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T2 breast cancer presenting with diffuse liver metastases and hepatic failure following fertility treatment. Cautionary report

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ABSTRACT

BACKGROUND: Diffuse hepatic metastases with hepatic failure as a presentation of a T2 breast cancer is rare. This is also remarkable seeing our case had been on fertility treatments before presentation. There are no documented reports of breast cancer patient on fertility treatment presenting with diffuse hepatic metastases and liver failure.

CASE SUMMARY: A 41 year old Para 1 Nigerian woman being managed for secondary infertility with an extended use of clomiphene presented with a 3 months history of a left breast lump, nipple bleeding and later, yellowness of eyes, right hypochondrial pain malaise and drowsiness. Abdominal USS showed an enlarged liver with diffuse metastatic nodules. Liver function tests showed persistently elevating liver enzymes and serum bilirubin. Serology showed Hepatitis B negative. She was diagnosed with a T2 left invasive ductal carcinoma, Er−, Pr+ Her2+ with deteriorating liver function from diffuse hepatic metastases She had chemotherapy but succumbed barely a week of presentation.

CONCLUSION: Breast cancer screening for patients before fertility treatments and continual surveillance while on such treatment is highly recommended.

1. Introduction

Although hepatic metastases from breast cancer is not an uncommon presentation with reported incidence at 40–50% [1] hepatic failure as a presentation of metastatic breast cancer is very rare. Rowbotham et al. has described an incidence at 0.44% for hepatic metastases for malignancies with very few cases reported in the literature. [2] Hepatic failure following hepatic metastases though rare has been reported more for non-Hodgkins lymphoma unlike metastatic breast cancer. [3] An aetiological association between fertility drugs and breast cancer has not been reported to exist. However increase in oestrogen levels is associated with use of clomiphene, a selective estrogen receptor modulator. We rationalize that this may promote the growth of a preexisting breast cancer. We report the case of a 41 year old para 1Nigerian woman, who had been managed for secondary infertility with clomiphene, that presented with a T2 tumour of 3 months duration which emerged as hepatic metastases with liver failure. Her demise occured barely a week from presentation (Figs. 1 and 2).

The rapidity of progression of this disease with subsequent demise within a week of presentation is remarkable. We believe that the prior use of clomiphene may have escalated the progression of this T2 tumour. Though it has been reported widely that clomiphene raises levels of oestrogen to supraphysiological levels [4] we are not aware of a report associating the prior use of this selective estrogen receptor modulator with the rapid progression of a previously existing breast cancer. Again previous reports of liver failure from hepatic metastases have occurred in subjects who have been managed for breast cancer in the past. In addition, our case deserves mention being a fresh diagnosis following a 3 month history of a T2 breast tumour.

2. Presentation of case

A 41 year old para 1 lady was referred from a fertility clinic with a 3 months history of a left breast lump and nipple bleeding. She had been managed for secondary infertility with an extended use of clomiphene having visited other fertility clinics. She had no previous history of liver disease. Initial general examination findings were unremarkable. Breast examination showed bloody nipple discharge and a hard left breast lump measuring 4 by 3 cm with no attachment to skin or underlying tissue. There was a single discrete left axillary lymph node. Abdominal examination showed an enlarged liver 6 cm from costal margin. Breast biopsy revealed an invasive ductal carcinoma, positive progesterone receptor and doubly overexpressed human epidermal growth factor receptors. Abdominal ultrasound scan showed diffuse metastatic liver nodules. Abdominal CT or MRI was not immediately available. She was staged T2N1M1. In the course of investigation, she developed fever, increasing scleral icterus, malaise, drowsiness and right

