Case Report

Malignant Glomus Tumor (Glomangiosarcoma) of Intestinal Ileum: A Rare Case Report

Ahmed Abu-Zaid,1 Ayman Azzam,2 Tarek Amin,2 and Shamayel Mohammed3

1 College of Medicine, Alfaisal University, P.O. Box 50927, Riyadh 11533, Saudi Arabia
2 Department of Surgical Oncology, King Faisal Specialist Hospital and Research Center (KFSH&RC), P.O. Box 3354, Riyadh 11211, Saudi Arabia
3 Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Center (KFSH&RC), P.O. Box 3354, Riyadh 11211, Saudi Arabia

Correspondence should be addressed to Ahmed Abu-Zaid; aabuzaid@alfaisal.edu

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Glomus tumors are rare mesenchymal neoplastic lesions arising from glomus bodies that are involved in skin thermoregulation [1, 2]. These neoplasms are extremely rare accounting for roughly 2% of all soft tissue neoplasms [3]. They mostly occur in the peripheral soft tissues with high tendencies to involve the dermal and subdermal subungual zones of fingers and toes [1, 2]. Glomus tumors barely take place in visceral organs, such as the gastrointestinal tract, where glomus bodies are scarcely present or even absent [4]. Among the very few reported cases of gastrointestinal glomus tumors, stomach antrum and duodenum were the most frequent regions involved [5]. The vast majority of reported cases demonstrated benign lesions. Malignant variants of glomus tumors (aka glomangiosarcomas) are exceedingly rare [6] and account for less than 1% of all glomus tumor cases [7]. Glomus tumors specifically involving the intestinal ileum are exceptionally uncommon with no single case previously reported in the English medical literature. To the best of our knowledge, we report the first case of glomangiosarcoma of the intestinal ileum.

1. Introduction

Glomus tumors are mesenchymal neoplastic lesions arising from glomus bodies that are involved in skin thermoregulation [1, 2]. These neoplasms are extremely rare accounting for roughly 2% of all soft tissue neoplasms [3]. They mostly occur in the peripheral soft tissues with high tendencies to involve the dermal and subdermal subungual zones of fingers and toes [1, 2]. Glomus tumors barely take place in visceral organs, such as the gastrointestinal tract, where glomus bodies are scarcely present or even absent [4]. Among the very few reported cases of gastrointestinal glomus tumors, stomach antrum and duodenum were the most frequent regions involved [5]. The vast majority of reported cases demonstrated benign lesions. Malignant variants of glomus tumors (aka glomangiosarcomas) are exceedingly rare [6] and account for less than 1% of all glomus tumor cases [7]. Glomus tumors specifically involving the intestinal ileum are exceptionally uncommon with no single case previously reported in the English medical literature. To the best of our knowledge, we report the first case of glomangiosarcoma of the intestinal ileum.

2. Case Report

A 29-year-old female patient was referred to our hospital with a 1-month history of a pelvi-abdominal mass, constipation, vomiting, and melena. Upon presentation, the patient was anemic and had a tender palpable mass at the right lower quadrant. Laboratory investigations showed plasma hemoglobin (Hb) of 69 g/L (normal range values: 110–160 g/L) and plasma CA-125 of 85 U/mL (normal range values < 35 U/mL). The patient was admitted and subjected to further investigations.

An abdominal X-ray was done and showed multiple dilated small bowel loops associated with air-fluid levels. The appearance was highly suggestive of partial intestinal obstruction. An enteroscopy was done and showed a huge
Figure 1: Computed tomography (CT) of the abdomen. (a) Coronal section and (b) axial section showing a huge 12.8×10.2×13.1 cm heterogeneous, aggressive-looking intraperitoneal pelvic mass lesion, most likely arising from intestinal ileum, with areas of lobulations, hemorrhagic cystic changes, gas locules, fluid-fluid levels, and proximal small bowel dilatation due to partial obstruction.

Macroscopic and microscopic examinations of the appendix showed no pathological diagnosis.

Grossly, the resected intestinal tumor of the ileum measured 14 cm in the maximum dimension with no definitive lymphovascular invasion was identified. Microscopically, the tumor was composed of multiple cellular nodules separated by streams of smooth muscle cells or fibrous bands. The tumor ulcerated the overlying mucosa, involved mucosa, submucosa, and muscularis propria, and extended to the serosa. The tumor nodules showed a relatively solid pattern with pericytoma-like gaping capillary vessels. Cytoplasmic clearing was noted. The tumor cells showed sharply defined cell membranes and centrally located round, uniform nuclei with delicate chromatin and inconspicuous nucleoli with focal areas of spindled cells. Areas of coagulative necrosis were observed. Mitotic activity was approximately 4-5/50 high-power field (HPF) (Figures 2(a)–2(f)).

