Original Works

Ewing's Sarcoma Family of Tumors Arising in the Pancreas Head of a 3-year-old boy

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Abstract: Herein we report an extremely rare case of a 3-year-old boy with Ewing's sarcoma family of tumors (ESFT) arising in the pancreatic head. He had a huge mass in the upper abdomen after playing with his brother. He was initially diagnosed with a large pancreatic hematoma; however, a CT scan showed a huge heterogeneous mass in the pancreas head that measured 11 cm in diameter and multiple liver metastases. An incisional biopsy was performed, but histological and immunohistochemical examinations could not confirm an exact diagnosis. Molecular analyses showed the presence of EWS/FLI-1 fusion gene transcripts, and the patient was definitively diagnosed with ESFT. Neoadjuvant chemotherapy with PBSCT allowed us to perform a complete tumor resection with a pylorus-preserving pancreatoduodenectomy without postoperative complications. He was treated with radiation therapy (15 cycles of 2.0 Gy each) and adjuvant chemotherapy immediately after surgery without major complication. Currently, he is doing well and has had no radiological evidence of local recurrence or metastases 20 months after completing the treatment.

Key Words: Ewing's sarcoma family tumors, Pancreas, FLI-1 fusion gene, Pancreatoduodenectomy.

Introduction

Ewing's sarcoma family of tumors (ESFT) is a malignant, poorly differentiated, small round cell tumor that arises in the bone and soft tissues in children and adolescents. ESFT includes Ewing's sarcoma of the bone and outside bone, primitive neuroectodermal tumor (PNET), neuroepithelioma, and Askin's tumor. ESFT is a rare tumor but can arise in the spine and bone of children, especially when it originates in the pancreas. Herein we report a 3-year-old boy with ESFT that arose in the pancreas head and was associated with multiple liver metastases. The diagnosis and treatment of this patient are...
discussed.

Case report

A 3-year-old boy complained of abdominal pain with upper abdominal distention after falling while playing with his brother at home. He was diagnosed with a large traumatic hematoma of the pancreatic head and transferred to our department. He did not complain of nausea or vomiting and his vital signs were stable. A physical examination revealed that his abdomen was partially distended with moderate tenderness in the upper right quadrant. There was no apparent jaundice or anemia.

Laboratory studies conducted upon admission showed the following: white blood cell count 8,700/μl, red blood cell 422 × 10³/μl, hemoglobin 10.3 g/dl, hematocrit 37.5%, platelet count 279,000/μl, CRP 0.05 mg/dl, total bilirubin 0.44 mg/dl, AST 29 IU/l, ALT 9 IU/l, ALP 424 IU/l, LDH 776 IU/l, and serum amylase 89 IU/l. An examination of serum tumor marker levels showed that only NSE was elevated to 200 ng/ml.

After admission, computed tomography scan and magnetic resonance imaging of his abdomen showed a huge heterogeneous mass in the pancreas head that measured 11 cm in diameter and multiple liver metastases (Fig. 1). There were no apparent findings of a hematoma or hemorrhagic ascites.

Based on the diagnosis of pancreatoblastoma with multiple liver metastases, we performed an incisional biopsy and inserted a central venous catheter. A histological examination of the biopsy specimen revealed a small round cell tumor (Fig. 2). An immunohistochemical examination did not confirm the tumor diagnosis. However, molecular analyses successfully detected EWS/FLI-1 fusion gene transcripts, which led to a definitive diagnosis of Ewing's sarcoma family of tumors. After an

![Fig. 1. Magnetic resonance imaging of the abdomen showing a huge mass in the pancreas head that measured 11 cm in diameter and had heterogeneous enhanced effects.](image-url)
Incisional biopsy, the patient immediately received chemotherapy consisting of cisplatin and tetrahydropyranyl-adriamycin. After the patient was definitively diagnosed with ESFT of the pancreas, the therapeutic protocol was changed to seven courses of VDC [vincristin, tetrahydropyranyl-adriamycin, cyclophosphamide] and IE [ifosfamide, etoposide] for eight months. Then, high-dose chemotherapy [Hi-MEC (etoposide, cisplatin, L-PAM)] and PBSCT markedly reduced the size of the main tumor in the pancreas head and the liver metastases disappeared (Fig. 3). After chemotherapy
with PBSCT, we performed a total extirpation of the tumor with a pylorus-preserving pancreaticoduodenectomy with the Child procedure. The postoperative course was uneventful.

After surgery, the patient was treated with radiation therapy (15 cycles of 2.0 Gy each) and adjuvant chemotherapy consisting of four cycles of VDC and IE for four months. He was discharged after multidisciplinary therapy, and he is currently in good condition without radiological evidence of local recurrence or metastases 20 months after completing the treatment.

