Case Report-I

Pancreatoblastoma: A Case Report and Review of Literature

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ABSTRACT

Pancreatoblastoma is a rare tumour of childhood. We report a case of two year old boy who presented with jaundice, abdominal swelling and anorexia for three months. CECT abdomen showed a 7x6 cm mass involving pancreatic head causing biliary obstruction. He was subjected to choledochoduodenostomy and biopsy of the mass which was suggestive of pancreatoblastoma. In view of unresectable lesion, he was started on chemotherapy with cyclophosphamide and vincristine. After four cycles his symptoms subsided and mass regressed to 5x5 cm but it was still inoperable. We planned to continue chemotherapy but after fifth cycle his condition worsened rapidly and died due to sepsis. This case is being reported on account of its rarity. Different authors have used various chemotherapy regimens with inconsistent results.

INTRODUCTION

Pancreatoblastoma (juvenile adenocarcinoma of pancreas) is an uncommon tumour occurring in childhood. Diagnosis of this upper abdominal mass is rarely, if ever, made preoperatively, and other more common conditions are generally considered in differential diagnosis like neuroblastoma, hepatoblastoma, malignant lymphoma, pseudocyst and Wilms' tumour. Surgical resection plays key role in the management of this tumour.[1,2] Some studies tried to define the place of radiotherapy[1,2,3] and chemotherapy in management of pancreatoblastoma.[4,5,6,7] However, there is a paucity of information on the tumour behavior and about their sensitivity to chemotherapy.

CASE: A two year old boy presented in October 2005 with gradually progressive abdominal swelling followed by insidious onset cholestatic jaundice and anorexia for past three months. There was no history of pain, fever, vomiting, weight loss, hematemesis, melena, altered bowel habit, polyuria, or polydipsia. The family history was negative for neoplastic disease. He was poorly nourished with icterus and ascites. On palpation a 7x5 cm size, round, firm, non tender epigastric mass was palpable. The lesion was fixed to the depth of abdomen but was separable from liver edge.

Routine blood investigations revealed anemia Hb=9 gm %) and raised serum bilirubin level (Total bilirubin = 12 mg/dl, Direct bilirubin = 7.6 mg/dl). Ultrasonography of abdomen revealed a huge retroperitoneal mass involving head of pancreas. CAT Scan of abdomen revealed 74 x 63 x 65 mm mass with irregular margins in the region of head of pancreas, abutting on the hepatic surface and encasing portal vein, splenic vein, inferior vena cava and aorta with obstruction of distal CBD and proximal biliary dilatation. Mild hepatomegaly and distended gall bladder were also noted (Fig. 1). In view of above findings a differential diagnosis of pancreatic pseudocyst, pancreatic hematoma and pancreatoblastoma

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CT Scan showing huge mass arising from head of pancreas

was made. Exploratory laparotomy and choledochoduodenostomy along with trucut biopsy was performed which showed small cell carcinoma with squamoid differentiation suggestive of pancreatoblastoma. His jaundice subsided after bypass surgery. (S) AFP was within normal range. He was then started on chemotherapy with cyclophosphamide 100 mg/ m^2 IV on day 1, 4 and 8 and vincristine 0.6 mg/ m^2 IV on day 1 and 8. After one cycle of chemotherapy child became comfortable clinically, ascites subsided and abdominal girth decreased but on ultrasound the mass was almost same in size (70 x 60x63 mm) and extent. He was continued chemotherapy with ultrasound monitoring of the disease. After four cycles the mass regressed in size and measured 50x48 mm on ultrasound. He was reassessed for surgery but found inoperable. He was continued on same drugs which he tolerated well except for mild neutropenia. Suddenly after fifth cycle his condition worsened. He developed high grade fever, pain abdomen and signs for sepsis and expired within two days despite broad spectrum antibiotics and aggressive resucitation.

DISCUSSION

Pancreatic carcinoma are classified on basis of cell of origin into: (a) ductal cell (b) islet cell (c) acinar cell and (d) uncertain histogenesis.[7] Except for islet cell tumour, the three year survival of pancreatic tumour is 2% Notable exception to this prognostic statistics is a tumour of uncertain histogenesis that was variously reported as pancreatoblastoma or infantile type pancreatic carcinoma.[7] The terminology is unacceptable to some because histologically this tumour does not have a typical blastemal appearance and it has good prognosis. Pancreatoblastoma is a rare tumour comprising 0.5% of epithelial neoplasm of pancreas.[8] It is actually the most common pediatric pancreatic neoplasm, more frequent in males than females with a ratio of 2.1.[9,10,11] Though no age prevalence has been reported in previous reports[2,5] recent studies show that mean age at presentation is about 6 years.[4,9,10] Some rare cases have been described during early infancy[2] and in adults.[12] The tumour is more common in the Asian (two third of cases) than in the white population.[11]

