HCC, it is clear that South Sudan is a country in a belt with a high risk of HCC. It is therefore worth investigating patients with suspicious liver lesions on imaging or liver enzymes. It is also worth maximizing our clinical senses in obtaining detailed risk history (to complement our limited investigations) as well as maximally using the available resources. Research is definitely needed in this field to determine common causes of HCC in South Sudan and their distribution nation-wide.

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