Primary Liposarcoma of the Duodenum: A First Case Presentation

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Abstract

A 55-year-old man suffering from melena was admitted to our hospital. A blood test showed severe anemia. Contrast-enhanced computed tomography (CT) revealed a huge lesion in the duodenum and dilatation of the common bile duct. Upper gastrointestinal endoscopy also identified hemorrhaging from the tumor in the duodenum. Due to the low density of the tumor mass, we performed emergency pylorus-preserving pancreaticoduodenectomy. Histology revealed an area of well-differentiated liposarcoma as well as an area of high-grade spindle cells and pleomorphic sarcoma without obvious differentiation. The final pathological diagnosis was dedifferentiated liposarcoma. This is the first case report of primary liposarcoma of the duodenum.

Key words: liposarcoma, duodenum, CDK4, MDM2, pancreaticoduodenectomy

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Introduction

Liposarcoma is the most common soft tissue sarcoma and includes a number of subtypes that differ in their histological, biological and molecular features (1). This tumor often occurs in the thigh, behind the knee or in the retroperitoneal region of the abdomen, although it can also be found in other parts of the body (2-4). The World Health Organization recognizes five subtypes of liposarcoma: well-differentiated, dedifferentiated, myxoid/round cell, pleomorphic and mixed-type. The myxoid/round cell subtype is among the most prevalent and typically occurs in younger individuals (5). Atypical lipomatous tumors/well-differentiated and dedifferentiated liposarcoma together form a larger subgroup of liposarcoma that is considered to represent a morphological and behavioral spectrum of the same disease (6).

Since surgical resection remains the only promising treatment for liposarcoma, performing total removal of the tumor

with negative surgical margins is mandatory (7). Wide resection, including the neighboring organs, should be performed without hesitation in selected cases. The survival of patients with extremity tumors is favorable. However, the difficulty in obtaining wide margins in the retroperitoneum predisposes the patient to local recurrence and ultimately death from unresectable disease (8). We herein document the case of a patient suffering from primary liposarcoma of the duodenum with severe hemorrhage. To the best of our knowledge, this is the first report of primary liposarcoma of the duodenum. The patient underwent emergency pancreaticoduodenectomy with partial resection of the transverse colon. The surgery and postoperative course were uneventful, primarily due to the scrupulous preoperative evaluation.

Case Report

A 55-year-old man suffering from melena was referred to our hospital for an evaluation and treatment. He had no clinical evidence of any past malignancy. An examination

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Figure 1. a: Abdominal contrast-enhanced CT revealed a large mass in the duodenum. b: CT also demonstrated both dilatation of the common bile duct and direct invasion into the transverse colon.

Figure 2. a: Upper gastrointestinal endoscopy identified hemorrhaging from the tumor in the duodenum. b: Endoscopic hemostatic procedures using clipping and ethanol injection failed to control the hemorrhage.

revealed a hard palpable mass in the abdomen and conjunctiva that were both icteric and markedly anemic. Laboratory blood test results demonstrated the following findings: Hb, 6.7 g/dL (normal: 13.4-17.4 g/dL); hematocrit, 21.2% (39.8-51.8%); albumin, 2.6 g/dL (3.8-5.3 g/dL); total bilirubin, 4.7 mg/dL (0.2-1.2 mg/dL); alkaline phosphatase (ALP), 3,636 IU/L (115-359 IU/L); and γ -glutamyl transpeptidase (GTP), 832 IU/L (16-73 IU/L). Other laboratory tests, including a blood smear, tumor marker analysis (carcinoembryonic antigen, carbohydrate 19-9 and carbohydrate 15-3) and serologic tests for viral infection, were within the normal ranges.

Abdominal contrast-enhanced computed tomography (CT) revealed a large and heterogeneous extraluminal mass measuring 9.5 cm in diameter arising from the second portion of the duodenum (Fig. 1a). CT demonstrated both dilatation of the common bile duct and direct invasion into the transverse colon (Fig. 1b). Upper gastrointestinal endoscopy identified hemorrhaging from the tumor, apparently originating from the duodenal submucosa; however, endoscopic hemostatic procedures using clipping and ethanol injection failed to control the hemorrhage (Fig. 2a, b). Due to the low density

of the tumor mass, complete embolization of the arteries around the duodenum would potentially have had no effect and may have induced necrosis of the adjacent organs. The hemorrhage mass was diagnosed as a primary gastrointestinal stromal tumor based on the abdominal-enhanced CT findings, rather than a non-functioning endocrine tumor or leiomyosarcoma of the duodenum. Therefore, we performed emergency pylorus-preserving pancreaticoduodenectomy with partial resection of the transverse colon.

An evaluation of the resected specimen revealed a 9.8×7.5-cm tumor in the duodenum (Fig. 3a). Macroscopically, the tumor was large, multilobular, well-circumscribed and appeared to be a white, solid, firm mass containing a yellow fatty area (Fig. 3b). Histologically, the tumor contained an area of well-differentiated liposarcoma in addition to an area of high-grade spindle cells and pleomorphic sarcoma without obvious differentiation (Fig. 3c). In the area of well-differentiated liposarcoma, atypical spindle and stellate cells with large, irregularly shaped hyperchromatic nuclei were scattered in loose fibrous tissue and between mature-looking adipose cells (Fig. 3d). On the other hand, the area of high-

Figure 3. a: Evaluation of the resected specimen. b: Macroscopic findings. c: Gross appearance of the tumor. d: Well-differentiated liposarcoma. e: Area of high-grade spindle cells and pleomorphic sarcoma. f: Immunohistochemical staining for MDM2. g: Immunohistochemical staining for CDK4.

