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Rosai–Dorfman disease involving gallbladder and liver—Report of a case

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ABSTRACT

INTRODUCTION: Rosai–Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic disorder of unclear etiology. Lymphadenopathy commonly affects the lymph nodes of the neck and the head, but extranodal involvement has been observed too.

PRESENTATION OF CASE: We describe an unusual case of RDD with involvement of the gallbladder, liver and cystic lymph node, clinically manifested as an exacerbated cholecystitis. The patient underwent a cholecystectomy with atypical liver resection because the finding was macroscopically suspected of gallbladder cancer. The diagnosis of RDD was confirmed by immunohistochemical study.

DISCUSSION: Histological features of RDD include histiocytic proliferation, emperipolesis and positive immunostaining for S-100 protein and typically negative for CD1a. Gastrointestinal localization of RDD, especially in the liver and pancreas, is extremely rare. Typically, the liver is affected as a part of systematic spread of RDD. We have not found reports for involvement of the gallbladder.

CONCLUSION: The presented case is valuable due to its rarity and difficulty in differential diagnosis.

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1. Introduction

Rosai–Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic disorder of unclear etiology [1,3,4]. It was described for the first time by Destombes in 1965 [1], but Rosai and Dorfman determined it as a distinct clinicopathological disorder in 1969 [2]. Histological features of RDD include histiocytic proliferation, emperipolesis and positive immunostaining for S-100 protein and typically negative for CD1a [2–4]. RDD usually presents as a painless, massive, bilateral enlargement of the neck lymph nodes, often combined with fever and leukocytosis [3]. Lymphadenopathy more frequently affects the lymph nodes of the neck and the head, but extranodal involvement has been observed too. The most common extranodal sites are the skin, upper respiratory tract and soft-tissue. Involvement of central nervous system, kidney, breast, thyroid gland and testis has been also reported [3,4]. Gastrointestinal localization of RDD, especially in the liver and pancreas, is extremely rare [3–6].

Abbreviations: RDD, Rosai–Dorfman disease; CT, computer tomography; H&E, hematoxylin and eosin.

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We have not found reports for involvement of the gallbladder. We describe a rare case of RDD presented with tumor mass involved the cystic lymph node, gallbladder and liver and clinically mimicking the exacerbated cholecystitis.

2. Presentation of case

A 58-year-old female patient presented with intermittent complaints including pain in right upper abdominal quadrant, nausea, vomiting and fever for approximately 3 years. The symptoms had started after consuming high-fat and spicy food. Previous ultrasound imaging revealed gallbladder stones. So the patient was admitted to our clinic for surgical treatment. The last symptomatic episode was 3 months before hospitalization. The physical examination demonstrated an afebrile patient with mild abdominal pain in the right hypochondrium and negative Murphy's symptom. No lymphadenopathy was noted. Results from laboratory tests were in reference values, excluding the white blood cell count – $10,89 \times 10^9$ cells/L (reference $3,5\text{--}10,5 \times 10^9$ cells/L). The ultrasound investigation revealed liver steatosis and a folded gallbladder with thickened walls, blurred outlines and presence of small stones in the lumen (Fig. 1).

On the basis of a presumptive clinical diagnosis of exacerbated cholecystitis with gallstones the patient underwent surgical treat-

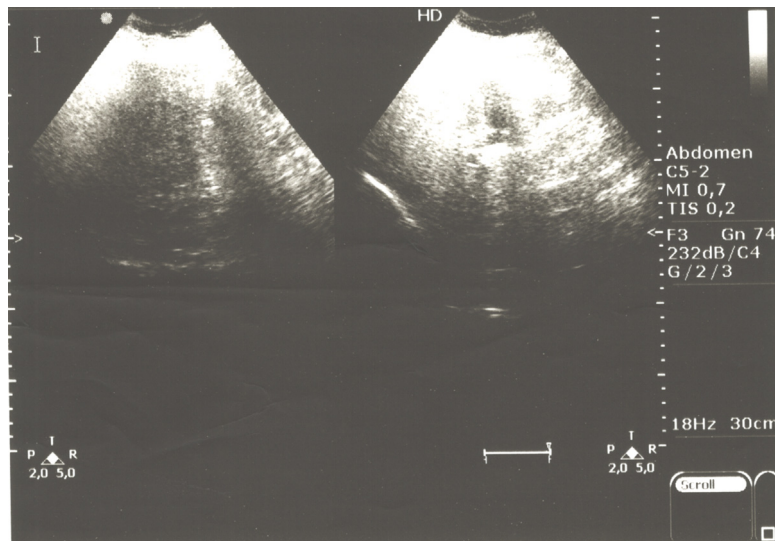


Fig. 1. Preoperative ultrasound image of the liver/gallbladder of the patient.

