Case Report

Hepatocellular Carcinoma in Pregnancy; Still Rare, Still Occurring Still Devastating - A Case Report in A Pregnant Nigerian Woman

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Abstract

Although hepatocellular carcinoma or hepatoma is estimated to cause about one million deaths annually, it is a very rare condition in pregnancy. Despite its being rare in pregnancy, it still occurs with a lot of devastation to afflicted patients. Some authorities say that morbidity and mortality have improved over time as diagnoses have tended to be made earlier and patients have received surgical and other treatments. Other workers have however reported a maternal mortality of one hundred percent with death occurring either antenatally or immediately postpartum. The rarity of this cancer coupled with the often times vague way of presentation make the diagnosis to be often missed or the disease to be detected late when cure is impossible. We present one such case, the 57th reported case in the world in English literature in a pregnant Nigerian woman with hepatoma in pregnancy.

Keywords: Hepatocellular carcinoma; Pregnancy; Rare cancer

Introduction

Although hepatocellular carcinoma causes an estimated one million deaths annually [1], it is a very rare condition in pregnancy [2,3]. Though, less uncommon in the female population, it is even rarer in pregnant women. Some authorities say that morbidity and mortality have improved over time as diagnoses have tended to be made earlier and patients have received surgical and other treatments [4]. Other workers have however reported a maternal mortality of one hundred percent with death occurring either antenatally or immediately postpartum. We present a case, the 57th reported case in the world in English literature in a pregnant Nigerian woman.

The Case

We report a 27 year old Gravida 2 para1^{+0} Nigerian from the Ibo tribe, a health worker with one living child who had hepatocellular carcinoma in pregnancy and died three months after delivery. She presented at our booking clinic at a gestational age of 26 weeks and five days and had no complaint. The index pregnancy was said to be uneventful before this time. She neither took alcohol nor tobacco in any form and did not use any family planning methods though she was aware of them. She was not hypertensive or diabetic, was not on any drugs, either herbal or orthodox and had no family history of malignancy. She had no past history of yellowness of the eyes or blood transfusion. The past medical and surgical histories were not significant. She was examined and was healthy looking, afebrile, anicteric and not pale. Her symphysio-fundal height was 24cm which corresponded with her date. She was given her routine drugs and a four-week appointment. She kept her appointment and complained of feeling dizzy on standing for a while. There was no fever, blood loss or any other associated symptoms. Investigations showed that she had 3 pluses of malaria parasites and her packed cell volume (PCV) was 25%. A diagnosis of symptomatic anemia with malaria in pregnancy was made and she was treated for malaria with Arthemesinine-combination therapy and given hematinics which she opted for instead of blood transfusion. Her PCV eventually rose to 29%. At 34 weeks and 5 days gestation, she complained of feeling dizzy again and upper abdominal pain which was discomforting but did not prevent her from carrying out her house hold chores. There was no fever or bleeding from any orifices and no urinary, gastro-intestinal or any other symptoms, systemic or local.

Examination revealed a healthy-looking young lady in no obvious distress who was afebrile, anicteric and mildly pale. She had mild pitting edema but there was no lymphadenopathy. The liver was palpable, 13cm below the right mid-clavicular line, slightly tender, irregularly-surfaced with a sharp edge. The spleen was not palpably enlarged and the kidneys were not ballotable. The symphisio-fundal height was 33cm which corresponded to her gestational age. The uterus habored a singleton fetus in longitudinal lie, cephalic presenting in right occipito-anterior position. The fetal heart was heard and regular. A diagnosis of hepatomegaly in pregnancy ? cause, to rule out liver cirrhosis was made and she was referred to the Physicians.

The initial liver function test, serum electrolytes, urea, creatinine and lipid profile were normal. In the second liver function test done 2 months later, the Aspartate transaminase was elevated, 60u/L (8 to 18 U/L), as well as total bilirubin, 27.8Nm/L (5 to 21) Nm/L and conjugated bilirubin which was 10.4 Nm/L (less than 8/Nm/L). The retroviral screening,

VDRL, HbsAg and HCV were negative. The alpha feto-protein was elevated 37.6ug/L (less than 15ug/L). Serum proteins were normal. Prothrombin time was 11 seconds (10 – 15 seconds) and bleeding time was 3 minutes and 51 seconds.