grade spindle cell and pleomorphic sarcoma, mimicking so-called malignant fibrous histiocytoma, exhibited a more cellular and atypical histology lacking obvious lipogenic differentiation (Fig. 3e). The tumor cells in the high-grade area showed positive immunostaining with antibodies to MDM2 (Fig. 3f) and CDK4 (Fig. 3g). The CDK4 staining was distributed diffusely, whereas MDM2-positive cells were scattered throughout the area and fewer in number than CDK4-positive cells. The area of well-differentiated liposarcoma demonstrated the same immunohistochemical findings. The final pathological diagnosis was dedifferentiated liposarcoma. The patient's postoperative course was uneventful, and he was discharged four weeks after the surgery. Because liposarcoma was observed in the extremities and often metastasizes, the patient was followed by our department using systemic examinations, such as CT and magnetic resonance imaging, once every two months after discharge. There were no signs of recurrence of either the primary liposarcoma of the duodenum or gastrointestinal hemorrhage 10 months after emergency pancreaticoduodenectomy.

Discussion

We herein presented the first case report of primary liposarcoma arising in the duodenum that was successfully treated with emergency pylorus-preserving pancreaticodu-

denectomy.

Liposarcoma constitutes one of the most common soft tissue sarcoma groups in adults, of which well-differentiated liposarcoma and dedifferentiated liposarcoma comprise major subtypes. The histological diagnosis of adipocytic tumors has traditionally relied on morphology alone, with immunohistochemistry being of limited value; however, in recent years, the use of immunohistochemical staining for CDK4 and MDM2 has gained popularity, capitalizing on the distinct genetic background of well-differentiated/dedifferentiated liposarcoma compared with other adipocytic neoplasms (9-11). Like most immunohistochemical markers, MDM2 and CDK4 are not of absolute diagnostic value, and, as always, it is important to use these parameters as part of an immunostaining panel when approaching a particular case. However, in the appropriate clinical and pathological context, immunoreactivity for these markers can facilitate the accurate diagnosis of atypical lipomatous tumor/well-differentiated liposarcoma and dedifferentiated liposarcoma. Ultimately, the primary duodenum tumor in this case was diagnosed as dedifferentiated liposarcoma, with typically scattered MDM2-positive nuclei, increased numbers of positive cells in the cellular areas and CDK4 reactivity that was stronger and more diffuse.

Surgical resection is the mainstay of curative treatment for patients with well-differentiated or dedifferentiated

liposarcoma (12, 13). The present patient received emergency pylorus-preserving pancreaticoduodenectomy as a life-saving procedure and the most appropriate management for primary liposarcoma of the duodenum with active hemorrhage. Subsequent gastrointestinal endoscopy detected the hemorrhage from the tumor; however, it was difficult to control the bleeding endoscopically. Recent reports suggest the usefulness of catheter intervention for treating gastrointestinal hemorrhage or periampullary neoplasms (14, 15). Due to the complex arterial anastomosis around the pancreatic head, the use of catheter intervention for tumors of the periampullary region is not sufficient. Complete embolization of the arteries around the duodenum may also be ineffective and was furthermore anticipated to induce necrosis of the adjacent organs in this case. Emergency pancreaticoduodenectomy is not a common procedure due to the associated rates of morbidity and mortality (16-19); however, recent advances in surgical techniques and improvements in perisurgical management have made it relatively safe, especially when performed by experienced surgeons in training centers.

New therapeutic modalities for treating liposarcoma, particularly aggressive tumors, including myxoid/round cell liposarcoma, are therefore needed. First, the expression of protein-coding genes in eukaryotes involves a number of tightly regulated steps, each of which is controlled by various proteins to ensure that the transcripts are appropriately expressed and processed. Protein translocation plays a significant role in the pathogenesis liposarcoma via the expression of a number of RNA polymerase II transcription genes, and the identification of several RNA polymerase II promoters in patients with liposarcoma has confirmed some target genes, including *INTS3*, *RAS family*, *ZNF294* and *MECP2* (20). The function of these target genes translocated in liposarcoma indicates their regulatory roles in processes as diverse as transcription, cell-cycle progression, DNA repair, genomic stability and neurodegeneration. Second, there has been a focus on identifying potential antigens for immunotherapy in patients with liposarcoma. NY-ESO-1 has been successfully targeted in trials of antigen-specific adoptive T-cell therapy, and complete responses have been observed in melanoma trials targeting NY-ESO-1 using both vaccines and adoptive transferred T-cells. Indeed, the discovery that synovial sarcoma expresses NY-ESO-1 was rapidly translated into a clinical trial (21). Furthermore, Pollack et al. (22) reported another soft tissue sarcoma subtype with a pattern of the NY-ESO-1 expression that is even more prevalent than that observed in synovial sarcoma. This latter study demonstrated that, like synovial sarcoma, myxoid/round cell liposarcoma can be used as a model disease for the study of NY-ESO-1-directed therapy (22).

In conclusion, we herein reported the first case study of primary liposarcoma arising from the duodenum that was successfully treated with emergency pylorus-preserving pancreaticoduodenectomy for tumor bleeding that was not controlled with endoscopic intervention. This case suggests that

pancreaticoduodenectomy can be selected as an appropriate treatment for aggressive hemorrhage from tumors of the pancreatic head as a life-saving procedure in specific situations.

The authors state that they have no Conflict of Interest (COI).

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