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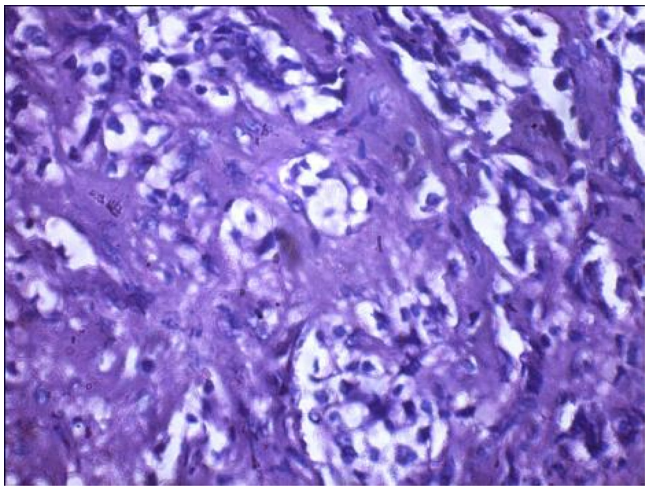

Fig. 1. Photomicrograph showing invasive ductal carcinoma.

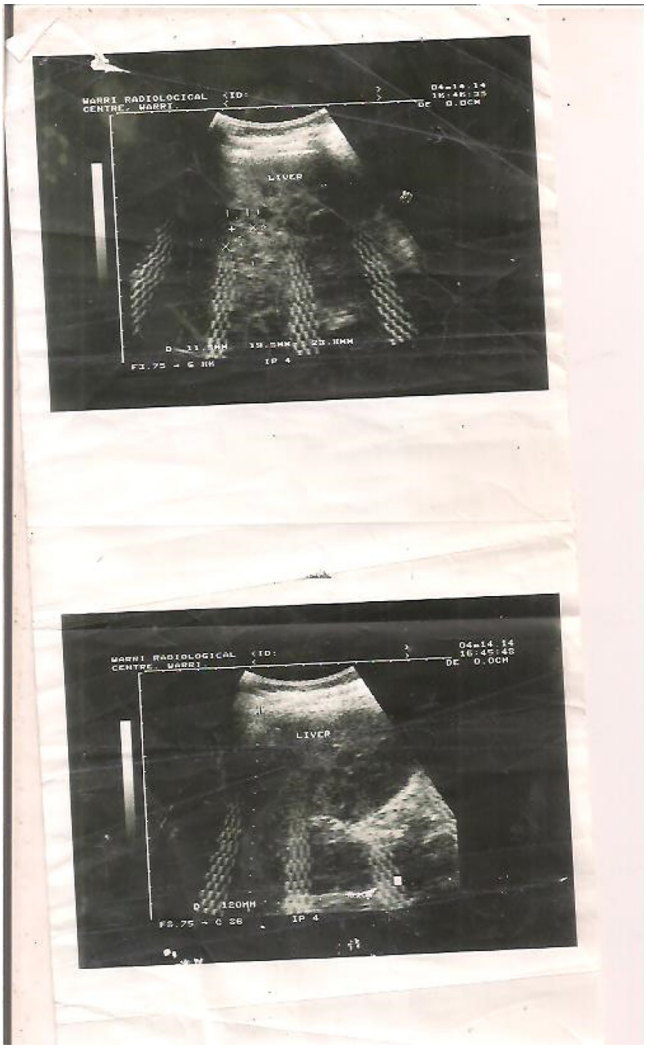

Fig. 2. Abdominal ultrasound photo showing a nodular liver.

hypochondrial pain. Liver function tests showed progressively elevating serum bilirubin and elevating aminotransferases. Viral hepatitis and HIV screening were negative. She was assessed as having decompensating liver function from diffuse hepatic metastases. She received taxane chemotherapy while anticipating herceptin administration. She continued to deteriorate with deepening scleral icterus, drowsiness and confusion dying within 9 days following presentation.

3. Discussion

Our case was being managed for infertility at other fertility clinics before presenting with a 3 months history of a breast lump/nipple bleeding and diagnosed with a T2 tumour with diffuse liver metastases. This is considered a short duration for such metastases and a rational explanation would be the presence of a growth promoter, a history of clomiphene use which would result in exponential increases in oestrogen levels, the breast cancer being a hormone positive tumour.

