Autologous stem cell transplantation as first line treatment after incomplete excision of pancreatoblastoma

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Pancreatoblastoma is a rare tumor and surgery with complete resection is the main treatment approach. Prognosis for patients with residual disease after surgery is usually dismal. A 14-year-old girl with pancreatoblastoma in the pancreatic body and tail was submitted to preoperative chemotherapy. She underwent surgery and the tumor was resected with microscopic margins. Postoperative chemotherapy was followed by high dose chemotherapy and autologous hematopoietic stem cell transplantation. After four years she remains very well with no evidence of disease. This is the first case reported of pancreatoblastoma that was treated with autologous hematopoietic stem cell transplantation as first line treatment without radiotherapy at the site of the microscopic disease.

Keywords: Hematopoietic stem cell transplantation; Pediatrics; Pancreatic neoplasms; Drug therapy, combination; Primary treatment

Introduction

Pancreatoblastoma (PBL) is an extremely rare pancreatic tumor of childhood comprising 0.5% of pancreatic non-endocrine tumors; it occurs almost exclusively in infants and young children[1]. Like in hepatoblastoma, most patients present raised α-fetoprotein levels both in the serum and tumor. Symptoms are related to mechanical obstruction, leading to vomiting, jaundice and gastrointestinal bleeding. Metastatic disease at diagnosis is more common in the liver and lymph nodes; lung and brain metastases are rarer[2]. Ultrasound (US) shows lesions with mixed or low echogenicity, sometimes containing small fluid areas. An abdominal computed tomography (CT) scan usually shows well-defined, hypodense lesions which show mild enhancement and internal enhancing septations; calcifications within the lesion are either rim-like or clustered[3]. Abdominal magnetic resonance imaging (MRI) or positron emission tomography (PET)/CT helps in the evaluation of small hepatic metastases, not always seen by CT. PET/CT provides an average specificity and sensitivity of 70% in pancreatic tumors. The optimal treatment of PBL in pediatric patients has not been established yet but complete resection is considered the main step in the treatment of this tumor[3,4]. Prognosis is dismal when there is metastasis or when it is inoperable[3]. The benefit of adjuvant chemotherapy has not been fully elucidated but it is commonly used for unresectable tumors at diagnosis and metastatic disease[2-4]. Radiotherapy is usually recommended for patients with unresectable tumors or after incomplete surgical resection[6,7]. High dose chemotherapy with regimens such as melphalan, carboplatin and etoposide combined with autologous hematopoietic stem cell transplantation (ASTC) has been suggested as an alternative for patients with lesions not completely resected but its role is not yet fully defined[7,8].

This report presents the case of a 14-year-old girl with local advanced disease treated successfully with induction chemotherapy, surgery and ASCT for microscopic disease, without radiotherapy.

Case report

A 14-year-old girl was hospitalized with nausea, vomiting and abdominal pain. An abdominal CT scan showed a heterogeneous mass located in the pancreatic body and tail, measuring 13.5 x 10.0 x 7.0 cm, spleen enlargement and ascites. Serum α-fetoprotein was 1.2 IU/mL (reference: < 11.3 IU/mL) and the carbohydrate antigen (CA) 19.9 was 4.5 IU/mL (reference: < 37 IU/mL) and no evidence of metastatic disease. As surgical resection of the tumor was not feasible, a biopsy was performed reaching the histopathologic diagnosis of PBL and immunohistochemical markers were positive for AE1+AE3, vimentin (focal), α-1-antitrypsin and CEA. Familial adenomatous polyposis and other genetic diseases were investigated and discarded. Following four cycles of a chemotherapy regimen with cisplatin (80 mg/m²) and doxorubicin (60 mg/m²) abdominal CT showed that the lesion had decreased to 6.2 x 4.5 x 4.8 cm. She therefore underwent a surgical attempt to resect the tumor; intraoperative findings revealed that the tumor was attached to the meso and with a large quantity of peritumoral fibrosis and splenic vessels adhered to it. The tumor was removed with a microscopic
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Discussion

The optimal treatment of PBL has not been established but generally it includes a combination of surgery, chemotherapy and radiotherapy. A recent report from the European Cooperative Study Group for Rare Paediatric Tumors describes the first international joint series of this very rare tumor(11). Radiotherapy may have a role in PBL in the case of incomplete excision or unresectable disease non-responsive to chemotherapy or relapsed disease(2,10) but this conduct has been associated with pancreatic dysfunction and other upper-abdominal organ dysfunctions(11). Patients treated with surgery only have the risk of local recurrence with invasion of the duodenum and lymph nodes and can be treated with conventional or high-dose chemotherapy, radiotherapy and surgery. Patients previously treated with chemotherapy, surgery and/or radiotherapy have a poor prognosis in the case of relapse. Delayed resection after preoperative chemotherapy was performed in this patient. After sufficient tumor shrinkage, operative resection was attempted leaving microscopic residue. As the long-term outcome of unresectable cases is dismal(5,7,9) and high dose chemotherapy and ASCT rescue has been used for high-risk pediatric solid tumors(12,13), it was decided to offer this as first line treatment rather than radiotherapy. As for some other high-risk solid tumors, ASCT may play a role in selected cases of PBL, either improving survival or reducing toxicities. Given the paucity of such cases, further studies are required to understand the role of ASCT in PBL. It is very difficult to draw an absolute conclusion from one case, but in situations where there is incomplete resection, reducing the chances of patient survival, high-dose chemotherapy can be considered as an option in first-line treatment instead of radiotherapy for microscopic disease in chemosensitive tumors.

The adoption of an intensive multidisciplinary approach is required and referral to highly experienced centers to improve clinical care in these rare tumors.

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