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RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Zi-Hang Xu; Production Department Director: Xiang Le; Cover Editor: Jia-Ru Fan.

NAME OF JOURNAL
*World Journal of Gastrointestinal Surgery*

ISSN
ISSN 1948-9366 (online)

LAUNCH DATE
November 30, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Peter Schemmer

EDITORIAL BOARD MEMBERS

PUBLICATION DATE
April 27, 2024

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E-mail: office@baishideng.com  https://www.wjgnet.com
Blastomas of the digestive system in adults: A review

Yu Liu, Tony El Jabbour, Jonathan Somma, Yukihiro Nakanishi, Saverio Ligato, Hwajeong Lee, Zhi-Yan Fu

Abstract

Blastomas, characterized by a mixture of mesenchymal, epithelial, and undifferentiated blastematous components, are rare malignant neoplasms originating from precursor blast cells. This review focuses on digestive system blastomas in adult patients, including gastroblastoma, hepatoblastoma, and pancreatoblastoma. Gastroblastoma is a biphasic, epitheliomesenchymal tumor, with only sixteen cases reported to date. In addition to the characteristic histology, metastasis-associated lung adenocarcinoma transcript 1 - glioma-associated oncogene homolog 1 gene fusion is typical, although recently novel ewing sarcoma breakpoint region 1 - c-terminal binding protein 1 and patched 1 - glioma-associated oncogene homolog 2 fusions have been described. Hepatoblastoma is exceptionally rare in adults and can show a variety of histologic patterns which may cause diagnostic difficulty. Pancreatoblastoma, primarily a pediatric tumor, displays acinar differentiation and squamoid nests with other lines of differentiation also present, especially neuroendocrine. Diagnostic approaches for these blastomas include a combination of imaging modalities, histopathological examination, and molecular profiling. The treatment generally involves surgical resection, which may be supplemented by chemotherapy or radiotherapy in some cases. Prognoses vary with gastroblastoma generally showing favorable outcomes post-surgery whereas hepatoblastoma and pancreatoblastoma often have poorer outcomes, particularly in the setting of metastases. This review highlights the complexity of diagnosing and managing these rare adult blastomas as well as the need for ongoing research to better understand their pathogenesis and improve treatment strategies.
INTRODUCTION

A blastoma is a malignant neoplasm consisting of a combination of mesenchymal, epithelial, and undifferentiated blastematous components. It originates from precursor cells called blasts. Blastomas arise at a variety of sites, and typical examples include medulloblastoma and neuroblastoma. However, the primary digestive system blastomas, hepatoblastoma, pancreaticoblastoma, and gastroblastoma, are uncommon, and the literature on these tumors is limited, particularly for cases arising in adults. In fact, no comprehensive resource is presently available. Thus, we aim to present a thorough review of digestive system blastomas in adults which, among other things, will highlight up to date information regarding the complexity of diagnosis, molecular pathogenesis, and management.

Gastroblastoma is a rare tumor, first described by Miettinen et al[1] in 2009. It was added to the World Health Organization (WHO) Classification of Tumors of the Digestive System in 2019. Only sixteen cases have been reported to date, most occurring in young adults. However, six have been reported in patients over 30, and the oldest reported case was in a 74-year-old[2]. Gastroblastoma is an epitheliomesenchymal neoplasm primarily developing in the gastric body and antrum[3]. Diagnosis typically relies on the presence of the metastasis-associated lung adenocarcinoma transcript 1 - glioma-associated oncogene homolog 1 gene fusion and its biphasic (epitheliomesenchymal) histology[3]. However, recent discoveries, such as the ewing sarcoma breakpoint region 1 - c-terminal binding protein 1 (EWSR1-CTBP1) gene fusion in a patient with Wiskott-Aldrich syndrome[4] and the patched 1 - glioma-associated oncogene homolog 2 (PTCH1-GLI2) gene fusion[5,6], suggest more genetic diversity than was originally thought.

Hepatoblastoma accounts for 79% of all pediatric malignant liver tumors. Almost 90% of tumors appear before the age of 5, and only 3% occur in patients older than 15 years[7]. Adult hepatoblastoma was first reported by Marx[8] in 1904, and, to date, only about 75 cases of adult hepatoblastoma have been reported[9,10]. Compared to childhood hepatoblastoma, where the 5-year overall survival rates exceed 70%[11,12], adults have a high rate of mortality and poor prognosis, with a 1-year survival rate of 24%[13]. Frequently, patients present with an elevated serum alpha-fetoprotein (AFP) level, which can be used to monitor response to therapy[14]. Although the etiology and pathogenesis of hepatoblastoma are poorly understood, mutations in the β-catenin gene, which plays a critical role in the WNT signaling pathway, are commonly observed in both pediatric and adult cases[15]. Due to its rarity in adults, treatment is not as standardized as it is in children, but surgical management is the mainstay of therapy in both populations[12].

