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Case Report / Приказ болесника

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Follicular lymphoma originating from the gallbladder – case report and literature review

Фоликуларни лимфом пореклом из жучне кесе – приказ болесника и преглед литературе

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SUMMARY

Introduction Follicular lymphoma belongs to the group of indolent lymphoid neoplasms originating from mutated germinal center B cells, characterized by a nodular or follicular histological pattern of infiltration. Primary involvement of extranodal sites is rare. The aim of this study is to present the clinical, histological, and immunohistochemical features of a rare case of gallbladder follicular lymphoma, along with a literature review, highlighting key diagnostic and therapeutic considerations.

Case outline We present the case of a 60-year-old female patient who underwent laparoscopic cholecystectomy for ultrasound-confirmed gallbladder calculosis. Based on the morphological findings, supplemented by immunohistochemical analysis, the lesion identified in the tissue samples corresponded to follicular non-Hodgkin lymphoma.

Conclusion Gallbladder lymphoma is a rare malignancy often found incidentally. Diagnosis relies on histology and immunohistochemistry, which distinguish it from adenocarcinoma and other lymphomas. Accurate classification is essential for proper management and prognosis.

Keywords: follicular lymphoma; MALT; gallbladder; non-Hodgkin lymphoma; immunohistochemistry

САЖЕТАК

Увод Фоликуларни лимфом спада у групу индолентних лимфоидних неоплазми порекла мутираних Б ћелија герминалног центра са карактеристичним нодуларним или фоликуларним хистолошким типом инфилтрације. Примарно захватање екстранодалних локализација је ретко. Циљ рада је приказати клиничке, хистолошке и имунохистохемијске карактеристике ретког случаја фоликуларног лимфома жучне кесе, уз преглед литературе, са нагласком на кључне, дијагностичке и терапијске аспекте.

Приказ болесника Представљен је случај болеснице животне доби 60 година код које је ради ултразвучно верификоване калкулозе жучне кесе урађен оперативни захват лапароскопске холецистектомије. На основу морфолошког налаза употпуњеног имунохистохемијском анализом описана промена у добијеним исечцима одговара фоликуларном нехочкинском лимфому.

Закључак Лимфом жучне кесе је малигна болест која се често открива случајно. Дијагноза се заснива на хистологији и имунохистохемији, што га разликује од аденокарцинома и других лимфома. Прецизна класификација је неопходна за правилно лечење и прогнозу.

Кључне речи: фоликуларни лимфом; *MALT*; жучна кеса; нехочкински лимфом; имунохистохемија

INTRODUCTION

Follicular lymphoma is an indolent lymphoid neoplasm originating from mutated germinal center B-cells, characterized by a nodular or follicular histological pattern of infiltration [1]. The tumor is composed of a mixture of centrocytes and centroblasts (small cleaved follicular center cells and large non-cleaved follicular center cells) (Figure 1). Follicular lymphoma is the second most common subtype of all non-Hodgkin lymphomas (NHL) and the most common indolent lymphoma. It accounts for 20–25% of adult NHL cases in the United States, with an annual incidence of approximately 14,000 new cases. The median age at diagnosis is 59 years, and it is more common in women, with a female-to-male ratio of 1.7:1.0 [2]. The classic cytogenetic abnormality in follicular lymphoma is the translocation t(14;18)(q32;q21), resulting in juxtaposition of the *BCL-2* gene on chromosome 18q21 with the immunoglobulin heavy chain gene on chromosome 14 [3, 4]. Initial diagnostic workup includes a thorough

medical history, detailed physical examination, laboratory tests, lymph node biopsy, bone marrow aspiration and biopsy, and computed tomography (CT)[5]. In 2004, an international cooperative group proposed the Follicular Lymphoma International Prognostic Index (FLIPI) [6, 7]. The estimated five-year overall survival for patients with high FLIPI scores is approximately 50%. Patients with follicular lymphoma may be treated with mono- or polychemotherapy [8, 9]. The introduction of Rituximab has significantly altered the disease course.

