Pancreatic neuroendocrine tumour in pregnancy

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ABSTRACT

Cancer is rare during pregnancy. Often the diagnosis is delayed due to the non-specific presentations and overlapping of symptoms that are common during pregnancy. Unawareness and hesitation to perform invasive investigations also contribute to the delay. We report the case of a 31-year-old pregnant lady (G_3P_2 33+ weeks, previous molar pregnancy) who presented with upper gastro-intestinal bleed and obstructive jaundice on the background of chronic gastrointestinal symptoms since early pregnancy and found to have a non-functional neuroendocrine tumour. She underwent biliary stenting and was treated with palliative chemotherapy. Unfortunately, her condition progressed rapidly and repeat imaging showed progressive disease. This case highlights the importance to consider evaluation in pregnant patients whose symptoms do not resolve despite treatment.

Keywords: Pancreatic neoplasms, neuroendocrine tumour, pregnancy, gestation

INTRODUCTION

Cancer in pregnancy is rare. However, the incidence has been estimated to be as high as 1 in 1,000 gestations for any tumor with the breast, cervix, skin (malignant melanoma) and lymphatic (lymphoma) being the most commonly affected sites, accounting for almost 90% of all cancers in pregnancy. [1, 2] Cancer of the gastrointestinal tract during pregnancy is rare and colon and stomach are the most commonly affected sites. Pancreatic cancers during pregnancy is much less common with less than 40 cases reported in the literature; the most common being cystic neoplasms and adenocarcinomas. Similar to non-pregnancy state, pancreatic cancer is often associated with significant mortality and are often diagnosed late. Symptoms are often non-specific and the diagnosis not considered, compounded by unawareness and reluctance to perform invasive investigations such as endoscopy or radiological imaging. We report the rare case of a 31-year-old pregnant lady with a metastatic non-functional pancreatic neuroendocrine tumour.

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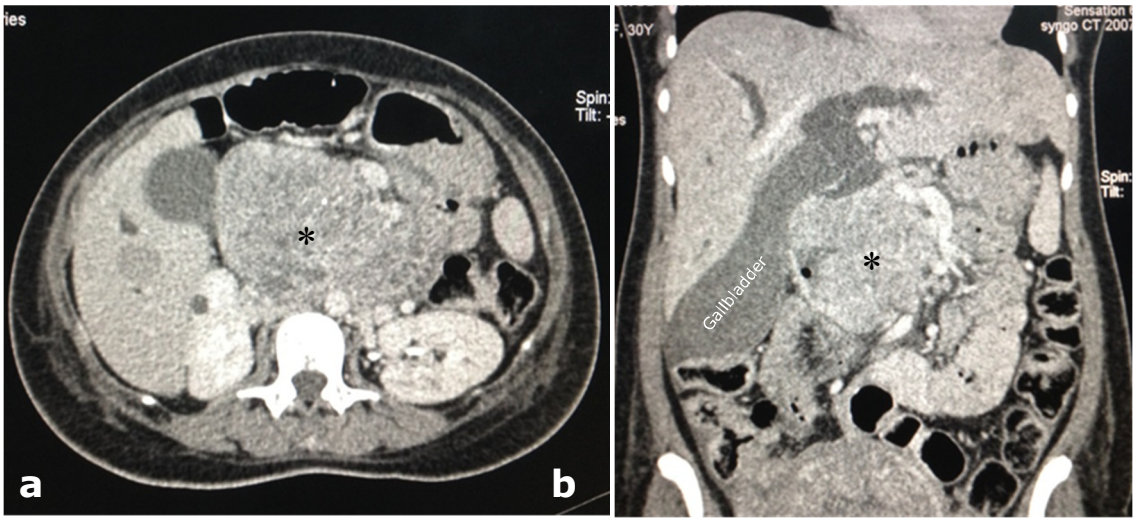
CASE REPORT

A 31-year-old (G_3P_2, 33+) with no past medical history apart from a previous molar preg-