Pancreatoblastoma is a rare malignancy, accounting for less than 1% of all exocrine neoplasms of the pancreas[16]. It is characterized by a multilinage cellular proliferation predominantly showing acinar differentiation with distinctive squamoid nests often present. Additionally, neuroendocrine differentiation is common whereas ductal and mesenchymal components are less pronounced[17]. It is most prevalent in pediatric patients, comprising 25% of pancreatic neoplasms in children in the first decade of life[18]. In adults, however, pancreatoblastoma is uncommon, with an incidence rate of just 0.004 per 100000 individuals aged 19 and older, and less than 80 such cases have been reported in the literature to date[19-22]. The genetic landscape of pancreatoblastoma often involves somatic alterations, including the loss of chromosome 11p, which is also implicated in Beckwith-Wiedemann Syndrome, and mutations in the Wnt/β-catenin signaling pathway[16,23,24]. Notably, the clinical course of pancreatoblastoma in adults is more aggressive than in children. Metastasis and/or invasion of adjacent structures contribute to 58% of adult pancreatoblastoma cases, leading to three-year survival rates of less than 40%. This sharply contrasts with the 94.4% 5-year overall survival observed in children[25-27].
CLINICAL MANIFESTATIONS

In most cases of gastroblastoma, adult patients present with non-specific symptoms and, in some, the diagnosis is incidental. Reported symptoms include fatigue, abdominal mass, abdominal and/or epigastric pain, and hematemesis [28]. Similarly, hepatoblastoma has non-specific initial clinical manifestations. Pain is the most common symptom including epigastric, abdominal, and low back pain. Fever, vomiting, nausea, anorexia/weight loss, and hepatomegaly/abdominal mass are also reported. Rarely described manifestations are gastrointestinal bleeding, dyspnea, and lower extremity edema [29]. Pancreatoblastoma is frequently asymptomatic early on; late manifestations include abdominal pain/mass, splenomegaly, obstructive jaundice, fever, diarrhea, melena, weight loss, and occult blood in urine [26].

LABORATORY/IMAGING FINDINGS

The imaging findings of blastomas are similar to those of more common tumors of the digestive system. Gastroblastomas appear heterogeneous on abdominal computed tomography (CT) [30], and magnetic resonance imaging (MRI) offers superior soft tissue contrast to clarify the tumor's extent and relationship to adjacent structures. Gastroendoscopy typically reveals an ulcerated, submucosal based mass [4,31]. Although not specific for gastroblastoma, serum markers like Carcinoembryonic Antigen and Carbohydrate Antigen 19-9 (CA19-9) can be elevated in some cases and can be helpful in monitoring for disease recurrence.

Hepatoblastoma may be detected as unifocal or multifocal lesions by imaging. On ultrasound, the tumor is reported as a hyperechoic and solid mass [32]. CT scans and MRIs provide superior delineation of tumor characteristics, extent, and vascular involvement. The use of contrast agents, particularly during the arterial phase, can highlight tumor vascularity. Serum AFP level is usually increased but nonspecific [10,33].

Pancreatoblastomas are single, large, well-delineated, circular or lobulated masses with scattered or aggregate calcifications visible on both CT and MRI. Heterogeneous character may reflect a cystic component of some tumors [34]. Contrast imaging shows enhancement in the arterial phase that can mimic a hypervascular neuroendocrine tumor [34-36]. Common bile duct involvement (i.e., dilatation) is apparent in some pancreatic head tumors [34,35,37,38]. Serum AFP has been noted to be increased in 68% cases [18,39] and may be used to monitor the effectiveness of therapy [40]. In the case reported by Li et al. [35], the patient showed elevated CA19-9 and Cancer Antigen 125 levels [35,38]. Rarely adrenocorticotrophic hormone can be secreted from the tumor [40-42].

CASE REPORTS

Table 1 summarizes adult gastroblastoma case reports from 2009 to present [43-48]. Patients were on average 37-years-old (range 19-74 years old) at the time of diagnosis. Surgical management was the primary treatment modality, and the gastric antrum was the most common tumor site. Molecular testing was not conducted in the majority of cases, but among those cases tested, all had the MALAT1-GLI1 gene fusion except for one case with a PTCH1-GLI2 gene fusion. Although reported follow-up times varied substantially, ranging from 3 months to 14 years, the clinical course was favorable in the majority of patients.

A total of 12 adult hepatoblastoma cases have been reported in the English literature from 2013 to 2023 (Table 2) [49-56]. The average age was 44 years old with a wide range from 22 to 84 years old, and tumors were more frequently right sided. Twelve cases demonstrated elevated serum AFP, and hepatitis B infection and liver cirrhosis were present in 40%. Metastasis at the time of disease presentation was infrequent. Histologically, 75% of cases exhibited mixed epithelial and mesenchymal patterns, and the remainder were purely epithelial. Surgical resection constituted the primary treatment modality, often followed by adjuvant chemotherapy. Follow-up periods were generally short. However, this may be due to the aggressive course of most patients; short term recurrence or metastasis and death were frequent outcomes.

