Leiomyosarcoma of the gallbladder—A case report and a review of literature

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ABSTRACT

INTRODUCTION: Primary sarcomas of the gallbladder (GB) are a rare disease that were first described by Griffon and Segall in 1897. Leiomyosarcomas (LMS), as described in the case report at hand, are considered a major subgroup.

PRESENTATION OF CASE: A 62-year-old female was referred to our hospital with intermittent right upper quadrant pain. A 45 mm mass arising from the neck of the GB was diagnosed by ultrasound. No distant metastases were revealed. We successfully removed the GB and the surrounding liver tissue. We also performed a lymphadenectomy of the hepatoduodenal ligament. The histopathological and immunohistochemical examination revealed an R0 resected epithelioid LMS of the GB.

DISCUSSION: Our review of literature shows only 20 publications of LMS of the GB. The majority of the patients are female with an average age of 65.95 years. In a non-metastasized stage, a cholecystectomy with a wedge resection of the surrounding liver tissue, accompanied by a lymphadenectomy of the hepatoduodenal ligament, is described as a successful surgical approach.

CONCLUSION: The LMS should be taken under consideration when diagnosing a tumor of the GB.

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1. Introduction

Primary sarcomas of the gallbladder (GB) are a rare disease that were first described by Griffon and Segall in 1897 [1]. Women are more often affected than men. In the majority of published cases, primary sarcomas of the GB appear between the 6th and 7th decade of life [2,3]. Leiomyosarcomas (LMS), as described in the case report at hand, are considered a major subgroup [2–4].

The work has been reported in accordance with the SCARE criteria [5].

2. Presentation of case

A 62-year-old female was referred to our hospital due to intermittent right upper quadrant and epigastric pain for 7 days in 2015. Her medical history consisted of hypothyroidism and pyelonephritis. Her surgical history included an appendectomy. During the clinical examination a positive murphy sign was found. The laboratory tests demonstrated an elevated bilirubin, y-glutamyl transferase, alkaline phosphatase, and lipase. Additionally, the inflammatory markers were elevated. The patient underwent an abdominal ultrasound. An inflamed GB with multiple gallstones was detected. Moreover, a 45 mm mass arising from the neck of GB was found (Fig. 1). Therefore, we conducted an upper endoscopy. No choledocholithiasis was detected. The 45 mm sized tumours had a space-occupying effect on the stomach. The endosonography, MRI and abdominal CT scan did not show distant metastases (Figs. 1 and 2). The mass of unknown dignity showed a contrast agent uptake, but no signs of an infiltrative growth pattern. After a multidisciplinary discussion within our tumor board, the decision was made to remove the mass, with the suspicion of finding a malignant entity. Intraoperatively, neither liver metastases nor the infiltration of the omental fat were revealed. We resected the inflamed gallbladder, as well as the fossa. Additionally, we performed a lymphadenectomy of the hepatoduodenal ligament. The frozen section analysis of the excision margins of the cystic duct did not show any malignant cells.

2.1. Pathological findings

The histopathological examination diagnosed an R0 resected 40 mm smooth bounded spindle-shaped epithelioid tumor in a chronic inflamed GB. The liver tissue and lymph nodes did not contain malignant cells (Fig. 3, Picture 1).
**Fig. 1.** A 4.5 cm mass of the neck of the GB can be seen (marked with a star) on the left side. A gallstone is located next to the tumor. The MRI reveals a tumor marked by the black arrow.

**Fig. 2.** Case report timeline.

| Date       | Event                                                                 |
|------------|----------------------------------------------------------------------|
| October 2015 | The patient suffered from abdominal pain of the epigastrium and the right upper abdomen |
| November 2015 | Referring of the patient to our hospital                              |
| November 2015 | Radiological detection of a 45 mm sized tumour of unknown dignity arising from the gallbladder infundibulum with no distant metastasis |
| November 2015 | Explorative laparotomy with tumour removal and lymphadenectomy        |
| December 2015 | Histopathological and immunohistochemical diagnosis of a R0 resected epitheloid leiomyosarcoma of the gallbladder |

| Date       | Event                                                                 |
|------------|----------------------------------------------------------------------|
| July 2018  | No Radiological detection of a recurrence and metastasis            |

**Fig. 3.** Immunohistochemical detection of DOG1, Calponin and Caldesmon.
Table 1
Publications on Leiomyosarcoma (LMS) of the gallbladder.

