

Reviewer I

Abstract

1. I think there is too much detailed information in the abstract. My suggestion would be to shorten it. For example the place of the cyst (liver segments IV, V, VIII) is not so important that it needs to be mentioned in the abstract.

We thank the reviewer for this point and revised and shortened the abstract accordingly.

2. The end of the abstract concludes with a remark that pericystectomy should be performed, when? Under what circumstances? Is this the only treatment option? Or is liver resection also still a treatment nowadays? What about recurrence rate? May be the authors should mention something about the treatment options in the text and/or even add the given treatments of patients in the other case reports to table 1.

We included the medical treatment in the discussion of our manuscript. But since it is not a cure and carries the risk of severe side effects along with the long-term dependence on drugs, we do not recommend this treatment. It may be an option if, as in the case described by Inal et al, the patient refuses definitive operative therapy.

3. In the immunostaining an ... is German-English, please rephrase

We rephrased the sentence and hope it is more to the reviewers liking.

Core Tip

1. I think this paragraph provides us with several good arguments why this issue is interesting. I am left with the question why this case report and review is unique in comparison to the other 17 case reports.

As we are quite happy with the core tip, we did not change it and hope the reviewer will excuse this. We did, however, change the abstract and discussion to highlight the fact that in this case, even though the patient did receive three invasive procedures prior to surgery, no histological samples were retrieved. Thus the diagnosis of intrahepatic endometriosis was not reached until after the operation. This seems particularly important, since performing a pericystectomy earlier would have shortened the suffering of the patient considerably. We hope that we can raise awareness of this rare disease with our case report.

Introduction

1. The reference provided for prevalence of endometriosis in the first sentence is probably incorrect. Reference no. 1 does not describe any prevalence numbers.

2. Even if there were prevalence numbers in this first reference I would think there are more up to date epidemiological data about endometriosis, the article is from 1997. My advice would be to search for an accurate & up to date number, may be the prevalence has changed over the years?

We changed the reference and choose a recent New England Journal publication. We hope this is more to the reviewers` liking. Yet the prevalence of endometriosis, as assessed by the few epidemiologic studies available, still remains between 6 and 10% of women of reproductive age.

3. The authors give the prevalence in women of reproductive age, however you write that 6 of 17 patients were postmenopausal. Are the authors to give us some data on prevalence of endometriosis in postmenopausal women as well?

Haas et al found in a retrospective epidemiological study that 2.5% of postmenopausal women suffer from endometriosis. The number is even higher if one includes the group of "perimenopausal" patients, which includes patients 45-55 years of age in this study (prevalence is 17.1% in this group). We did update the manuscript accordingly.

4. I am not sure if starting the introduction with the importance of endometriosis is a logical start in a Journal with a GI focus. In my opinion it would be better to start with the definition

of endometriosis and then write something about the fact that intrahepatic endometriosis is a rare form of endometriosis.

We thank the reviewer for his valued opinion. Yet in order not to stress the limited space we decided not to elaborate on the basics of endometriosis. We are sure the interested reader will be able to follow our case report without this information.

Case Report

1. I would suggest to rewrite the first sentence because it should be formulated differently. Typographical error 1st line: “thirty-two year old” should be “A thirty-two year old” and if you read the sentence it feels like it is unfinished.

2. Typographical error 7th line: “ERPC” should be “ERCP”

3. Please mention Endoscopic Retrograde Cholangio Pancreaticography prior to the abbreviation (ERCP) the first time.

4. 13th line: ‘We could detect no further abnormalities during the operation’, my suggestion would be to write “We could not detect any other abnormalities during the operation” or “During the operation no other abnormalities were detected”

5. 18th line: I would suggest to combine the last two sentences. For example: “origin of the cyst and so the diagnosis of an intrahepatic endometriosis was confirmed”

Again, we thank the reviewer for his suggestions. We have changed the manuscript accordingly.