A total of 47 adult pancreatoblastoma cases have been reported since 2018 (Table 3) [57-68]. The average age of affected individuals was 45 years old (range 19 to 75 years old). Half of the patients were diagnosed with metastasis at the time of initial diagnosis, typically to the liver. Tumors arose throughout the pancreas with no discernable pattern. Primary treatment modalities included surgical resection and chemotherapy. Follow-up ranged from several months to a few years, and, although many patients experienced disease recurrence or metastasis, there were several instances of better outcomes during the follow-up period.

HISTOPATHOLOGY

Histopathological assessment plays a pivotal role in the diagnosis of blastomas of the digestive system. Gastroblastomas arise within the gastric muscularis propria, and neither component of its biphasic histology displays much cytologic atypia (Figure 1). The epithelial component consists of cells with round uniform nuclei, slightly eosinophilic cytoplasm, and inconspicuous nucleoli. These cells are arranged in sheets, nests, cords, and tubules. Notably, the epithelial component in some cases forms gland- or rosette-like structures that may contain mucin or dense eosinophilic globules. In contrast, the mesenchymal component consists of homogeneous and slender spindle cells often embedded within a myxoid matrix [28,30]. Immunohistochemistry can be helpful in highlighting these components and confirming the
### Table 1 Summary of reported cases of adult gastroblastoma

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Age/sex</th>
<th>Location</th>
<th>Molecular alteration (s)</th>
<th>Treatment</th>
<th>Follow-up</th>
<th>Recurrence or metastasis</th>
</tr>
</thead>
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<tr>
<td>Castr et al[43], 2019</td>
<td>74/M</td>
<td>Gastric antrum</td>
<td>MALAT1::GLI1</td>
<td>Partial gastrectomy</td>
<td>5 years</td>
<td>Recurrence after 5 years</td>
</tr>
<tr>
<td>Centoene et al[30], 2019</td>
<td>43/F</td>
<td>Gastric antrum</td>
<td>Not performed</td>
<td>Partial gastrectomy</td>
<td>100 months</td>
<td>No</td>
</tr>
<tr>
<td>Fernandes et al [44], 2014</td>
<td>19/F</td>
<td>Gastric antrum</td>
<td>Not performed</td>
<td>Partial distal gastrectomy</td>
<td>20 months</td>
<td>No</td>
</tr>
<tr>
<td>Graham et al[3], 2017</td>
<td>27/M</td>
<td>Stomach</td>
<td>MALAT1::GLI1</td>
<td>Partial gastrectomy</td>
<td>12 months</td>
<td>No</td>
</tr>
<tr>
<td>Graham et al[3], 2017</td>
<td>56/F</td>
<td>Stomach</td>
<td>MALAT1::GLI1</td>
<td>N/A</td>
<td>N/A</td>
<td>Metastasis to liver</td>
</tr>
<tr>
<td>McCammon et al [1], 2023</td>
<td>26/M</td>
<td>Gastric pylorus extending through the first and second portions of the duodenum</td>
<td>MALAT1::GLI1</td>
<td>Tumor resection from the mucosa of pylorus and duodenum</td>
<td>2 months</td>
<td>No</td>
</tr>
<tr>
<td>Miettinen et al[1], 2009</td>
<td>30/M</td>
<td>Gastric antrum</td>
<td>Not performed</td>
<td>Antrectomy, postoperative radiation</td>
<td>14 years</td>
<td>No</td>
</tr>
<tr>
<td>Miettinen et al[1], 2009</td>
<td>27/F</td>
<td>Gastric body</td>
<td>Not performed</td>
<td>Partial gastrectomy</td>
<td>5 years</td>
<td>No</td>
</tr>
<tr>
<td>Miettinen et al[1], 2009</td>
<td>19/M</td>
<td>Gastric body</td>
<td>Not performed</td>
<td>Subtotal gastrectomy</td>
<td>3.5 years</td>
<td>No</td>
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<tr>
<td>Pinto et al[31], 2019</td>
<td>53/F</td>
<td>Gastric antrum</td>
<td>Not performed</td>
<td>Partial gastrectomy</td>
<td>18 months</td>
<td>No</td>
</tr>
<tr>
<td>Poizat et al[45], 2012</td>
<td>22/F</td>
<td>Duodenum</td>
<td>Not performed</td>
<td>Partial resection of the distal duodenum</td>
<td>16 months</td>
<td>No</td>
</tr>
<tr>
<td>Toumi et al[46], 2017</td>
<td>29/F</td>
<td>Gastric body</td>
<td>Not performed</td>
<td>Partial gastrectomy + splenectomy</td>
<td>6 months</td>
<td>Local recurrence after 6 months</td>
</tr>
<tr>
<td>Wey et al[30], 2012</td>
<td>28/M</td>
<td>Distal stomach</td>
<td>MALAT1::GLI1</td>
<td>Preoperative chemotherapy + partial gastrectomy</td>
<td>3 months</td>
<td>Metastasis to lymph nodes, liver, pelvic clinically stable at 3 months</td>
</tr>
<tr>
<td>Gong et al[47], 2023</td>
<td>19/M</td>
<td>Gastric antrum</td>
<td>No gene break rearrangement detected by FISH</td>
<td>Partial gastrectomy</td>
<td>19 months</td>
<td>No</td>
</tr>
<tr>
<td>Zhu et al[48], 2018</td>
<td>65/F</td>
<td>Gastric body</td>
<td>Not performed</td>
<td>Full-thickness resection of the gastric wall</td>
<td>4 years</td>
<td>No</td>
</tr>
<tr>
<td>Chen et al[5], 2022 and Liu et al[6], 2022</td>
<td>58/M</td>
<td>Gastric body</td>
<td>PTCH1::GLI2</td>
<td>Endoscopic submucosal dissection</td>
<td>1 year</td>
<td>No</td>
</tr>
</tbody>
</table>

