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Case Report and Review of Primary Gallbladder Gastrointestinal Stromal Tumour

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1. Abstract

1.1. Background

Gastrointestinal stromal tumours (GIST) are mesenchymal tumours primarily located in the gastrointestinal tract, representing the majority of gastrointestinal mesenchymal tumours. Primary gallbladder GIST are exceptionally rare, with fewer than 20 cases documented in the existing literature.

1.2. Case Presentation

We report a unique case of a 25-year-old woman who exhibited symptoms and imaging changes consistent with gallbladder adenomyosis. The diagnosis was confirmed through histological examination. Additionally, we conduct a comprehensive review of the existing literature to elucidate this rare pathology.

1.3. Conclusion

This case underscores the significance of pathology in the diagnosis of primary gallbladder GIST. Further research and case studies are essential to enhance our understanding of its pathogenesis and to identify optimal treatment strategies.

2. Background

GIST was first described in 1960 as gastric epithelioid leiomyomas and were further classified as such by the World Health Organization (WHO) in 1969. The evolution of immunohistochemistry, electron microscopy, and molecular biology led Mazur and Clark [1] to identify these tumours as “gastrointestinal stromal tumours” in 1983, advancing the understanding of their histogenesis. It is believed that GIST originates from Cajal cells, essential stem cells of the gastrointestinal tract that are distributed between the muscle layers of the gastrointestinal tract and regulate visceral movement. These cells are found in the subepithelial and muscular layers of the gallbladder [2,3]. The first report of gallbladder GIST appeared in 2000 [4]. Due to the rarity of gallbladder GIST, their study is complex and primarily relies on histological findings and immunohistochemical detection.

3. Case Report

A 25-year-old woman presented with a 2-year history of subxiphoid pain, which worsened after the consumption of greasy foods. There was no reported history of jaundice or significant weight loss. Physical examination revealed no evidence of skin or scleral jaundice, and the Murphy sign was negative. Routine blood tests indicated a high leukocyte count (16.19x109/L) and an elevated neutrophil count (13.69x109/L). Liver function tests were within normal limits. Tumour markers were all in the normal range (carcinoembryonic antigen, alpha-fetoprotein, carbohydrate antigen 125, carbohydrate antigen 15-3, and carbohydrate antigen 19-9). Ultrasound examination showed that the gallbladder size was normal, although the wall of the basal gallbladder was thickened to approximately 4.5 mm. small honeycomb echoes and small strong echoes were observed in the thickened wall of the gallbladder, along with a strong sediment echo in the gallbladder cavity. These findings were thought to indicative of gallbladder adenomyosis and silt stones (Figure 1). Subsequently, laparoscopic partial cholecystectomy was performed.

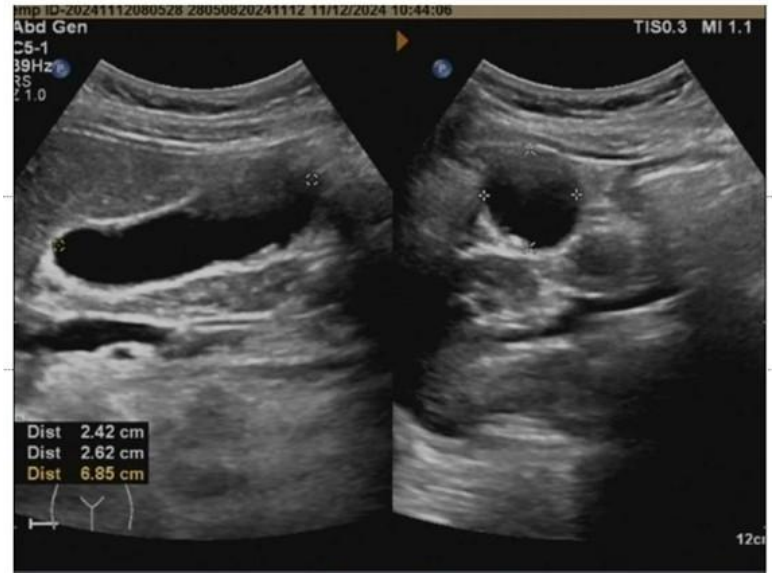

Figure 1: Preoperative ultrasound reveals a dilated gallbladder with wall thickening.