6. Tumor markers are normal. What about CA 125? Did you measure it? Literature about endometriosis mentions that it is often high although it is not a sensitive indicator of endometriosis.

Only the mentioned tumor markers were measured.

Discussion

1. The authors start the discussion with the difficulty of diagnosing hepatic endometriosis. I think it is worth mentioning which other diagnosis had been considered in this context (differential diagnosis).

Since the cyst seemed refractory to drainage and did not seem to invade any surrounding tissues, along with negative tumor markers and no apparent metastasis, we did not suspect it to be of malignant origin. The serology showed no signs of an echinococcal disease, yet we did consider this a major DD.

Reviewer II

Dear Editor: I have read with interest the manuscript entitled "Intrahepatic Endometriosis as Differential Diagnosis of Hepatic Cysts - Case Report and Review of Literature".

It is a very interesting manuscript for the readers of WJG. It can be accepted for publication after minor review.

Minor problems:

Is there any explanation for the lack of sample during two laparoscopic de-roofing surgery?

Sadly, no histology was obtained prior to the operation. The drainage and de-roofing did not occur in our hospital, so we can only speculate why no samples were obtained. Maybe at this point, the focus was on an infectious genesis of the cyst and only microbiological samples were obtained.

Can the MRI characteristic of the cyst be better described? Is there any differential diagnosis in the MRI image with other hepatic tumor and cyst? For example: early vs late peripheral nodular enhancement? Early arterial enhancement with rapid loss of enhancement and return to isointensity with the surrounding liver? Is the rapid loss of enhancement in the portal

venous phase? Delayed fill-in the center?

MRI demonstrated a well defined lobulated cystic lesion without enhancement after administration of liver-specific contrast material (gadoteric acid) in the arterial, venous or delayed phase. Particularly, no nodular enhancement was observed. So we did not include haemangioma in our differential diagnoses

In the Table 1 Inal M case no operation should be changed to no.

Thank you for this point, we changed the table accordingly.

Reviewer III

Major points to be taken:

1. There seemed to be more than 17 English publications currently online reporting clinical cases toward hepatic endometriosis, e.g.;

Ferdico Roesch-Dietlen et al., Hepatic Endometriosis, Annals of Hepatology, 2011

Roesch-Dietlen et al describe a case of extraparenchymal endometriosis, while we focus on intraparenchymal hepatic endometriosis. We did not include this work in the present manuscript.

Reid GD et al., Hepatic endometriosis: A case report and review of the literature, Australian and New Zealand Journal of Obstetrics and Gynaecology, 2003

Thank you for pointing out this interesting article, we did include it in our manuscript.

Nezhat C et al., Laparoscopic management of hepatic endometriosis: Report of two cases and review of the literature, The Journal of Minimally Invasive Gynecology, June 2005

Again, the authors describe two cases of extraparenchymal hepatic endometriosis. Since the peritoneal surface of the liver is easily accessible for endometrioma cells once they reach the peritoneal cavity, this form of extragonadal endometriosis is more frequent than intraparenchymal hepatic endometriosis.

2. As the author mentioned only one of the publication presented with cyclical pain in the upper right abdominal quadrant accompanying menstruation, this is not so certain – as Ferdico RD's finding also shown this.

Roesch-Dietlen et al do not describe a case of intraparenchymal endometriosis, but a case of endometriosis on the surface of the liver.

3. The positive result of the combination staining of CK7, progesterone and estrogen can also mean the presence of endometroid tumors, not just for defining epithelial cells only (ref: Zhao C et al., Am J Surg Pathol. 2007 Feb;31(2):255-66.)

We agree with you on this issue and included the information that no atypical cells were observed in the histology, thus the diagnosis of benign intrahepatic endometriosis was reached.

Minor correction needed:

1. In Table 1: Please add et al. followed by the author's name.

2. In Table 1: Misspelling of an author's surname to cause anonymity: should be Finkel L not Finke L.

Thank you again for attentively reading our manuscript and providing theses valuable points. We changed the table to your specifications.