F: Female; M: Male; N/A: Not available.

The histology of hepatoblastoma may reflect any stage of hepatic development and, thus, can be quite varied. Some tumors are purely epithelial while others show mixed epithelial and mesenchymal differentiation. The epithelial elements can range in appearance from that of early immature embryonal hepatocytes to a well differentiated hepatocellular phenotype. When present, fetal-type cells are characterized by eosinophilic cytoplasm and distinct cell borders, often arranged in cords or nests reminiscent of, but disorganized as compared to normal liver architecture. In contrast, embryonal components appear more basophilic and densely packed, with a tendency to form pseudococinar structures. Adding to the potential for diagnostic confusion, ductular (cholangioblastic) differentiation may also be found, and some cases show small cell undifferentiated (SCUD) histology. Mesenchymal components are also varied and can range from fibroblastic to heterologous elements such as bone or cartilage (Figure 2), and some tumors are divided into lobules by non-neoplastic fibrous bands. There is no definitive immunomarker to distinguish hepatoblastoma from other tumors.
hepatocellular carcinoma, although the latter is positive only for hepatocellular markers, usually occurs in a cirrhotic liver background, and will not contain immature or mesenchymal components. That said, immunohistochemical markers still play a role in the diagnostic and prognostic evaluation of hepatoblastoma[10,28,70,71] with at least some tumor cells, depending on their histologic appearance, expressing AFP, HepPar1, glypican 3, and/or β-catenin (nuclear and cytoplasmic). Pancytokeratins are variably positive in epithelial components, and CK7 and CK19 will highlight cholangiocellular elements when present. Importantly, SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1 (SMARCB1/INI1) is expressed in almost all cases of hepatoblastoma, throughout its varied components. SMARCB1 negative tumors are rare, limited to a subset of those with SCUD histology, and have a poor prognosis.

Histology of adult pancreatoblastoma is characterized by a multilineage cellular proliferation predominantly showing acinar differentiation with distinctive squamoid nests always present. Additionally, neuroendocrine differentiation is common whereas ductal, mesenchymal, or more primitive components are less pronounced. Its acinar component can mimic acinar cell carcinoma as well as the related typical histologic differential diagnosis of pancreatic endocrine tumors and solid pseudopapillary neoplasms too. However, none of these display the prototypical squamoid nests of pancreatoblastoma[22]. While the neuroendocrine component of pancreatoblastoma may be detectable as increased serum levels of hormones, this is uncommon in the adult population[21]. Immunohistochemistry plays a critical role in diagnosing pancreatoblastoma. Acinar differentiation is highlighted with immunolabeling for trypsin, chymotrypsin, and B-cell Lymphoma/Leukemia 10. Neuroendocrine differentiation is evidenced by the expression of Synaptophysin, Chromogranin, and Insulinoma-Associated Protein 1, but should not be diffuse as in the case of pancreatic endocrine tumors. The squamoid component is positive for EMA and beta-catenin (nuclear staining) whereas the latter would be diffusely evident in a solid pseudopapillary neoplasm. Although these tumors may be histologically complex, the synchronous presence of acinar differentiation with immunohistochemical confirmation plus squamoid nests typically allows for straightforward diagnosis in well sampled tumors[22] (Figure 3).