CASE REPORT

The patient is a 60-year-old woman referred to a hematologist with a diagnosis of non-Hodgkin lymphoma. Because of interscapular pain accompanied by nausea and loss of appetite, and in the context of gallbladder cholelithiasis confirmed by ultrasound one month earlier, a laparoscopic cholecystectomy was performed. Upon review of the histopathology report (macroscopic description): The material submitted for pathological analysis consists of an opened gallbladder with emptied contents, measuring approximately 7.0 × 2.0 cm. The external surface is partially smooth and shiny, and partially torn. The internal surface is yellow-green and velvety. In the region of the gallbladder body, beneath the mucosa, there is a poorly demarcated thickening (lesion) measuring 2.5 × 1.3 cm, appearing whitish, solid, and shiny on the cut surface. Microscopic description: The histologically examined material consists of gallbladder tissue samples. In the sections taken from the macroscopically described lesion within the gallbladder wall, a lesion is present that is composed predominantly of a uniform lymphoid cell population. The lymphoid infiltrate is made up of small to medium-sized cells with oval nuclei, granular chromatin, and visible nucleoli. The cytoplasm is scant. Focally, lymphoid cells are also present within the surface epithelium and within glandular epithelium. The described histologic appearance in the gallbladder samples is consistent with non-Hodgkin lymphoma. The differential diagnosis of gallbladder lymphoma includes several lymphoma subtypes: follicular lymphoma, diffuse large B-cell lymphoma (DLBCL) and MALT lymphoma. Although they arise in the same organ, these different lymphoma types have distinct morphological and immunophenotypic profiles. Based on morphological findings and immunohistochemical analysis (LCA+, CD20+, CD10+, BCL2+, CK7-, Synaptophysin-) the changes observed in the tissue samples were consistent with follicular non-Hodgkin lymphoma of B-cell phenotype, low-grade. Assess the extent of disease, a full clinical, laboratory, and radiological evaluation was performed, as well as PET/CT to evaluate disease activity.

Laboratory findings revealed mild neutropenia, mild thrombocytopenia, hypoalbuminemia, with normal levels of LDH, uric acid, and beta-2 microglobulin. PET/CT findings: Right occipital lymph node with an axial diameter of 10 mm and increased uptake of 18F-FDG (SUVmax 7.21). In the right axilla, multiple lymph nodes with the largest measuring 11 mm and increased uptake (SUVmax 4.21). On the left inguinal side, multiple lymph nodes with diameters up to 11 mm and increased uptake (SUVmax up to 9.6). On the right inguinal side, multiple sub-centimeter lymph nodes with moderately increased uptake (SUVmax up to 2.76). Multiple foci of increased 18F-FDG uptake in almost all bones of the axial skeleton (SUVmax up to 23.46 in the body of the Th6 vertebra). Compression fractures of Th7 and Th8 were previously documented on CT. The patient was presented to the Multidisciplinary Team with a diagnosis of non-Hodgkin lymphoma (follicular grade I), clinical stage IV B, ECOG performance status: 0, FLIPI 1: 2 (intermediate risk), FLIPI 2: 1 (low risk), R-IPI: 2 (good prognostic index). The council recommended initiation of immunochemotherapy (ICT) following the R-CHOP protocol, for eight cycles.

The patient received eight cycles of ICT per the protocol. A follow-up CT of the thorax, abdomen, and pelvis was performed. No enlarged lymph nodes. Compression fractures of Th7, Th8, and Th9. Remission of the primary disease was confirmed. The patient was again presented to the Multidisciplinary Team, which recommended maintenance therapy with Rituximab every three months for two years. She received four cycles of maintenance therapy, which was then discontinued due to COVID-19 infection. Clinical and laboratory evaluation is conducted every 3 months, and radiological evaluation every 6 months.

Ethics: Written informed consent was obtained from the patient for publication of this case report. Approval of the ethics committee under number 01-19-515-2/25.