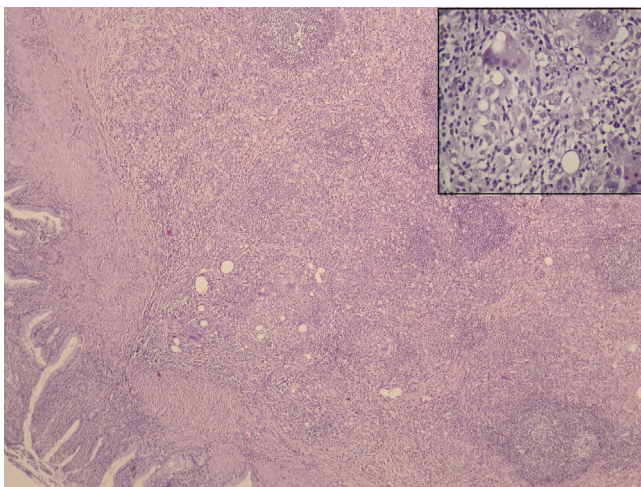


Fig. 2. Tumor mass involving cystic lymph node and the gallbladder (H&E,10×) Inset (upper right H&E, 20×) – histiocytes with emperipolesis; H&E=hematoxylin and eosin.

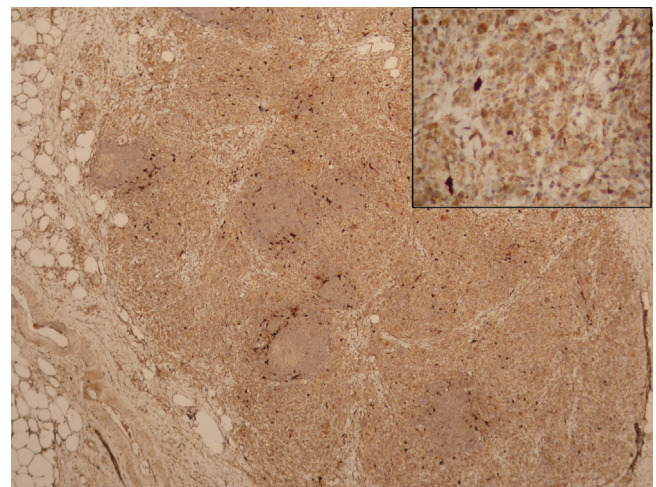


Fig. 3. Lymph node; strong immunoreactivity of histiocytes for S-100 protein; inset (upper right, 10×).

ment. The intraoperative exploration revealed severe adhesions surrounding the gallbladder, which was with almost intrahepatic location, thickened walls and palpable small stones inside it. The wall of the gallbladder in the infundibular part was extremely thickened and ocher colored. Because of the suspected gallbladder cancer we performed a cholecystectomy with atypical liver resection of IVth and Vth liver segments in macroscopically negative margins. The express histological examination rejected the malignant diagnosis. The permanent histological examination revealed Rosai–Dorfman disease with involvement of cystic lymph node, which lied in the angle formed by the cystic and common hepatic ducts (Mascagni’s lymph node), pericyclic tissues, liver and gallbladder (Fig. 2). Immunohistochemical labeling of the histiocytes for S-100 protein was positive (Fig. 3) and negative for CD1a. The microscopic resection margins were negative.

Postoperative period was uneventful. Because of the histological findings we performed a full CT scan of the patient – there were no enlarged lymph nodes or lesions in other organs. One year after the operation the patient was in good health without clinical, ultrasound and CT imaging data for recurrent disease.