**MOLECULAR PATHOLOGY**

A molecular hallmark of adult gastroblastoma is the MALAT1-GLI1 fusion, which is considered essential for diagnosis.
Figure 2 Mixed epithelial mesenchymal hepatoblastoma in an adult patient, showing a heterogeneous mix of epithelial and mesenchymal components. Well differentiated fetal-type epithelial component is characterized by their eosinophilic cytoplasm and cords or nests-like growth reminiscent of normal liver architecture. The mesenchymal part shows heterologous osteoid elements (100 ×).

Figure 3 Pancreatoblastoma in the pancreatic head of a 42-year-old male patient. A: The tumor is composed of acinar and ribbonlike morphology composed of relatively monotonous cells with basophilic nuclei, mimicking a pancreatic endocrine tumor (100 ×); B: In a few foci, squamoid nests, consisting of circumscribed whorled nests of polygonal cells with abundant eosinophilic cytoplasm and a squamous appearance, are present (200 ×).

Genomic sequencing studies have established that mutations in the Wnt-β-catenin signaling pathway are prevalent in hepatoblastoma, with alterations in the Catenin Beta 1 (CTNNB1) gene detected in about 90% of cases[15,72]. These mutations are central to disease pathogenesis and are often accompanied by changes in other Wnt signaling genes. Additionally, a subpopulation of high-risk hepatoblastomas exhibits alterations in the Nuclear Factor, Erythroid 2 Like 2 (NFE2L2) gene, indicating oxidative stress as a contributing factor to cellular transformation and disease progression. The Yap signaling pathway collaborates with β-catenin in tumor development. Nevertheless, the activation mechanism of Yap in hepatoblastoma cases is still unclear, necessitating further studies[72]. Such molecular profiling highlights the complex genetic landscape of hepatoblastoma, may impact patient management presently, and potentially has implications for
Table 2 Summary of reported cases of adult hepatoblastoma from recent 10 years (2013-2023)

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Age/sex</th>
<th>Location</th>
<th>Hepatitis B</th>
<th>Liver cirrhosis</th>
<th>AFP</th>
<th>Metastasis at diagnosis</th>
<th>Histology</th>
<th>Treatment</th>
<th>Follow-up</th>
<th>Recurrence or metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pagarigan et al[49], 2023</td>
<td>49/F</td>
<td>Right hepatic lobe</td>
<td>HBsAg (+); anti-HBc (+)</td>
<td>Yes</td>
<td>&gt; 50000 ng/mL</td>
<td>No</td>
<td>Mixed</td>
<td>Surgical resection + postoperative chemotherapy</td>
<td>4 months</td>
<td>Recurrence</td>
</tr>
<tr>
<td>Ibsan et al [10], 2022</td>
<td>26/F</td>
<td>Right Hepatic lobe</td>
<td>No</td>
<td>No</td>
<td>2275 ng/mL</td>
<td>No</td>
<td>Epithelial (the mixed fetal and embryonic pattern)</td>
<td>Surgical resection</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Ibsan et al [10], 2022</td>
<td>50/M</td>
<td>Entire liver</td>
<td>No</td>
<td>No</td>
<td>6386 ng/mL</td>
<td>No</td>
<td>Mixed</td>
<td>Surgical resection</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Park et al [50], 2015</td>
<td>36/F</td>
<td>Right hepatic lobe</td>
<td>HBsAg (+); anti-HBc (+)</td>
<td>Yes</td>
<td>676.5 ng/mL</td>
<td>No</td>
<td>Mixed</td>
<td>Surgical resection + postoperative chemotherapy</td>
<td>5 months</td>
<td>Intraperitoneal metastasis, died</td>
</tr>
<tr>
<td>Caso-Maestro et al[51], 2013</td>
<td>27/M</td>
<td>Right hepatic lobe</td>
<td>HBsAg +, HBcAb +, HBeAb +</td>
<td>No</td>
<td>116000 ng/mL</td>
<td>Mixed</td>
<td>Surgical resection</td>
<td>27 months</td>
<td>Left adrenal recurrence followed by total adrenalectomy; alive</td>
<td></td>
</tr>
<tr>
<td>Al-Jiffry et al[53], 2013</td>
<td>22/M</td>
<td>Left hepatic lobe</td>
<td>No</td>
<td>No</td>
<td>Normal</td>
<td>Diaphragm, pericardial, and IVC infiltration</td>
<td>Mixed</td>
<td>Surgical resection</td>
<td>16 d</td>
<td>Died</td>
</tr>
<tr>
<td>Cienfuegos et al[52], 2013</td>
<td>37/F</td>
<td>Segment 5 and 6 of the liver</td>
<td>HBsAg +, HBcAb +, HBeAb +</td>
<td>Yes</td>
<td>1556.3 ng/mL</td>
<td>No</td>
<td>Mixed</td>
<td>Surgical resection</td>
<td>10 months</td>
<td>Recurrence and died</td>
</tr>
<tr>
<td>Zhang et al [53], 2013</td>
<td>32/F</td>
<td>Left hepatic lobe</td>
<td>No</td>
<td>No</td>
<td>Normal</td>
<td>Epithelial, neuroendocrine differentiation</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Park et al [50], 2015</td>
<td>36/F</td>
<td>Right hepatic lobe</td>
<td>HBsAg +, HBcAb +, HBeAb +</td>
<td>No</td>
<td>676.5 ng/mL</td>
<td>No</td>
<td>Mixed</td>
<td>Surgical resection + postoperative chemotherapy</td>
<td>12 months</td>
<td>Left subphrenic area metastasis; died</td>
</tr>
<tr>
<td>Celotti et al [54], 2016</td>
<td>68/M</td>
<td>Left hepatic lobe</td>
<td>No</td>
<td>No</td>
<td>1231 ng/mL</td>
<td>Pericardial metastasis</td>
<td>Mixed</td>
<td>Left lobectomy + diaphragm resection + extended pericardiectomy</td>
<td>21 months</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Urdiaín et al[55], 2019</td>
<td>65/M</td>
<td>Right hepatic lobe</td>
<td>No</td>
<td>No</td>
<td>N/A</td>
<td>No</td>
<td>Epithelial</td>
<td>Surgical resection</td>
<td>10 months</td>
<td>Recurrence, died</td>
</tr>
<tr>
<td>Dave et al [56], 2019</td>
<td>84/M</td>
<td>Left hepatic lobe</td>
<td>N/A</td>
<td>N/A</td>
<td>708 IU/mL</td>
<td>Metastatic to left lower bronchus, left descending pulmonary artery and left descending pulmonary vein</td>
<td>Mixed</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