The abdominal ultrasound done showed a grossly enlarged liver with irregular and distorted parenchymal echo-pattern and multiple echogenic nodular masses affecting more of the left lobe with infiltration to the right lobe. There was probe tenderness. Hepato-billiary radicles were not visualized. There was no significant increased vascular flow on doppler interrogation. The gall bladder was not enlarged but showed thickened walls. Both kidneys, spleen and pancreas appeared normal. There was no ascites or lymph nodes seen. The uterus harbored a single viable fetus in longitudinal lie, presenting cephalic with fetal biometry showing a gestation of 37 weeks with reduced liquor volume and an antero-fundal placenta. The internal os was closed. Impression: A viable intra-uterine pregnancy at 37 weeks gestation with hepatic parenchymal disease ? cause. Cytology was advised.

Fine needle aspiration biopsy was done.

Histology Report

Histology smears showed clusters of discohesive large epithelial cells with coarse vascular nuclei and prominent nucleoli in areas. Also seen were mononuclear inflammatory cells especially plasma cells and lymphocytes. Also noted in areas were some neutrophils and fibrous tissues.

Diagnosis: Hepatocellular carcinoma.

Labor was induced at 37 weeks and six days gestation and she was delivered of a life 3.2 kg female baby that was normal with Apgar scores of ten in one and five minutes respectively.

Patient was discharged two days after delivery to continue her management with the Physicians. She kept her six weeks postnatal visit appointment. Though emaciated now with mild icterus with the liver now 20cm below the right mid-clavicular line, nodular, moderately tender and sharp-edged, the uterus was well involuted. The baby was well and had received her due immunization. She was encouraged to continue her treatment with the Physicians who had started her on chemotherapy. The liver eventually enlarged to the level of the anterior-superior iliac spine with a span of 30cm.
She at some point signed against medical advice and left the hospital. She eventually died three weeks after (three months after delivery)

Discussion

Hepatocellular carcinoma is a Primary solid malignancy of the liver [1] which is a leading cause of cancer deaths all over the world [2]. It occurs less commonly in women and very rarely in pregnancy [3,4] with an estimated incidence of one in 100,000 [5] most of whom reside in Africa and Asia [6]. Our patient comes from Nigeria in Africa. Hepatocellular carcinoma is a very rare tumour in pregnancy. This patient of ours was the 57th reported person in English literature to have hepatocellular carcinoma in pregnancy. Since Roddie's first report of a case of hepatocellular carcinoma in pregnancy in 1957 [7], Choi et al. [8] in 2011 reported four cases and analyzed another 44 cases they could find in the

literature making their series the 48 cases reported all over the world up till 2011. Our search through the literature from 2011 when Choi et al reported the 48 cases in world literature till date only revealed an additional 8 cases bringing the total number of reported cases of hepatocellular carcinoma all over the world in English Literature to 56. Ours is the 57th reported case world over.

Ndububa et al. [9] in Nigeria found Hepatocellular carcinoma to occur in an age range from 22 to 37 years with a mean age of 28.2 years. Our patient was 27 years and fitted into this age range.

The risk factors for hepatocellular carcinoma in pregnancy include race – being an African or Asian especially Chinese is more likely to predispose a pregnant woman to this carcinoma, Hepatitis virus infection (both B and C), cirrhosis of the liver, non-alcoholic fatty liver disease, associated obesity and type 2 diabetes mellitus [5], aflatoxin, alcohol, combined oral contraceptives pills [10] and increasing parity [11], family history [10,11] late menopause [13], early menarche [14] etc. It is however important to note that some women who have hepatocellular carcinoma in pregnancy do not have any of these risk factors [10]. The only risk factor for hepatocellular carcinoma in our patient was her African origin; she is an Ibo from southeastern Nigeria.

At times, investigations may not be helpful in making a diagnosis of hepatoellular carcinoma as liver function tests and maternal alpha fetal protein levels may be normal [3] or only slightly elevated. Although alpha fetoprotein may be markedly elevated in some cases of HCC, its being elevated in pregnancy [4] and in other conditions renders its use in the diagnoses of HCC further confusing and unhelpful. Laboratory tests were initially unhelpful in our case as the first liver function test and alpha feto-protein, prothrombin time etc done were normal. However, by the time the tests were repeated two months later they became abnormal.