Immunohistochemically, the intestinal ileum tumor cells were stained positive for alpha smooth muscle actin (α-SMA), h-caldesmon, and calponin. Pericellular net-like positivity for collagen type IV reticulin was also noted. The tumor cells were negative for CD117, CD34, cytokeratin, S100, desmin, human melanoma black-45 (HMB-45), chromogranin, and synaptophysin (Figures 3(a) and 3(b)). The histopathological diagnosis was consistent with malignant glomus tumor of the intestinal ileum.

A postoperative 6-month followup failed to show any evidence of tumor recurrence. Plasma hemoglobin (Hb) and CA-125 were within the normal ranges. The patient is doing fine and is to be followed up after 6 months.

3. Discussion

Glomus tumors are unusual soft tissue mesenchymal neoplasms composing 2% of all soft tissue neoplasms [3]. They originate from customized smooth muscle cells of the normal perivascular glomus bodies, which are modified arterio-venous anastomotic apparatuses involved in skin thermoregulation [1, 2]. They are frequently observed in the peripheral soft tissues, predominantly in the distal segments of extremities (i.e., subungual zones of fingers and toes) where glomus bodies are mostly abundant in the dermal and subdermal skin layers [1, 2]. Glomus tumors involving deep visceral organs are exceptionally unusual due to the relative deficiency or near absence of glomus bodies in these locations [4]. As such, diagnosis is often deferred or even missed.

Gastrointestinal glomus tumors are very uncommon, and the stomach antrum is the most frequent site of involvement followed by intestinal duodenum [5]. The majority of reported cases are of a benign nature, and malignant variants are considerably uncommon and almost vanishing [2], accounting for approximately 1% of all glomus tumor cases [7]. Moreover, gastrointestinal glomus tumors involving the intestinal ileum are exceedingly rare. In our search of the medical literature using PubMed, only a single case of intestinal ileum glomus tumor was reported in the Russian medical literature [8], whereas none was found in the English medical literature. To the best of our knowledge, this is the...
first reported case of a malignant glomus tumor (glomangiosarcoma) of intestinal ileum officially documented in the English medical literature.

Gastrointestinal glomus tumors present with a diversity of symptoms. In the setting of ulcerating overlying mucosa, upper (hemoptysis/hematemesis) or lower (hematochezia/melena) gastrointestinal tract bleeding is the main presenting symptom causing varying degrees of anemia with cardiopulmonary complications [2]. Other presenting symptoms may include nonspecific ulcer-like symptoms (retrosternal epigastric discomfort), nausea, and bilious vomiting secondary to bowel obstruction, while many other patients may remain symptom-free [9].

There are two forms of glomus tumors: solitary and multiple forms. Solitary forms are the most common accounting for roughly (90%) of all cases, occur most frequently in adults [10]. Multiple forms (i.e., multiple glomus tumor syndrome) are less common accounting for roughly (10%) of all cases and occur most frequently in children [10], and are believed to be inherited in an autosomal dominant manner with incomplete penetrance [11].

According to the microscopic morphology, glomus tumors can be divided into typical and atypical glomus tumors. Typical glomus tumors are histologically composed of glomus cells, blood vessels, and smooth muscle cells [11]. Histopathologically, typical glomus tumors can be further
subdivided into solid tumors, glomangiomas, and glomangio- 
giomyomas based on the proportional abundance of round 
glomus cells, vascular smooth muscle cells, and spindle- 
shaped smooth muscle cells, respectively [12].

Several classifications of atypical glomus tumors have 
been proposed. In 1990, Gould et al. [6] proposed the fol-
lowing categorization of atypical glomus tumors: locally 
infiltrative glomus tumor (LIGT), glomangiosarcoma arising 
in a benign glomus tumor (GABG), and glomangiosarcoma 
 arising de novo (GADN). LIGT has the typical glomus his-
tological characteristics with an increased propensity to 
aggressively invade adjacent tissues. GABG and GADN 
are cytologically malignant lesions. The distinction between 
GABG and GADN is established by the presence or absence 
of a benign glomus tumor, respectively. GABG largely 
exhibits focal “spindling” of cells with cytologic neoplasia 
and hence is fairly simple to identify. Conversely, in GADN, 
the histopathological features suggestive of glomus tumors 
are often too minimal to be adequately recognized and 
distinguished from the round cell sarcomas [13]; and hence, 
establishing the correct diagnosis is fairly difficult and often 
missed.