AFP: Alpha-fetoprotein; F: Female; M: Male; HBsAg: Hepatitis B surface Antigen; HBcAb: Hepatitis B core antibody; HBeAb: Hepatitis B e-antibody; N/A: Not available; IVC: Inferior vena cava.

Adult pancreaticoblastomas exhibit loss of heterozygosity on chromosome 11p in 86% of cases and alterations in the APC/β-catenin signaling pathway in 67% of cases, including biallelic inactivation of APC and activating CTNNB1 mutations[23]. Interestingly, there is an overlap here with the molecular pathology of hepatoblastoma. Most recently, studies have identified alterations in the Fibroblast Growth Factor Receptor (FGFR) signaling pathway, including FGFR1 mutations and FGFR2 rearrangements, in pancreaticoblastomas[54]. Additionally, high-level amplification of Myeloid Cell Leukemia Sequence 1 (MCL1) has been identified in a small percentage of pancreaticoblastoma patients. The patients with MCL1-amplified pancreaticoblastoma could potentially benefit from targeted MCL1 inhibition[73].

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<table>
<thead>
<tr>
<th>Ref.</th>
<th>Age/sex</th>
<th>Location</th>
<th>Metastasis before treatment</th>
<th>Treatment</th>
<th>Follow-up (months/years)</th>
<th>Recurrence/metastasis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rojas et al</td>
<td>45/F</td>
<td>Pancreatic tail</td>
<td>No</td>
<td>Pancreatectomy and splenectomy; Chemotherapy;</td>
<td>3 months</td>
<td>Liver metastasis</td>
<td>N/A</td>
</tr>
<tr>
<td>[22], 2023</td>
<td></td>
<td></td>
<td></td>
<td>stem cell transplant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Machado et al[57], 2023</td>
<td>3 patients (2F, 1M); avg age: 51</td>
<td>Tail and body of pancreas</td>
<td>Liver and lung metastasis</td>
<td>Surgical resection</td>
<td>6 years 2 months</td>
<td>Regional or distant metastasis</td>
<td>2 died; 1 alive after 6 years 2 months following surgery</td>
</tr>
<tr>
<td>Hussain and Farrukh [58], 2023</td>
<td>75/M</td>
<td>Pancreatic head</td>
<td>Liver metastasis</td>
<td>Chemotherapy; stent insertion</td>
<td>5 months</td>
<td>No</td>
<td>Stable</td>
</tr>
<tr>
<td>Wu et al [34], 2022</td>
<td>7 patients (2M, 5F); avg age: 56.71</td>
<td>Pancreatic head (n = 3), tail (n = 2), gastric antrum (n = 1), neck (n = 1)</td>
<td>Liver (n = 2), Lymph node (n = 2), kidney adrenal (n = 1)</td>
<td>N/A</td>
<td></td>
<td>Not reported in 3 cases, 24, 26, 4, 4 months in others</td>
<td>N/A</td>
</tr>
<tr>
<td>Suemitsu et al[69], 2021</td>
<td>74/M</td>
<td>Tail of pancreas</td>
<td>No</td>
<td>Open distal pancreatectomy and splenectomy</td>
<td>36 months</td>
<td>No</td>
<td>Recurrence-free</td>
</tr>
<tr>
<td>Li et al[35], 2021</td>
<td>60/F</td>
<td>Tail of the pancreas</td>
<td>Right liver metastasis</td>
<td>Resection and chemotherapy</td>
<td>16 months</td>
<td>N/A</td>
<td>Death</td>
</tr>
<tr>
<td>Morales et al[30], 2021</td>
<td>76/M</td>
<td>Pancreatic head</td>
<td>Lymphovascular and perineural invasion</td>
<td>Chemotherapy</td>
<td>32 months</td>
<td>No</td>
<td>Stable</td>
</tr>
<tr>
<td>Raoul et al [60], 2021</td>
<td>33/F</td>
<td>Pancreas</td>
<td>Invading gastric wall</td>
<td>Pancreatectomy, Chemotherapy</td>
<td>14 months</td>
<td>Liver metastasis</td>