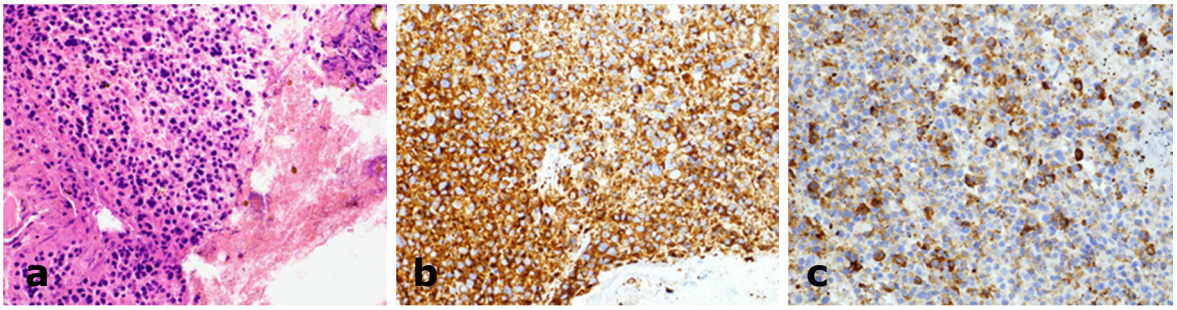
nancy was referred with coffee ground haematemesis. She previous had been admitted to the obstetric service with non-specific abdominal discomfort thought to be premature contractions. Both times she was discharged after uneventful short stays after exclusion of premature contractions and unconfirmed liquor leak.

She had been previously well prior to the pregnancy. During her first pregnancy, she had upper gastrointestinal symptoms of heartburn and reflux which settled after the first trimester. However, in the latest pregnancy, her symptoms had improved but persisted despite treatment. She had presented to the clinic and was treated symptomatically. An abnormality scan done mid-trimester was normal. In the latest presentation, she reported to have lost some weight, persistent nausea, vomiting of altered coffee ground fluid later becoming more fresh. Physical examination revealed her to be lethargic, anaemic and was mildly jaundiced. She was otherwise haemodynamically stable. Abdominal examination revealed a gravid uterus and vague epigastric mass but not features of chronic liver disease. Laboratory work-up confirmed anaemia (Hb 8.1 gm/dL, MCV 93.5 FL and platelets 390x 10^9), deranged liver (Bilirubin 55.6 umol/L, ALP 698 U/L, GGT 583 U/L, albumin 19 gm/L and total protein 44 gm/L) and clotting profiles (prothrombin time 28.3 sec and INR 2.5). The liver profiles showed cholestatic picture with elevated bilirubin and reduce serum albumin. In association with the deranged clotting profiles, chronic liver disease and possible portal hypertension related bleeding was suspected. An urgent ultrasound scan (USS) showed multiple liver lesions (largest 4cm) and mildly dilated perigastric vein.

The patient was given blood transfusions and intravenous omeprazole infusion, fresh frozen plasma and a dose of intravenous vitamin K. Dexamethasone steroid priming to mature the fetal lung was also given. After stabilisation, the patient proceeded to an urgent upper gastro-intestinal endoscopy. This was done in the operating theatre with anesthetic and obstetric supports. This showed some altered blood in the stomach but was



Figs. 1: a) Axial computed tomography (CT) scan showing a large enhancing tumour at the head of pancreas (*) and, b) Coronal view showing the pancreatic tumour with dilated common bile duct and gallbladder.



Figs. 2: a) Histology showing tumor formed of round cells containing thin rim of cytoplasm and hyperchromatic nuclei, arranged in ribbons and vague glandular pattern, b) Immunohistology stains showing strong cytoplasmic positivity for synaptophysin, and c) Immunohistological staining with chromogranin focal granular cytoplasmic positivity.

atic tumour with liver metastases was made. In view of the USS finding and the vascular nature of the duodenal tumour, neuroendocrine tumour was suspected.

A multidisciplinary approach involving the gastroenterology, oncology, obstetric and gynecology and radiology team was adopted. The patient was counseled for urgent delivery. An uncomplicated emergency lower section cesarean section and delivered a baby girl. The baby was well but was transferred to the Neonatal Intensive Care Unit for support and monitoring. Following the delivery, a repeat upper GI endoscopy revealed the ulcerated tumor and was biopsied. A computed tomography (CT) scan was done showed a 7.6 x 8.6 cm mass in the head of pancreas displacing the duodenum producing luminal narrowing, dilated biliary tree and multiple low attenuated nodules in both lobes of liver (Figure 1). The distal pancreatic duct was dilated. Apart from the liver metastases, there was no evidence of metastases elsewhere.

