CASE REPORT

Case Report: Rare presentation of pancreatic ductal adenocarcinoma with severe depressive disorder with catatonia [version 1; peer review: awaiting peer review]

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Abstract
Pancreatic cancer is a highly lethal malignancy with symptoms such as abdominal pain, back pain, loss of appetite, bloating, weight loss, jaundice, nausea, vomiting, etc. It has a relatively late presentation, which makes its only potentially curative treatment, surgical resection, impractical for most patients. However, the prognosis is poor despite complete resection. The occurrence of depression and anxiety is rather common in patients with pancreatic cancer and a biological basis for this is suspected, although not studied in detail. We herein report a case of pancreatic ductal adenocarcinoma in a 57-year-old man who suffered from abdominal pain, constipation, and significant weight loss. The computerized tomography (CT) scan and successive endoscopic ultrasound (EUS) guided biopsy with histopathology confirmed a mass arising from the mid-body of the pancreas with tubular and cystic glands lined by moderately pleomorphic columnar epithelial cells. The patient underwent chemotherapy with the FOLFIRINOX regimen. He eventually developed severe depression with psychotic symptoms and catatonia, which further exacerbated the challenges in the management of the malignancy. In spite of widely available therapeutic options for the management of depression described in the literature, the effectiveness of those in pancreatic cancer patients with concomitant depression is not well established. Hence, more studies are imperative in addressing the neuropsychiatric associations of pancreatic cancer and formulating a protocol for their apt management.
Keywords
Catatonia, FOLFIRINOX, pancreatic cancer, pancytopenia

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**Introduction**

Pancreatic ductal adenocarcinoma (PCAD) is one of the major causes of cancer-related mortality (fourth globally) with the 5-year survival rate being around 9%.[1,2] It is responsible for 3.2% of cancer incidence rates, but it contributes to 8% of all cancer deaths.[3] According to GLOBOCAN, the incidence of pancreatic cancer in Nepal in 2020 was 357 (rank-16), while case mortality was 346 (rank-11) with the 5-year prevalence being 250 on average. All of this indicates the late onset of concerning symptoms, probably at the stage of metastasis, and the aggressive and refractory nature of the disease to the treatment[4]. While the combination of chemotherapy, like FOLFIRINOX and gemcitabine/nab-paclitaxel, has improved the outcome over the years, survival in most patients is still less than a year.[4] Another major issue with pancreatic cancer is mental health; cancer patients and survivors go through a range of emotional and psychological turmoil like depression, anxiety, and various other issues.[5]. Fras et al. conducted a study in 1967 that suggested pancreatic cancer is the highest contributor of depression, anxiety, and unpleasant premonitions among overall cancer patients.[6] Depression not only hinders the coping process with the disease and its impact, it also impacts the patient’s acceptance to the treatment, their quality of life, hospital stay, and increases the risk of suicide.[7] Here we discuss a case of pancreatic adenocarcinoma under palliative treatment, an atypical presentation of depressive catatonia with psychotic symptoms, and multiple complications that arose with the disease and treatment process.

**Case report**

Our patient was a 57-year-old man of Khas ethnicity, an administrative officer in government office, from Kanchanpur, Nepal, who presented to the Nepal Cancer Hospital and Research Center with abdominal pain, constipation, loss of appetite and significant weight loss for about three months. He had no co-morbidities, no past history of any psychiatric illness or a family history of malignancy and was a non-smoker and a social drinker. Ultrasonography (USG) of the abdomen was done initially, which showed peripancreatic and hepatic focal lesion. Subsequently, a computed tomography (CT) scan showed an ill-defined heterogeneously enhancing lesion arising from the mid-body of the pancreas measuring 6.1 cmx5.5 cmx4.4 cm, which caused dilation of the distal main pancreatic duct up to 13 mm. The lesion was seen encasing the coeliac trunk, the origin point of the splenic and proper hepatic arteries, and approaching the superior mesenteric artery. Multiple ill-defined enhancing lesions in the liver were noted as well, the largest one measuring 3.5 cmx3.3 cm in segment VII (Figure 1). An endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) was done to confirm the diagnosis of pancreatic malignancy (Figure 2). The histopathological examination was consistent with ductal adenocarcinoma, showing tubular and cystic glands lined by moderately pleomorphic columnar epithelial cells. The cells had moderate amount of cytoplasm, round to oval nuclei and prominent nucleoli.

After discussing the diagnosis, management and prognosis aspects, the patient was admitted for palliative chemotherapy.

Intravenous (IV) continuous infusion regimen of FOLFIRINOX was started constituting of folinic acid (400 mg/m² over two hours every 14 days), fluorouracil (400 mg/m² bolus on day one followed by 2,400 mg/m² over 46 hours every 14 days), irinotecan (180 mg/m² over 90 minutes every 14 days) and oxaliplatin (85 mg/m² every 14 days) in combination. The first two cycles were tolerated well by the patient. On follow-up, patient was noted with leucopenia (total leucocyte count of 2,956 with absolute neutrophil count (ANC) of 444) and was treated with subcutaneous filgrastim (5 mcg/kg/day), which was maintained for 10 days. The patient’s initial study of serological tumor marker CA 19-9 before commencing the treatment was 1555 u/ml, which had improved to 133.3 u/ml through the course of treatment (Reference range <45 u/ml).