<td>Stable</td>
</tr>
<tr>
<td>Raoul et al [60], 2021</td>
<td>33/F</td>
<td>Pancreatic tail</td>
<td>Liver metastasis</td>
<td>Chemotherapy</td>
<td>20 months</td>
<td>No</td>
<td>Stable</td>
</tr>
<tr>
<td>Elghawy et al[61], 2021</td>
<td>23/F</td>
<td>Pancreatic tail</td>
<td>Liver metastasis</td>
<td>Chemotherapy; autologous hematopoietic cell transplant</td>
<td>57 months</td>
<td>N/A</td>
<td>Stable</td>
</tr>
<tr>
<td>Zhang et al [34], 2020</td>
<td>7 patients (7M); Avg age: 44.71</td>
<td>Pancreatic head (n = 3), neck (n = 1), body (n = 1), tail (n = 2)</td>
<td>Only 1 patient liver metastasis</td>
<td>Surgical resection</td>
<td>1.5 months, 6 months, 8 months, 8.5 months, 10 months, 2 years, 4 years</td>
<td>3 patients developing liver metastasis</td>
<td>Alive = 2, lost to follow-up = 5</td>
</tr>
<tr>
<td>Snyder et al [62], 2020</td>
<td>28/F</td>
<td>N/A</td>
<td>Liver metastasis</td>
<td>Chemotherapy; left suboccipital craniotomy</td>
<td>More than 51 months</td>
<td>Brain metastasis</td>
<td>Alive</td>
</tr>
<tr>
<td>Morrissey et al[63], 2020</td>
<td>69/M</td>
<td>Pancreatic head</td>
<td>No</td>
<td>Adjuvant chemotherapy; Surgical resection</td>
<td>10 weeks</td>
<td>No</td>
<td>Alive (tumor-free)</td>
</tr>
<tr>
<td>Berger et al [64], 2020</td>
<td>32/F</td>
<td>Pancreatic head</td>
<td>Liver metastasis</td>
<td>Pancreatectoduodenectomy and Lymphonodecetomy; Right hemihepatectomy for liver metastasis; Chemotherapy</td>
<td>14 months</td>
<td>Lung metastasis</td>
<td>Died</td>
</tr>
<tr>
<td>Berger et al [64], 2020</td>
<td>19/M</td>
<td>Pancreas</td>
<td>No</td>
<td>Chemotherapy, pylorus-preserving</td>
<td>24 months</td>
<td>Liver and abdominal lymph node metastasis</td>
<td>Died</td>
</tr>
<tr>
<td>Berger et al [64], 2020</td>
<td>30/M</td>
<td>Pancreatic head</td>
<td>No</td>
<td>Complete pancreatectomy; adjuvant chemotherapy; Immunotherapy</td>
<td>17 months</td>
<td>Liver metastasis</td>
<td>Died</td>
</tr>
<tr>
<td>Berger et al [64], 2020</td>
<td>20/F</td>
<td>Pancreatic tail</td>
<td>Diffuse liver metastasis</td>
<td>Chemotherapy</td>
<td>14 months</td>
<td>N/A</td>
<td>Died</td>
</tr>
</tbody>
</table>
**TREATMENT AND PROGNOSIS**

Surgical resection is the primary treatment approach in all blastomas of the digestive system with chemotherapy or radiotherapy considered for some patients. Generally, post-surgical outcomes are favorable in adult gastroblastoma patients. However, in some cases, local recurrence, metastasis, and death have been reported[30,43]. The case report by Liu et al[6] demonstrating successful treatment with endoscopic submucosal dissection offers an insight into less invasive treatment for localized disease[6].

Outcomes are markedly different in adult hepatoblastoma. For unresectable tumors, the one-year survival rate is 0% whereas it is 41% for resectable tumors[69]. Prognosis is dependent on various factors including patient age, extent of resection, and stage of disease. Outcomes are much better in patients who had complete surgical resection before the age of 45 years compared to those who were treated after that[69]. Adjunctive chemotherapy including vincristine, 5-fluorouracil, and cisplatin have improved the 5-year survival rate[69].