Acute liver failure with liver metastases is rare being seen with diffuse parenchymal infiltration as in our case. [5] Very few cases have been reported in the literature with the prognosis more or less dismal. The fertility treatments before presentation may explain the aggression of this disease within the short duration of three months. Although several reports have not determined an aetiological association between fertility drugs and breast cancer, other reports do not deny a growth promotion in a preexisting breast cancer being hormone dependent especially in our case which was hormone positive. Again the tumour in our case was overexpressing for the Her 2neu protein another factor in its aggression and rapidity of spread. Our case tested negative for hepatitis B, a common case of hepatic failure in our environment. Our case did not respond to hormonal manipulation with tamoxifen and continued to deteriorate. This further reiterates the need for breast cancer screening before women are placed on fertility drugs. A much needed call in this era of an upsurge in fertility treatments.

Patients who had been adequately treated for breast cancer in the past have been the subject of most reports with invasive ductal carcinoma being the histological type as in our case. [5] However our case was exceptional being a diagnosis at first presentation thus had not received any treatment nor had a history of liver disease. Prodromal symptoms of fever, malaise, right upper quadrant pain have been reported to precede the onset of liver failure as occurred in our case prior to commencing any treatment. [2]. Even though our case had chemotherapy to attempt to curtail the metastases, the patient's presentation with signs of deteriorating liver function; elevating liver enzymes, increasing bilirubin levels, right hypochondrial pain, drowsiness predated the administration of chemotherapy. Although we were unable to obtain an abdominal CT to determine the extent of liver involvement of the liver metastases, the abdominal ultrasound scan findings showed extensive hepatic involvement.

Nieto et al. reported the peculiar case of fatal acute liver failure from a previously 4 year old indolent breast neoplasm in a patient with a previously known liver disease [6]. The patients liver metastases was reported to be widely infiltrating as in our case with diffuse metastatic liver nodules. The occurrence of diffusely infiltrating liver nodules has been reported to be most commonly associated with acute liver failure [5]. Anorexia, jaundice, and different levels of altered mental status have all been described as features in these cases of diffuse liver parenchymal involvement from an aggressive breast cancer as occurred in our case [1]. Martelli et al. have reported a metastatic breast cancer with rapidly progressive liver failure but radiographically occult liver lesions; massive hepatic infiltration being demonstrated at autopsy [7]. Another worker described hepatic failure occurring from an occult breast carcinoma [8]. Our case had hepatomegaly with demonstrable diffuse liver nodules on abdominal ultrasound scan. Biochemical elevations in the levels of aminotransferases, lactate dehydrogenase and alkaline phosphatases were prominent features in our

case as has been reported [5]. However coagulopathy, disseminated intravascular coagulopathy and thrombocytopaenia were not observed in our case as has been described by other reports [5].

A rapid and aggressive course of the disease is described for this disease with a very poor prognosis. The reported cases were described as uniformly succumbing to the condition in a short time. Some workers have suggested that up to 80–90% involvement of hepatic parenchyma by the tumour with hepatic failure likely provides explanation for the early demise of these reported cases [9], as in our case. We believe that the elevation of oestrogen levels from fertility drugs over a period of time may have promoted the growth of this tumour and its consequent liver metastases with widespread liver nodules within an observed 3 months clinical history. With the increase in utilisation of fertility drugs, there comes a need for pre-treatment screening and increased surveillance for breast cancer in patients managed with fertility drugs.

4. Conclusion

Breast cancer screening for patients before infertility treatments and continual surveillance while on such treatment is highly recommended. The poor prognosis of metastatic breast cancer with acute hepatic failure with no effective treatments in published literature marks it as requiring more studies in a bid to upturn its dismal outlook.

Conflicts of interest

We declare no conflict of interest.

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Ethical approval

Not applicable.

Author contribution

Dr E.A. Sule, managed the patient, conceived and wrote up the report.

Guarantor

Dr E.A. Sule.

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