DISCUSSION

Primary extranodal involvement of follicular lymphoma is rare. In the domestic literature, there has not been a previously reported case of follicular lymphoma diagnosed by cholecystectomy. In 2003. Ferluga et al. [10] published and describing a 63-year-old woman with symptoms of biliary obstruction. Ultrasound raised suspicion of a Klatskin tumor. Based on histopathology and immunohistochemical analysis, the tumor was classified as extranodal follicular lymphoma, grade 2. This was the first reported case worldwide of extranodal follicular

lymphoma in this location. In this case the postoperative follow-up of more than 3 years has been completely uneventful without any symptoms or signs of disease recurrence. In 2004. Jelić et al. [11] published a case report describing an isolated primary extranodal lymphoma limited to the gallbladder in a 70-year-old woman with symptomatic cholelithiasis. According to the literature, the most common type of lymphoma in this location is MALT (mucosa-associated lymphoid tissue). However, this case demonstrated follicular lymphoma in an organ (gallbladder) that typically lacks lymphoid tissue. At that time it was sixteenth case described. In 2024. Nakagaki et al. [12] published an article reporting on a 70-year-old man with an ultrasound-verified polypoid lesion in the gallbladder without specific symptoms and no abnormalities in laboratory data. Histopathology with immunohistochemistry confirmed follicular lymphoma (CD10+, CD20+, bcl2+, CD23+). This case report illustrates how difficult it can be to diagnose follicular lymphoma originating from gallbladder. In 2025. Mikayla et al. [13] presented an 82-year-old male with acute abdominal pain. Computed tomography, ultrasound, and magnetic resonance imaging, detected a suspicious gallbladder mass and regional lymphadenopathy. Fine needle biopsy and immunophenotyping confirmed a diagnosis of follicular lymphoma. Toshikatsu et al. [14] presented 71-year-old Japanese woman with a gallbladder polyp detected on ultrasound in 2024. Pathology revealed aggressive follicular lymphoma of the liver and gallbladder. Immunohistochemical staining was positive for CD10, CD20, CD23, CD79a, BCL-2, and BCL-6. Nishida et al. [15] presenting male patient in his 70s. During follow up, a gallbladder tumor was detected on CT scans. Immunohistochical staining demonstrated that lymphocytes were positive for CD10, CD20, and bcl-2. The final pathological diagnosis was primary follicular lymphoma of the gallbladder.

Gallbladder lymphoma is a rare malignancy, most often discovered incidentally after cholecystectomy. Clinically and radiologically, it can mimic benign conditions or adenocarcinoma, making histological and immunohistochemical analysis essential for diagnosis. The differential diagnosis includes follicular lymphoma, MALT lymphoma, and diffuse large B-cell lymphoma, each distinguishable by morphology and immunophenotype. Timely recognition and accurate classification of the lymphoma are crucial for guiding appropriate management and prognosis. Future research should focus on optimizing diagnostic techniques, refining therapeutic strategies, and conducting longer-term follow-up studies to better assess patient outcomes in such a rare disease. This case highlights the need for heightened clinical suspicion and comprehensive evaluation in atypical presentations of extranodal lymphoma.

Conflict of interest: None declared.

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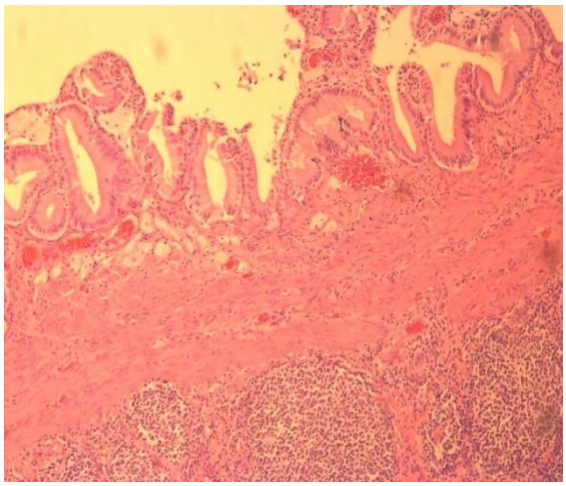

Figure 1. Follicular lymphoma of the gallblader (H&E; × 10)