Pancreatoblastoma is an encapsulated or partly encapsulated tumour with nests of uniform cells separated by a fibrous stroma with peripheral lobulation and central necrosis. The tumour cells may have acinar, glandular or undifferentiated appearance.[19] The presence of small areas of squamous differentiation (squamoid corpuscles) is typical.[11,14] Presence of acinar cells containing zymogen like granules on electron microscopy helps in confirmation of diagnosis. Histochemical and ultrastructural studies reported in the literature are consistent with the fact that some forms of pancreatoblastoma may have both exocrine and endocrine components associated with presence of both zymogen and neuro-endocrine granules, sometimes in the same cells, or in different cells.[4,8,20] This differentiation may predict good prognosis.[20]

Certain imaging features are suggestive, but not diagnostic of pancreatoblastoma. Most pancreatobalstomas arise from the body and/or tail of the pancreas, or involve the entire organ,[10,11] rather than being universally or predominantly located in the pancreatic head as reported previously.[14,21] Ultrasound shows a heterogenous or predominantly hypoechoic mass,[16,22] sometimes containing small fluid areas.[16,23] Biliary dilatation is uncommon. Vascular encasement and calcification are

common.[16,22] It usually involves the mesenteric vessels and/or inferior vena cava but not aorta (which is commonly encased in neuroblastoma). However this case was a notable exception having aortic encasement.

CT scan shows well encapsulated pancreatic mass that is hypodense to liver[16,21,22] with mild enhancement[22,23] and areas of calcification or hemorrhage and necrosis. Prominent central necrosis in tumour and hepatic metastasis have been described but occur in minority of cases only. Magnetic resonance imaging may show tumour as hypointense to liver on T1-W images and iso or hyper intense on T2-W images.[18,22] Contrast enhancement is variable. The reported angiographic appearances of pancreatoblastoma are not consistent.[24]

The criteria for diagnosis of pancreatoblastoma should include infantile carcinoma of the pancreas with an encapsulated mass derived from ventral pancreas; histological identification of epithelial differentiation, including acinar, glandular or trabecular architecture, as well as distinct organoid pattern containing globular structures with elongated cells (squmoid corpuscles); and the presence of acinar cells with zymogen granules.[1]

Though all three aspects of treatment may be considered, but surgery is the only means of cure.[3] Surgery requires complete resection of tumour, sometimes a pancreato-duodenectomy (Whipple procedure) is needed.[2,13] Chemotherapy, alone or in combination with radiotherapy may be considered in pre-operative or palliative setting in inoperable or metastatic cases. Local radiotherapy has been proposed before or after surgery in some studies.[1,2] Camprodon and Quintanilla suggested that this tumour may be cured by radiotherapy only.[3] There are few reports about chemotherapy. One patient was treated with 5 fluorouracil and another was treated by actinomycin D and vincristine as adjuvant chemotherapy with no possible evaluation of the response.[2,5] A regression was reported in a patient with cyclophosphamide plus vincristine sulfate and in two patients with combination of cyclophosphamide, vincristine, methotrexate and 5 fluorouracil.[6,7]

In 1964, Moynan reviewed 16 cases of childhood pancreatic carcinoma.[25] The first case of infantile pancreatic carcinoma was reported in 1971.[26] In 1973, Tsukinorto reviewed 12 cases from the Japanese literature including their own case.[6] Camprodon and Quintinalla were able to collect 28 cases from the Western literature.[3] Tsukimoto et al collected 12 cases from Japan,[6] and Lack et al reported five cases from Boston.[5] Horie et al[1] and Benjamin and Wright[27] have documented two each, and multiple single cases have been reported.[8,20,28]

The clinical signs in our patient were limited to icterus, ascites and palpable lump in epigastric region. Diagnosis of pancreatoblastoma was confirmed only after laparotomy and biopsy. Alpha fetoprotein was within normal range. As patient had huge retroperitoneal mass encasing portal vein, splenic vein, inferior vena cava and aorta he was found inoperable. Only option left was use of chemotherapy or radiotherapy. As radiation would have required a very large field encompassing the whole abdomen with high morbidity and, lack of literature about effective use of radiation in pancreatoblastoma prompted us to use chemotherapy in this child. We started chemotherapy using cyclophosphamide and vincristine with palliative intent. After first cycle itself child showed positive response as he was cheerful, comfortable and ascites had resolved. He was continued on chemotherapy with ultrasound monitoring of the disease. After four cycles though mass regressed in size but he was found inoperable. After fifth cycle his condition worsened suddenly as he developed sepsis and expired after two days despite aggressive treatment.

As pancreatoblastoma is very rare tumour, information about standard management is lacking in literature. We, on review of literature opine that surgery must be considered as treatment of choice if tumour is resectable. Chemotherapy and radiation therapy should be reserved for palliation and sometimes pre-operatively to make tumour resectable. Exact doses of radiation is not well defined. Even chemotherapy regimen used by different authors vary and there is no standard regimen.

Most of the authors have used drugs like cyclophosphamide, vincristine, 5 flurouracil, acinomycin D, methotrexate etc. in various combinations. None of the regimen was found superior to other. The evaluation of the other drugs is difficult because of low frequency of pancreatoblastoma.. We used a combination of cyclophosphamide and vincristine in our patient and achieved good palliation with minimum morbidity.

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