In 2001, Folpe et al. [7] suggested the following classifi-
cation of atypical and malignant glomus tumors: malig-
nant glomus tumor (glomangiosarcoma), glomus tumor of 
uncertain malignant potential, symplastic glomus tumor, and 
glomangiomatosis. Folpe and colleagues [7] proposed the 
following criteria for classification of glomangiosarcomas: (a) 
deep tumor location and size more than 2 cm, (b) presence 
of atypical mitotic figures, or (c) combination of moderate-
to-high nuclear grade and mitotic activity (5 mitoses/50 
high-power fields). Although our patient had a deeply 
located, very large mass (14 cm in the maximum diameter) 
and increased mitotic activity (4-5 mitoses/50 high-power 
fields), interestingly, our patient did not develop distant 
metastasis.

Generally, glomangiosarcomas are strongly stained pos-
itive for ki-67 (proliferation index marker), bcl-2 (anti-
apoptotic marker), and p53 (antiproliferative and apoptosis-
inducing marker) than the benign glomus tumors [13, 14]. 
Glomangiosarcomas have an increased likelihood to recur 
locally [13]; and hence, long-term followup is greatly rec-
ommended. Regardless of bearing cytological characteristics 
of malignancy, glomangiosarcomas generally have a benign 
indolent clinical course and rarely metastasize, therefore 
providing excellent prognosis [2]. Nevertheless, malignant 
potential to aggressively invade distant organs is very pre-
dictable and cannot be ruled out; and therefore, long-
standing followup is highly advised. Tumor location, mass, 
cellularity, nuclear atypia, spindle cell change, mitotic activ-
ities, atypical mitotic figures, necrosis, and angiolymphatic 
invasions have been fundamentally recognized as probable 
factors determining propensity for malignancy. Wide surgical 
excision is curative and remains the most effective treatment 
[2].

Gastrointestinal glomus tumors must be differentiated 
from the other closely cytology-related tumors such as 
gastrointestinal stromal tumors (GISTs), carcinoid tumors, 
hemangiopericytomas, paragangliomas, and lymphomas [1, 
2, 15]. Immunohistochemical staining can be effectively used 
to facilitate a definitive diagnosis of a given neoplastic 
lesion. Gastrointestinal glomus tumors are nearly always 
positive for alpha-smooth muscle actin (α-SMA), calponin, 
h-caldesmon and vimentin [2, 7]. Gastrointestinal stromal 
tumors (GISTs) are almost always positive for CD117 (c-
KIT) and very frequently (70%) positive for CD34, whereas 
gastrointestinal glomus tumors are persistently negative for 
CD117 and occasionally positive for CD34 [2]. Carcinoid 
tumors stain positively for keratin 18, chromogranin A, and 
synaptophysin. Gastrointestinal glomus tumors by no means 
express keratin 18 and chromogranin A proteins, whereas 
synaptophysin is only hardly ever expressed focally [3]. 
Hemangiopericytomas stain negative for alpha-smooth mus-
cle actin (α-SMA) [2, 16], which is a satisfactory evidence to 
rule out a diagnosis of gastrointestinal glomus tumor. Para-
gangliomas stain substantially positive for chromogranin A 
and synaptophysin and exclusively positive for S-100 proteins, 
while gastrointestinal glomus tumors barely stain positive for 
S-100 proteins [2, 16]. Malignant lymphomas stain positive 
for CD20 and CD45 leukocyte-specific markers, both of 
which stain negative in gastrointestinal glomus tumors [2]. In 
short, immunohistochemical studies can simply and rapidly

**Figure 3: Immunohistochemistry of excised intestinal ileum tumor.** (a) Tumor cells are positive for alpha smooth muscle actin (α-SMA). (b) Uniform pericellular type IV collagen expression.
characterize the neoplastic profile of any given malignant lesion.

4. Conclusion
To the best of our knowledge, we report the first case of a malignant glomus tumor (glomangiosarcoma) of the intestinal ileum in the English medical literature. Glomus tumors of intestinal ileum are exceedingly rare but should be considered in the differential diagnosis in any patient presenting with a pelvi-abdominal mass. Moreover, histopathological examination of the excised lesion is fundamental for determining a definitive diagnosis. Glomangiosarcomas generally have a benign clinical course. Although glomangiosarcomas occasionally recur locally and rarely metastasize distally, long-term followup is greatly recommended as the recurrence, and malignant potentials cannot be excluded. Wide surgical resection is curative and remains the mainstay of treatment.

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References
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