| Author               | Year of publication | Gender | Age  | Location                  | Size cm          | Pathological findings | Treatment                                                                 | Outcome                  |
|----------------------|--------------------|--------|------|---------------------------|------------------|------------------------|---------------------------------------------------------------------------|--------------------------|
| Guo et al.           | 2016               | female | 41   | NR                         | 5 × 4.2 × 2.5    | Secondary              | CCE                                                                       | >30                      |
| Savilania et al.     | 2012               | female | 50   | Fundus and Corpus          | 5 × 4 × 3        | Primary                | CCE, Resection of liver segment IVb + V                                  | 12                       |
| Im et al.            | 2014               | male   | 82   | Corpus                     | 5.5              | Primary                | CCE, Hepatic wedge resection via laparotomy                              | NR                      |
| Park et al.          | 2012               | female | 54   | NR                         | 7 × 5.5          | Primary                | CCE, Resection of liver segment IVb + V, Omentectomy, small bowel segmental resection, lymphadenectomy ligamentum hepatoduodenale | 3                       |
| Sherine et al.       | 2010               | female | 50   | Fundus and Corpus and liver segment of IVb + V | NR              | Primary                | CCE                                                                       | NR                      |
| Al-Daraji et al.     | 2009               | female | 36   | NR                         | 3.0              | Primary                | CCE, Hepatic wedge resection via laparotomy                              | 20                       |
| Garcia et al.        | 2009               | male   | 79   | Fundus and Corpus          | 4.4              | Primary                | CT-guided percutaneous drainage due to abscess and cholecystitis         | < 1, DOD                 |
|                      |                    | female | 81   | NR                         | NR               | Primary                | Explorative Laparotomy with gastrojejunostomy and ileotransversostomy and biopsy of GB | < 1, DOD                 |
|                      |                    |        |      | Invasion of liver, duodenum | 4               | Primary                | Chemotherapy                                                             | NR                      |
|                      |                    |        |      | Invasion of liver, duodenum |                  | sPrimary               | CCE, Distal gastrectomy, Hepatectomy of the IVa, V, partial resection of transverse colon and duodenum | NR                      |
|                      |                    | female | 82   | NR                         | 2 × 2 × 1.5      | Primary                | CCE, Resection of liver segment                                           | > 24                     |
|                      |                    | female | 78   | Fundus with liver extension | NR              | Primary                | CCE, Lymphadenectomy                                                      | NR                      |
|                      |                    | female | 64   | NR                         | 7 × 5 × 2        | Primary                | CCE, Liver biopsy                                                        | > 21                     |
|                      |                    | female | 73   | NR                         | NR              | Primary                | CCE, wedge resection of the liver                                        | > 12                     |
|                      |                    | female | 56   | NR                         | NR              | Primary                | CCE                                                                       | 6; DOD                   |
|                      |                    | female | 72   | Liver and bowel infiltration | NR              | Primary                | CCE, wedge resection of the liver, resection of transverse colon and affected parietal peritoneum | < 2; DOD                 |
|                      |                    | female | 69   | NR                         | 6.5 × 6.2        | Primary                | Laparotomy with CCE                                                      | NR                      |
|                      |                    | female | 91   | Fundus                     | 2 cm             | Primary                | NR                                                                        | PMD                     |
|                      |                    | male   | 77   | NR                         | 8 cm             | Primary                | CCE                                                                       | NR                      |
|                      |                    | female | 72   | NR, metasta to liver and lung | NR              | Primary                | NR                                                                        | NR                      |

CT: Chemotherapy; CCE: Cholecystectomy; GB: Gallbladder; DOD: Death of disease; LMS: Leiomyosarcoma; NR: Not recorded; PMD: Post mortem diagnosed.
2.2. Immunohistochemical findings

The immunohistochemical examination revealed the expression of DOG1, Calponin and Caldesmon (Fig. 3, Picture II–III).

The postoperative course was uneventful. We discharged our patient 12 days after surgery.

As a follow-up approach, we decided to perform a CT scan every 6 months. No tumor recurrence or metastases were detected up to this day. Our patient remains alive and in good health.

3. Discussion

Primary sarcomas of the GB are a rare malignancy. The majority of these sarcomas are leiomyosarcomas. An incidence is estimated as 1.4 per 1000 malignancies of the GB [6,7].