Ultrasonography is very important in making diagnosis of hepatocellular carcinoma in pregnancy [4] as it detects hepatic mass and can to some extent help in characterizing hepatic pathologies in ways that can help raise enough suspicion to warrant further investigations and enable the taking of steps that will enable biopsies to be taken and pathology confirmed. It is indispensable in early diagnosis which offers much hope in these patients for early resection where possible and has improved survival. Ultrasonography really helped us in the management of our patient both as it assisted us to make a tentative diagnosis, proffered extent of spread of the pathology and prodded us to make further investigations toward definitive diagnoses.

The diagnosis of hepatocellular carcinoma in pregnancy can be difficult as it may be asymptomatic [14] especially in the early stages. At times, it can be discovered incidentally on abdominal examination or in response to the patient complaining of upper abdominal pain or as incidental finding of a liver mass on ultrasonography which might be the only finding that might lead to the eventual diagnosis of the disease. Diagnosis therefore calls for a high index of suspicion on the part of the Obstetrician.

Also diagnosis during pregnancy is difficult because many of the physiologic symptoms of pregnancy such as fatigue, nausea and vomiting can be similar to those of hepatocellular carcinoma especially at the early onset [3]. Equally

important is that, as pregnancy progresses, a palpable liver mass may become less evident [4] contributing to difficulty in diagnosis. The diagnosis of this disease in our patient was difficult as it was initially asymptomatic as patient did not have any complaint initially.

One month after booking at 30 weeks and 5 days, she complained of dizziness and was treated for malaria which was the only finding in addition to the anaemia she had.

In symptomatic cases, the commonest presenting symptom is right upper quadrant abdominal discomfort or pain [18]. Presence of a mass in the upper abdomen, weight loss and hepatomegaly have been the most frequent presentation [14]. Our patient complained of right upper abdominal pain.

One month after our patient complained of dizziness, she still complained of the dizziness and upper abdominal pain/discomfort that did not prevent her from carrying out her normal household functions. It was at this point that abdominal examination revealed hepatomegally.

Hepatocellular carcinoma has accelerated course in pregnancy than in the none pregnant women [8,15,16]. This is attributed to the increased levels of estrogen in pregnancy which accelerates the growth of hepatocellular carcinoma and the immune suppression that occurs in pregnancy [17]. Hepatocellular carcinoma had an accelerated course in our patient because from being asymptomatic on presentation at 26 weeks and 5 days, She deteriorated very fast and died within six months of presentation.

Available treatment for HCC in pregnancy include liver resection which has now been accepted as the main stay of treatment and the gold standard [4,13,14]. Other treatment modalities include chemotherapy, radio frequency ablation, ethanol injection etc. [4]. Treatment should be multi-disciplinary. Any treatment modality must take into consideration the mother and the baby. Adjunctive treatment before delivering the baby like giving surfactants or steroids for fetal lung maturity is important. At term the mother should be delivered so that she could receive the full benefits of any treatment modality that could be offered to her. In our patient, the baby was almost term at 37 weeks and 6 days weeks and was delivered to enable the mother get chemotherapy which was the treatment modality that was adopted for her given the extent of spread of the disease, also management was multi-disciplinary. We did not have to give any adjunctive treatment to the baby as the lungs were considered to have matured before delivery.

Some works attribute almost 100% maternal mortality to it [9]. However, recent literature show that the prognosis is better now with a fetal rate survival of 57% [10] and this has been attributed to earlier diagnosis and application of different treatment modalities including surgical resection of the tumors [18]. In our patient, though the baby survived, the mother died three months after delivery.

Hepatocellular carcinoma though rare in pregnancy still occurs. It may initially be asymptomatic or insiduos and vague in presentation further tasking the Obstetrician while it carries on its devastation. Obstetricians should therefore develop a high index of suspicion to be able to diagnose this disease early when there is still some hope of cure in the rare instance

when a woman will be unfortunate to suffer it.

Conflict of Interest

There was no conflict of interest

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