3. Discussion

Rosai–Dorfman disease is a rare disorder characterized by emperipolesis (lymphocytic penetration of and movement into the histiocyte), massive sinusoidal dilatation in affected lymph nodes containing histiocytes with an abundant pale eosinophilic cytoplasm, lymphocytes and plasma cells [2–4,7]. Immunohistochemically RDD histiocytes are positive for S100 and are typically negative for CD1a [3].

Etiology of the disease is still unclear and controversial. Some studies have demonstrated that pathogenesis of RDD is related to viral infections, such as human herpesvirus (HHV), parvovirus B19, and Epstein–Barr virus (EBV) [3,4,8]. However, other studies have not confirmed these results [3,9]. RDD has been reported in patients with immunoglobulin (Ig) G4-related disease, but there is no clear evidence that these disorders have a common etiopathogenesis [3,4,10].

Commonly, RDD occurs during the first or second decade of life, but any age group can be affected [8]. African Americans are more frequently affected [2,3,8]. Lymphadenopathy usually affects the lymph nodes of the neck and the head. Extranodal involvement by RDD was initially thought to be uncommon, but some recent

reports suggest that it may be present in up to 40% of cases [3,11]. Gastrointestinal localization of RDD, especially in the liver and pancreas, is extremely rare [3–6]. Typically, the liver is affected as a part of systematic spread of RDD with nodal and wide extranodal involvement, like the 5 cases reported by Lauwers et al. [6,7]. Di Tommaso et al. presented a case of RDD exclusively involved the liver, but in several foci and the disease was synchronous with non-Hodgkin lymphoma [6]. We have not found any reports for RDD with isolated affection of the gallbladder. Our case is unusual, because RDD was limited in cystic lymph node, the surrounding liver parenchyma and the gallbladder, and manifested by the clinical picture of exacerbated cholecystitis.

The differential diagnosis of RDD in this specific case is with other rare histiocytic diseases involving the liver and gallbladder cancer. Microscopically, there are no difficulties RDD and gallbladder cancer to be distinguished. In regards to Langerhans' cell histiocytosis, it is a systematic disease with proliferation of positive to S100, CD1a and langerin histiocytes combined with an intense inflammatory infiltrate [4,6]. The phenomenon of emperipolesis is not observed [4,6]. Xanthogranulomatosis also can be mistaken with RDD because of the the accumulation of lipid-laden, foamy histiocytes, but they are S100 negative [4,6]. It should also be noted that focal RDD-like changes can sometimes be seen in lymph nodes involved by other processes, such as Hodgkin's or non-Hodgkin's lymphoma [15].

Treatment for the RDD is recommended only in patients who are symptomatic or have vital organ or systemic involvement [3]. Sometimes, in 20% of cases the disease is self-limited and shows spontaneous regression [3,12]. Complete surgical resection, like in our case, is the best option for treatment of the localized RDD [3]. In symptomatic cases of extensive RDD steroids are the first-line therapeutic option [3]. Radiotherapy can be used in cases with orbital, airway, and central nervous system involvement but till now no guidelines have been established for that management [3,13]. In cases of disseminated RDD or those refractory to surgery or other modalities, chemotherapy has been used with varying degrees of success [3,14].

4. Conclusion

We have presented a unique case of RDD presenting as a mass involving cystic lymph node, gallbladder and the surrounding liver parenchyma and clinically mimicking the exacerbated cholecystitis. This case is valuable due to its rarity and difficulty in differential diagnosis.

Conflicts of interest

The authors declare that they have no conflicts of interest to disclose.

Funding

None.

Ethical approval

The patient's approval has been given for this case report.

Consent

An informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

written consent is available for review by the Editor-in-Chief of this Journal on request".

Author contribution

Elena Arabadzhieva wrote the paper. Dimitar Bulanov collected the literature for the review in the report. Sasho Bonev analysed the review. Atanas Yonkov and Ivanka Taneva performed the operation of the patient described in this report. Tatyana Pirdopska performed the histological examination. Ivan Terziev carried out the immunohistochemical study and confirmed the diagnosis. Violeta Dimitrova revised the manuscript for important intellectual content and technical details. All authors have read and approved the final manuscript.

Research registry

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Guarantor

Violeta Dimitrova, MD, PhD, DMSc and Atanas Yonkov, MD, PhD would be the guarantors.

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