To reveal further knowledge on epidemiology, therapy and outcome of patients with LMS of the GB, we reviewed the literature using the search terms “Sarcoma,” “Leiomyosarcoma,” and “Gallbladder”, with Google Scholar and PubMed. The search yielded 30 relevant publications [1,2,4,6–26]. We excluded publications without available abstracts or insufficient information regarding the patient’s medical history. 10 publications were excluded (Table 1). The articles’ publication dates range from 1982 to 2018. Among the 20 publications, the medical history of 24 patients who suffered from a LMS of the GB was reported. In 23 cases, the LMS occurred primarily in the GB. 18 patients were female, and 6 patients were male with an average age of 65.95 years. The diameter of the mass ranged between 2 and 8 cm. Egorov et al. published a case of a large LMS that weighed 1500 g [22]. In 4 cases, the LMS infiltrated the surrounding organs.

The diagnosis of a LMS is established in accordance with the World Health Organization classification for soft tissue tumors [3]. This tumor entity consists of cells showing distinct smooth muscle features. Macroscopically, the LMS forms a white and grey coloured fleshy mass. The microscopic pattern typically consists of intersecting, sharply margined groups of spindle cells. Usually, the LMS is immunohistochemically positive for desmin, h-caldesmon, and SMA. Immunostainings may be focally positive for CD34, epithelial membrane antigen (EMA), keratin, and S100 [3,10].

Patients who suffered from a LMS of the GB often present with abdominal pain, fever, jaundice, and weight loss [6]. In certain cases, as the one presented here, an acute or chronic cholecystitis, accompanied by cholelithiasis led to the diagnosis of a GB tumor. Predisposing factors regarding the pathogenesis of the LMS may be gallstones and chronic inflammation of the GB [6]. Our review revealed that the majority [13,24] of patients were referred to the hospital suffering from gallstones with an acute or chronic inflammation of the GB [1,2,7,11,12,14,15,17,19,20,23].

As a diagnostic approach, an ultrasound examination, a CT scan, as well as a PET–CT scan are recommended. The LMS may occur as a polypoid mass protruding into the lumen with an irregularly thickened wall. Nevertheless, the lack of specific radiological features makes the differentiation from an adenocarcinoma challenging [6].

Similar radiological, histological and immunohistochemical features make the adenocarcinoma, the rhabdomyosarcoma, the liposarcoma, the Kaposi sarcoma, and the angiosarcoma an important differential diagnosis to consider [12,13].

The therapy depends on the tumor extension. In a non-metastatic stage, the cholecystectomy combined with a wedge resection of the surrounding liver tissue, as well as a lymphadenectomy of the hepatoduodenal ligament seems to be a sufficient surgical approach [6,9,10,15,19,25]. Contrarily, Guo et al. and Perez-Montiel et al. treated a LMS of the GB by performing a solely cholecystectomy. Their patients survival rate was about 2 years [8,14]. Our review revealed that an extensive surgery was performed in cases of a local tumor invasion [1,10,13]. There is not sufficient evidence in the literature regarding the effectiveness of adjuvant chemo- or radiation therapy. However, some authors reported that chemotherapy with doxorubicin, mitomycin C may improve the long term survival following surgery [1,17,26].

The LMS of the GB has a very poor prognosis, particularly in a metastatic stage [1,17]. By removing the LMS in an early tumor stage, a long term survival for several years, as shown in our case report, has been described [8,14].

4. Conclusion

Particularly when diagnosing a tumor of the GB in elderly women, a leiomyosarcoma should be taken under consideration.

In a non-metastatic stage, the cholecystectomy with a wedge resection of the surrounding liver tissue, as well as a lymphadenectomy of the hepatoduodenal ligament is described as a sufficient surgical approach.

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Ethical approval

No ethical approval necessary.

Consent

I have obtained written consent for publication of this case report from the patient and I can provide this should the Editor ask to see it.

Author contribution

Dr. med. Christoph Paasch (corresponding author): Contribution to the paper: author, data collection, data analysis and interpretation, writing the paper.

Dr. med. Muharrem Salak (co-author): Contribution to the paper: surgical treatment of the patient.

PD Dr. med. Thomas Mairinger (co-author): Contribution to the paper: data analysis.

PD Dr. med. Franz Theissig (co-author): Contribution to the paper: Histopathological examination, interpretation of the histological pictures, immunohistochemically examination.

Registration of research studies

The case report at hand is not a first-in-man case report of a novel technology or surgical technique, therefore a registration of these case reports according to Declaration of Helsinki 2013 is not required.

Guarantor

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Declaration of Competing Interest

None.

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