4. Materials and Methods

The 3.5 μm paraffin sections were utilized for haematoxylin as well as eosin staining and immunohistochemical analysis. Immunohistochemical analyses were performed using biotin-peroxidase complex methods with appropriate positive and negative controls. The primary antibodies included CD117 (monoclonal, ready-to-use), DOG-1 (monoclonal, 1:100), CD34 (monoclonal, 1:80), smooth muscle actin (SMA) (monoclonal, 1:80), desmin (monoclonal, 1:150), S-100 (monoclonal, 1:150), CD68 (monoclonal, 1:200), CK (monoclonal, 1:250), STAT6 (monoclonal, ready-to-use), Bcl-2(monoclonal, ready-to-use), β-catenin (monoclonal, 1:200), and Ki-67 (monoclonal, 1:300). All antibodies were obtained from Maxin Biotech Co., Ltd. in China

4.1. Pathological Findings

In the pathological review, the partial gallbladder (basal part) measured 2.5 cm×2.5 cm×1.6 cm. The maximum wall thickness reached 10 mm, exhibiting a pale, gelatinous appearance. Microscopically (Figure 2), tumour cells infiltrated the entire wall of the gallbladder, displaying a spindle shape and arranged in fascicles and bundles. The tumour did not involve the serous membrane. There was partial necrosis and a low mitotic count [maximum 3⁄5mm2]. Immunohistochemical detection included CD117, DOG-1, CD34, Vimentin, S-100, SMA, desmin, CD68, ck, STAT6, Bcl-2, β-catinin and Ki-67. The tumour cells exhibited diffuse staining for CD117, DOG1, CD34, vimentin and SDHB (Figure 2). SMA and other markers tested negative. Ki-67 labelling index was approximately 1 per 100 cells, indicating a low proliferative index. The diagnosis of primary GIST of the gallbladder was established based on the criteria outlined in the existing literature for primary GIST of the gastrointestinal tract.

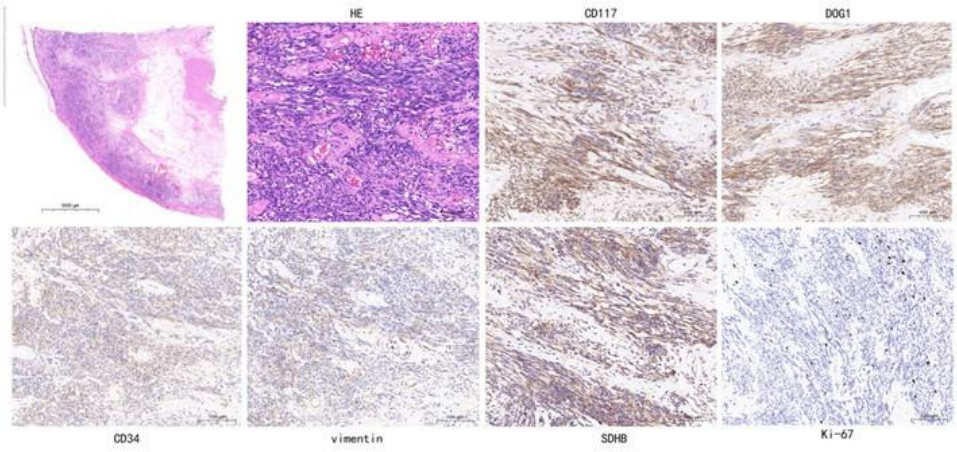

Figure 2: The wall of gallbladder is replaced by hypercellular spindle cells and partial necrosis (H&E, ×0.8). Spindle cells are interspersed with fascicle patterns (H&E, ×200). Tumour cells are stained diffusely for CD117, DOG1, CD34, vimentin and SDHB (Immunostain ×200). Ki-67 was in a low proliferative index, and the positive cells were mainly inflammatory cells (Immunostain ×200).