Adult pancreatobastoma, even with aggressive therapy, has poor outcomes and its optimal treatment strategy is not known. While controversial, adjuvant chemotherapy, including 5-fluorouracil/doxorubicin/mitoycin and dororubicin/carboplatin, and radiotherapy may be used as palliative treatment in advanced disease[41]. The average survival in adults is only 15-18 months[37,41]. Nearly half of patients have either local invasion and/or metastasis at diagnosis[41]. The most common site for metastasis is the liver, followed by regional lymph nodes and lung[41]. BRAF and MEK inhibitors such as Dabrafenib and Trametinib showed transient response at advanced stage, given the novel IQ Motif and Sec7 Domain 1 - Rapidly Accelerated Fibrosarcoma 1 (IQSEC1-RAFI) fusion in pancreatoblastoma[74].

**COMPARISON OF DIGESTIVE SYSTEM BLASTOMA IN PEDIATRIC AND ADULT POPULATIONS**

To date, only 16 cases of gastroblastoma in adults have been reported. Acknowledging the limited number of cases available for comparison, pediatric patients tend to present with more pronounced clinical symptoms, such as intermittent blood in stools and significant abdominal pain[75-77]. Moreover, a distinctive demographic difference is apparent, with all reported pediatric cases occurring in males[4,75-77], unlike the pediatric cases, which generally occur in both males and females. The remaining disease features are consistent between the two populations, and, regardless of age, patients generally show a favorable prognosis following surgical resection.

Hepatoblastoma exhibits distinct characteristics in adults. Pediatric patients typically show symptoms like abdominal swelling and pain, whereas adult symptoms are subtler[69]. Notably, about 40% of adult cases from 2013 to 2023 have underlying liver conditions like viral hepatitis or cirrhosis (Table 2), unlike the pediatric cases, which generally occur in patients without pre-existing liver disease. Histologically, adult cases also often show a more aggressive, undifferentiated histology whereas pediatric hepatoblastoma tends to show more typical epithelial and mesenchymal components including heterologous elements that indicate a favorable prognosis[65,78,79]. In adult hepatoblastoma, the presence of embryonal or undifferentiated cells often indicates a poorer prognosis[69]. Most significantly, adults are more prone to recurrence or metastasis than children despite similar treatment approaches.

Pancreatoblastoma certainly shows significant differences between adults and children. Because only 17% of pediatric cases demonstrate extrapancreatic disease at the time of diagnosis[80], presenting symptoms, like abdominal pain, palpable abdominal masses, jaundice, and vomiting, are all attributable to local tumor effect. In contrast, adults have a poorer prognosis and often present with symptoms and signs related to the more aggressive disease course, which includes frequent invasion of adjacent organs and structures as well as frequent metastases. Histology is similar in the age groups, but adult pancreatoblastomas typically contain less stroma[81]. Surgical resection is the primary treatment for both groups, often supplemented with chemotherapy and radiation therapy. However, adults generally have a poorer
prognosis, frequently due to the invasion of adjacent organs or metastasis at the time of diagnosis.

**CONCLUSION**

In this review, we focus on adult digestive system blastomas, covering aspects like histopathology, molecular pathology, and treatment outcomes, along with comparisons between pediatric and adult cases. Gastroblastoma is characterized by biphasic morphology and distinctive genetic features, notably the *MALAT1-GLI1* fusion. Hepatoblastoma shows diverse morphology and commonly exhibits mutations in the Wnt-β-catenin signaling pathway. Pancreatoblastoma is marked by acinar differentiation and squamoid nests, sharing molecular pathology similarities with hepatoblastoma. Treatment mainly involves surgery, possibly with adjunct chemotherapy or radiotherapy. This review underscores the importance of ongoing research for a deeper understanding and improved management of these rare blastomas.

**FOOTNOTES**

**Author contributions:** Liu Y and Fu ZY are acknowledged for their substantial contributions to drafting the work, conducting a comprehensive literature review for all discussed sections, revising critically important intellectual content, and giving final approval to the published version; Jabbour T and Lee H are credited for providing guidance on the topic; Jabbour T, Nakanishi Y, and Ligato S are acknowledged for their contributions to pathology imaging; Somma J is credited with aiding in the final polishing of content language; All authors have actively participated in the creation of the manuscript and agree with the final version of the manuscript.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

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**S-Editor:** Li L

**L-Editor:** A

**P-Editor:** Yu HG

**REFERENCES**


https://www.wjgnet.com
Review of adult GI blastomas

10.1007/s00247-005-0064-3


Cytologic and histologic analysis of 12 adult cases reveals helpful criteria in their diagnosis and distinction from common mimics.
Liu Y et al. Review of adult GI blastomas