Discussion

ESFT is an undifferentiated small round cell tumor with a high propensity to metastasize. ESFT is a rare malignant tumor that predominantly arises in the intra-abdominal organs of children. Ewing's sarcoma (ES) was first described as a diffuse endothelioma in 1921 1. Today, ES belongs to ESFT along with other tumors, such as PNET, neuroepithelioma, and Askin's tumor, which have the same cytogenetic abnormalities in most cases. ESFT is likely to increase in size and is associated with multiple metastases of the lung, liver, bone, or brain at the initial diagnosis, which are likely a major prognostic factor. Several studies have shown that the major clinical prognostic factors include tumor site, tumor volume, age at diagnosis, responsiveness to chemotherapy, and site of metastatic disease 2–4.

ESFT is usually diagnosed based on histological and/or immunohistological findings of the tumor. However, it may be difficult to confirm an accurate diagnosis of ESFT in some cases. Recently, molecular analyses have significantly contributed to definitive ESFT diagnoses 5. The chromosomal translocation t(11;22)(q24;q12) is present in about 85% of ESFT cases, which leads in all cases to the chimeric fusion gene EWS/FLI-1 6–7. EWS is an RNA-binding protein, and FLI-1 is a DNA-binding transcription factor that belongs to a gene family that contains an erythroblastosis virus transforming-sequence domain. In the present case, the patient was initially diagnosed with pancreaticoblastoma. However, molecular analyses of the EWS/FLI-1 fusion gene transcripts lead to a definitive and final diagnosis of ESFT arising in the pancreas head.

Multimodal treatment strategies, including surgery, multiagent chemotherapy, and radiation, are widely accepted as essential treatments to control localized ESFT. Controlling the primary tumor is very important to improve the prognosis of ESFT. In the present case, pancreaticoduodenectomy was absolutely essential to locally control ESFT of the pancreas head. Therefore, preoperative multiagent chemotherapy played an important role in reducing the tumor size and decreasing the possibility of surgical or postoperative complications.

ESFT arising from the pancreas is extremely rare in children. To our knowledge, which is based on English scientific literature, only seven cases of ESFT arising in the pancreas in children have been reported 8–12. The most frequent complaint associated with the disease is abdominal pain, however there are no characteristic symptoms. Therefore the size of tumor tends to enlarge at initial presentation. Six of these seven pediatric patients underwent excision of tumor including pancreaticoduodenectomy in three with or without multimodal chemotherapy. Because of the small number of patients, the appropriate therapeutic strategy for ESFT of the pancreas has not been established. We successfully managed ESFT of the pancreas with a combination of multiagent chemotherapy and a second-look operation, including an open incisional biopsy and pylorus-preserving pancreaticoduodenectomy. Open incisional biopsy should be considered as a method to avoid repeated biopsies and inadequate confirmation of the diagnosis 13. Efficient and appropriate chemotherapy with PBSCT allowed us
to perform a total and complete extirpation of the tumor with a pylorus-preserving
pancreatoduodenectomy without intra- and post- operative complications.

As noted above, one of the major prognostic factors of ESFT is the presence of metastases at the
time of the initial diagnosis, and some analyses have reported that the 3-year disease-free survival rate
of ESFT patients with initial metastasis is only approximately 25%\(^{13,14}\). Multimodal treatment
strategies combined with surgery, multiagent chemotherapy, and radiotherapy, have improved the
survival rate of ESFT patients. Thus, new therapeutic strategies with new treatments and local control
of the primary tumor site with aggressive surgery will be required to improve the prognosis of patients
with metastatic ESFT.

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Munzinger G, Vieth V, Burdach S, van den Berg H,
Juergens H, Dirkxen U. The value of local treatment in
patients with primary, disseminated, multifocal Ewing
脇頭部原発ヨーイング肉腫の3歳男児の1例

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脇頭部原発のヨーイング肉腫（ESFT）の3歳男児の1例を報告する。患児は腹部打撲を契機に腹部腫瘤に気付かれ、精査にて脇頭部に径11cm大の巨大腫瘍および多発肝転移が認められた。腫瘍生検が施行されたが、組織学的および免疫組織学的検査では確定診断が得られず、遺伝子解析にてEWS/FLI-1融合遺伝子が検出されESFTの確定診断を得た。PBSCTを用いた術前化学療法にて著明な原発巣の縮小および肝転移巣の消失が得られた後、幽門輪温存脇頭十二指腸切除術を施行し腫瘍の完全切除が可能であった。術後放射線療法および化学療法施行後、再発なく完全覚解が得られている。

キーワード：ヨーイング肉腫、FLI-1融合遺伝子、幽門輪温存脇頭十二指腸切除術。