5. Discussion

GIST is a gastrointestinal tumour derived from stromal precursor cells (Cajal stromal cells). Cajal stromal cells are located in the connective tissue of the muscular layer of the digestive duct. These cells are also present in the subepithelial and muscular layers of the gallbladder [2]. This is the histological basis for gallbladder stromal tumour. GIST can occur in any part of the gastrointestinal tract, and it is common in the stomach and small intestine [4]. Primary gallbladder GIST is very rare. Since it was first reported in 2000, about 12 cases have been reported in the indexed literature [4,6-17]. This study presents a rare case of gallbladder GIST confirmed by histological and immunohistochemical analyses.

We summarize the reported cases [4,6-17], including the one we reported (Table 1). Gallbladder stromal tumours are reported across a broad age range, 25-79 years old, the median age is 62.58. Most cases were reported in women (92.3%). Clinically, symptoms were non-specific, with patients typically experiencing abdominal pain (75%), jaundice (33.3%), fever (33.3%), or other dyspeptic symptoms. Ultrasonography may reveal thickening of the gallbladder wall or irregular hypoechoic masses, whereas computed tomography (CT) imaging may reveal enhanced, heterogeneous soft tissue lesions near the gallbladder. In this case, ultrasound images suggested gallbladder adenomyosis and gallstones without characteristic changes. Imaging findings are lacking in abnormal manifestations, and it is difficult to distinguish biliary carcinoma, gallbladder adenomyosis, and other tumours.

The diagnosis mainly depends on pathological examination and immunohistochemical testing. Pathologically, the gallbladder stromal tumor typically varies in size from 0.5 to 7.5cm, with a firm or slightly gelatinous texture. Microscopically, the cell morphology was spindle cell, epithelioid cell, or mixed, mainly spindle cell (69.2%). Most cases showed mitotic images, and 54.5% of the cases more than 5 mitotic per 50 high-power fields. Necrosis is often present (60%), regardless of tumour size. Immunohistochemical staining is critical for diagnosis, and markers such as CD117, DOG-1, CD34, and vimentin are typically expressed. Negative staining for SMA and S-100 helps differentiate GIST from other mesenchymal tumours. Interestingly, one case was negative for CD117 and C-KIT genetic test but positive for a mutation in the PDGFRA gene [16]. This findings light the importance of molecular assays, including PDGFRA and C-KIT mutation testing, as complementary diagnostic tools for cases with unusual immunohistochemical profiles.

In conclusion, primary gallbladder GIST is an exceedingly rare entity with non-specific symptoms and imaging findings, that often pose significant challenges in clinical practice, leading to delayed diagnosis. Accurate diagnosis mainly relies on pathological and immunohistochemical analysis in clinical. Although surgical resection is the primary therapeutic approach, further research and case studies are crucial to improve understanding of its pathogenesis and optimal treatment strategies.

6. Acknowledgments

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Table 1: Demographic, Clinical, Histopathological, and Immunohistochemical Characteristics of Reported Cases (Including Present Case).

Feature Category	Characteristic	Value / Proportion (n/N)
Demographics	Median age (years)	62.6
	Age range (years)	25–79
	Female	12/13 (92.3%)
	Male	1/13 (7.7%)
Clinical Features	Abdominal pain	9/12 (75.0%)
	Jaundice	4/12 (33.3%)
	Fever	4/12 (33.3%)
Imaging Findings	Gallstones	6/13 (46.2%)
	Thickened wall	11/13 (84.6%)
	Spread	2/13 (15.4%)
	Polypoid lesion	1/13 (7.7%)
Histopathology	Tumor size (max diameter)	0.5–7.5 cm
	Cell morphology: Spindle	9/13 (69.2%)
	Cell morphology: Epithelioid	2/13 (15.4%)
	Cell morphology: Mixed	2/13 (15.4%)
	Mitosis (>5/50 HPF)	6/11 (54.5%)
	Necrosis	6/10 (60.0%)
Immunohistochemistry	CD117 positive	11/12 (91.7%)
	CD34 positive	4/10 (40.0%)
	Vimentin positive	7/7 (100%)
	Desmin positive	2/6 (33.3%)

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