The biopsies showed neoplastic cells which stained positive for CK7, chromogranin A and synaptophysin. Staining for CK 20 was negative. The findings were that of neuroendocrine carcinoma (NEC) of the head of pancreas. Staining for estrogen and progesterone receptors was negative. The serum tumor markers that were taken before delivery which included CA 19-9, CA 125 and CEA were all normal.

An ERCP was attempted but this failed due to the tumor obstructing the lumen. She later underwent percutaneous biliary stent placement. Post decompression, she was started on oral everlolimus by the oncology service. Her baby was doing well but her condition progressed despite treatment and a CT scan done eight weeks later showed disease progression with multiple metastases in the liver, spleen and peritoneum. She died less than ten weeks after diagnosis.

DISCUSSION

Pancreatic neuroendocrine tumour is an uncommon malignancy accounting less than 2% of all pancreatic tumours with a reported incidence of less than 1 per 100,000 persons per year. [5-7] Pancreatic neuroendocrine tumours can be categorised into functional or non-functional. Functional tumour usually mani-

fests early when the tumour is still small with symptoms of hormone excess. [5, 7, 8] The most common type is insulinoma and the least common type is gastrinoma. [5-7] Non-functional tumours account for 40-80% of the total pancreatic neuroendocrine tumour. The non-functional type typically presents late with big lesions with or without metastases due to its indolent course. [7, 8]

Pancreatic neuroendocrine tumour in association with pregnancy is similar to those encountered in non-pregnancy state, with the exception that it is much less common. To date, there have only been over 20 cases of functional insulinoma in association with pregnancy reported in the literature. [9] Most manifested early in the pregnancies with symptoms of hormone excess and manifestations of hypoglycemia. On the other hand, there have only been three cases of non-functional neuroendocrine tumour of the pancreas in pregnancy reported in the literature. [10, 11] Our case represents the fourth case to be reported.

Sciscione *et al*. [10] reported a case of non-functional insulinoma that was incidentally detected through routine antenatal screening. Due to the size of the lesion, the patient underwent a Whipple's procedure. Although the procedure was uncomplicated, the patient post-surgery recovery was complicated by clostridium difficile colitis. This was later complicated by foetal death after delivery as a result of fetal intracerebral haemorrhage. Kamphues *et al.* [11] reported two cases; both presenting in the second trimester. One patient was evaluated for hypertension whilst the other presented with persistent vomiting and weight loss. Both underwent surgery during the second trimester without complications. Compared to reported cases, our case was diagnosed in the third trimester and presented with gastrointestinal bleeding and weight loss, and the disease was already very advanced (stage IV).

A well-differentiated non-functional pancreatic neuroendocrine tumour has a five-year survival rate of 30% to 63%. [7] Unfortunately more than half with nonfunctioning pancreatic neuroendocrine tumour would have an advanced disease at diagnosis, resulting in poor survival outcomes. [12] Our patient died less than ten weeks after diagnosis.

The key to management of pancreatic neuroendocrine tumour is early diagnosis. Our patient had nonspecific GI symptoms from the first trimester. GI symptoms such as heartburn, nausea, vomiting, regurgitation and dyspepsia are common in the first trimester, but most will resolve during second trimester. Unfortunately, no further investigations such as ultrasound scan were done. Although an abnormality scan carried out during the mid-second trimester, the scan only concentrated on the pregnancy. On retrospect, the pancreatic tumor could have been detected at this stage. It is particularly important for clinicians to consider investigations if symptoms do not improve or actually worsen. Investigations include blood investigations such as liver profiles and USS of the abdomen as the initial investigations. If further investigations are required, MRI and upper GI endoscopy can be considered.

In conclusion, pancreatic neuroendocrine tumours during pregnancy are rare and are often diagnosed in the advanced stages

during to the overlapping of nonspecific symptoms, confounded by the reluctance to do investigations and also unawareness of the rare causes. Clinicians should always consider the possibility of neoplasms and initiate investigations if symptoms persist despite appropriate treatments.

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