About a month later, the patient had developed low mood, slept most of the time, had no interest in his regular activities for about three weeks, complained of hearing voices that others could not hear (auditory hallucinations) for the last seven days, and had completely refused to eat or drink for two days. He was brought to the hospital when he had loss of consciousness with seizure-like episode, and decreased urine output. On examination, there was a lack of response to stimuli including painful stimuli and verbal commands. The patient’s right hand was in a peculiar position with elbow flexed and internally rotated and shoulder extended to 90 degrees, which remained in the same position on attempts to manipulate it. His urinalysis and culture showed infection by *Escherichia coli*. A CT scan of the head was done to rule out intracranial causation, however it showed abnormal morphology and parenchymal attenuation and electroencephalogram (EEG) showed normal rhythm. Psycho-oncology consultation was done, and he was admitted for severe depressive disorder with catatonia with uncomplicated cystitis. The patient was started on Tab.clonazepam (0.5 mg) once daily for five days and then tapered off, Tab.sertraline (50 mg) once daily.
Figure 2. Endoscopic ultrasound showing a large 46x24 mm hypoechoic mass in the body of the pancreas. The mass is poorly demarcated, and the pancreatic duct is proximally dilated at 10 mm. The mass encases the celiac axis and the whale tail, including the splenic artery. The splenic vein and the portal vein confluence was not visualized. There are a few peripancreatic lymph nodes, including in the celiac axis. The left lobe of the liver is normal, although the intrahepatic biliary radicals are prominent. This is suggestive of pancreatic adenocarcinoma and appears unresectable. FNA was performed and the cell block prepared from the smear was sent for histopathological examination. FNA, fine needle aspiration.

and Tab.olanzapine (5 mg) once daily, and Tab.cefixime 200 mg twice daily for five days for a urinary tract infection, all given orally. Electroconvulsive therapy was denied by the patient and family members despite explanation of its possible implications. After relative psychiatric stabilization, he was discharged on oral capecitabine tablets (1,250 mg/m² i.e., 2 grams). His psychiatric medications were continued, and blood counts were regularly monitored.

On follow-up, the patient’s psychotic features had improved but his depression and catatonia persisted. At this point the patient seemed to have no will to persevere and refused chemotherapy. The family members mentioned several episodes of unresponsiveness with no or minimal verbal response. The patient continued to refuse chemotherapy on subsequent follow-ups and was managed with palliative care at home, where he passed away following two years of diagnosis. This case had a very unique presentation, so we decided to do a literature review to look for similar cases in Nepal. We found no results when PubMed (PubMed, RRID:SCR_004846) was searched on July 18th, 2021, using keywords “depression”, “pancreatic cancer”, and “Nepal.

Discussion
We lack techniques for early diagnosis and treatment of pancreatic cancer and with late symptoms, patients usually present at the stage of local spread or metastasis where surgery is not an option, which is similar to our case. Our patient was diagnosed as having severe depression with psychotic features with catatonia according to the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) (DSM-5), after a thorough history taking, clinical examination and excluding other medical possibilities through blood labs, CT scan and EEG. Although studies have suggested associations between pancreatic cancer and major depressive disorder in the past, the presentation of catatonia was new and further challenging for the management of our patient.

Cancer is an extremely stressful reality for patients, which is life threatening and can result in multiple psychiatric disorders. Severe depression with catatonia in this case developed after the diagnosis of cancer at its incurable stage. The stress of imminent death and, the troubles and side-effects of chemotherapy the patient had to go through also contributed to it. The prevalence of depression is roughly 5% among the global population and 5.2% in Nepal. A prevalence study done in the USA showed around 6% prevalence in the general population, but when it comes to cancer patients, this percentage increases to 30%, and in pancreatic cancer, this number rises to 40%. A study conducted in a hospital in Nepal showed that depression had a prevalence rate of 28% in cancer patients, while a study in a cancer hospital reported moderate to severe depression in 49.2% of cancer patients. However, not enough studies have been conducted about ‘why the association exists?’ and
"how do we manage efficiently?". In fact, we could hardly find any study conducted in Nepal about the association of pancreatic cancer and depression when we searched.

It is evident that cancer and severe depression are both extremely challenging cases for management; co-existence of both can adversely affect the prognosis of each other. In addition, the presence of catatonia in our case created difficulties in counseling and communication with the patient and, in understanding his perspective for denying treatment. According to DSM-5, “Catatonia can be defined as the presence of three or more of 12 psychomotor features in the diagnostic criteria for catatonia associated with another mental disorder and catatonic disorder due to another medical condition.” The psychomotor features are stupor, catalepsy, waxy flexibility, mutism, negativism, maintaining posturing against gravity, odd mannerisms, stereotyped movements, agitation, grimacing, echolalia and echopraxia. Our patient had semi-stupor, catalepsy, mutism, negativism and posturing, and we ruled out any other medical cause for the symptoms. The exact pathogenesis of catatonia is not well understood but recent advances in imaging like functional magnetic resonance imaging (fMRI) has shown defects in the orbitofrontal and prefrontal cortex on the right side. The other issue in our case was myelosuppression. Since the start of chemotherapy, patient’s blood reports showed pancytopenia, specifically neutropenia, which waxed and waned throughout the treatment process. Hence, we maintained the dose of filgrastim and had to be cautious when we added Tab. olanzapine, as studies have shown multiple neuroleptic drugs causing decreased neutrophil count and other blood dyscrasias.

**Conclusions**

Our case reflects on a rare presentation of catatonic depression in pancreatic cancer. The objective of this case report is to shed light on both the psychiatric complications that arise in cancer patients as well as the association of pancreatic cancer with depression that can present in different complicated forms like this one. Several studies need to be conducted to understand the proper association between cancer and mental health, pancreatic cancer and depression in its different forms and severity levels. The lack of attention on this topic in Nepal is alarming. When searched on PubMed on July 18th, 2021, using keywords “depression”, “pancreatic cancer”, and “Nepal”, we found zero hits. The management presents with surmountable challenges, but studies should focus on exploring and directing the management of cancer-associated depression, its complications and issues that can arise during the management.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient’s wife.

**References**


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