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# A Synchronous Occurrence of Hepatocellular Carcinoma and Echinoccocal Liver Cyst – Can Parasite Promote Carcinogenesis? Literature Review and Classification Proposal

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**Rezumat**

***Prezența sincronă a carcinomului hepatocelular și a hidatidozei hepatice – Poate prezența paraziților să influențeze carcinogeneza? Revizuirea literaturii și propunerea unei clasificări***

Prezența concomitentă a unui chist hidatic și a carcinomului hepatic este un scenariu clinic foarte rar, în mod special la nivelul unui ficat anterior sănătos. Incluzând cazul raportat de noi, există 12 cazuri de prezență sincronă a carcinomului hepatocelular și a unui chist hidatic raportate în literatură, 3 dintre acestea la pacienți fără patologie hepatică anterioară. Oferim o analiză detaliată a tuturor cazurilor raportate până acum, precum și informații importante adiționale cu privire la etiologia, patogeneza, diagnosticul, tratamentul și rezultatele clinice ale acestora, atât în cazul carcinomului hepatocelular, cât și al echinococozei. Deși afectează un număr mic de pacienți, relația posibilă dintre cele două leziuni hepatice ar trebui investigată și o clasificare standardizată ar trebui stabilită. Acestea ne-ar ajuta să înțelegem natura carcinogenezei hepatice, să identificăm caracteristicile diagnostice ale leziunilor hepatice și să alegem tipul de tratament adecvat.

**Cuvinte cheie:** carcinom hepatocelular, chist hidatic, ficat, chirurgie

**Abstract**

Concomitant presence of hydatid cyst and hepatocellular carcinoma is a very rare clinical scenario especially in a previously non-diseased liver. Including our case here reported, there are 12 cases of synchronous HCC and hydatid cyst found in the scientific literature and 3 of them were found in a patient with non-diseased liver. We provide detailed review of all reported cases with additional highlights on etiology, pathogenesis, diagnosis, treatment and outcomes of both HCC and echinococcal disease. Although there is a small number of patients, possible relation between these 2 liver lesions should be investigated and standardized classification should be established. This will help us to understand the nature of HCC carcinogenesis, identify diagnostic features of liver lesions and choose the most appropriate type of treatment.

**Key words:** HCC, hydatid cyst, liver, surgery

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## Introduction

Hepatocellular carcinoma (HCC) is the most frequent primary malignant tumor of the liver, but with relatively low incidence of about 4-5 cases per 100,000. However, the incidence is constantly rising throughout the world. (1,2) Echinococcal cyst is a rare parasitic focal liver disease, especially in Western countries, while higher incidence is seen in some endemic areas such as in the Mediterranean, Baltics, Middle and Far East, South America. (3,4) Therefore, a concomitant cyst and HCC is an extremely rare clinical scenario especially in a non-diseased liver.

In most cases (85-90%) HCC occurs in cirrhotic livers due to viral hepatitis, alcoholism or other diffuse liver diseases while in only 10-15% of cases it occurs in non-cirrhotic liver (NCL).

The etiology of HCC in non-cirrhotic liver is still questionable, but recent studies showed that it is likely related to the metabolic syndrome and with alcohol intake. Epidemiological studies found that HCC in NCL are found predominantly in females (65%) and older aged patients (> 65). (5)

The only possible curative therapy for HCC is radical surgical resection or liver transplantation. Adjuvant or neoadjuvant chemotherapy has been used in some cases depending on the stage and grade of the tumor, but generally has limited and palliative role in the treatment. (6)

In humans, there are two main types of Echinococcal disease, cystic echinococcosis which is more common and caused by Echinococcus granulosus and the less frequent alveolar echinococcosis, caused by Echinococcus alveolaris.

In adults the liver is most commonly involved site of the infection (70%) followed by the lungs in 20–30% of cases. The incubation period of cystic echinococcosis (hydatid cyst) may be from several years to even 30 years, while many cases remain asymptomatic for lifetime. Other manifestations in the brain, spleen, kidneys or heart are rare in cystic echinoccocosis and bit more frequent in alveolar types. (7)

In some cases hydatid cysts are not easily differentiated from other focal liver lesions such as liver abscesses or benign and malignant liver tumors. In endemic areas, cavitary tuberculosis and mycoses should be considered as a differential diagnosis as well. In unclear cases, beside ultrasound and CT-scan, it is recommended to do a MRI scan which is a highly sensitive diagnostic tool which can reveal specific radiologic features of hydatid cysts and HCC. (8)

However, scenarios, where tumors and cyst are found as a single lesion, may still present a diagnostic challenge. If synchronous HCC and hydatid cyst occur as a single lesion, then it is very important to detect both pathologies since further treatment and prognosis depends on the right diagnosis.

Signs and symptoms of hydatid cyst are nonspecific and may include hepatomegaly, a palpable mass in the right upper quadrant, right epigastric pain, nausea, and vomiting, unexplained intermittent fever, systemic lymph node enlargement. Jaundice is less frequently reported in cases where cysts compress extrahepatic bile ducts. Rupture may occur, usually in larger cysts (> 10 cm) and it results in allergic manifestations. Nonspecific symptoms are a reason why liver echinococcosis may closely mimic cirrhosis or hepatic tumors and therefore imaging tests should help differentiate these 2 lesions. (4,9) The standard CT image of an echinococcosis infection shows a solid tumor with central necrotic areas and surrounding calcifications. Serologic test results usually confirm the infection. (10)

For simple cases of cystic echinococcosis, the preferred form of treatment is open surgical removal of the cysts combined with chemotherapy using albendazole and/or mebendazole 1 month prior to surgery. The benefit of post-surgical antihelmintic treatment is still debatable, but it is not routinely used if the cyst is removed completely.

Less commonly, segmental or major liver resection is required. It is clear that synchronous HCC necessitates more extensive liver resections, hepatectomies, extended hepatectomies or even liver transplantation.

Rarely, if there are cysts in multiple organs or tissues, or the cysts are in surgical risky locations, the condition may be inoperable and chemotherapy and/or percutaneous aspiration are the second choice of treatment.

Open surgery remains the standard for cystic echinococcosis treatment, but recent studies suggest that percutaneous alcohol injection or percutaneous thermal ablation with chemotherapy may be more effective than surgery in terms of disease recurrence, and morbidity and mortality. In inoperable cases, chemotherapy with antihelmintic therapy is used. (11)

### *Literature review*

For the purpose of this review, we searched the electronic database PubMed to identify all relevant studies. There are 12 reported cases of concomitant HCC and echinoccocal cysts in scientific literature and 7 of them had sufficient data for review analysis. In only two describe patients, this pathology was present without underlying liver disease or viral hepatitis (*Table 1* and *Table 2*). (12-18) A case of focal nodular hyperplasia and concomitant hydatid cyst was reported, but it was not included in our analysis.19 Considering the low incidence rates for both these diseases, such rarity is not surprising, however, some authors suggest the possible relation between echinoccocal cyst and HCC development especially in patients where no underlying liver disease is present.

Of 7 reported cases in the PubMed database, 4 patients were male and 3 were female. Patients were aged 27-74, averagely 62. In 5/7 (70%) of reported cases there was underlying liver disease (cirrhosis) caused by chronic viral infection. Only one patient had the alveolar cyst, while 6 other had cystic type of echinococcus. In 2 cases chronic viral B hepatitis was reported, in one case concomitant B and C virus and in one case chronic delta virus infection and alcoholism were identified as a cause of liver cirrhosis. In all patients, ultrasound and CT scans were performed, while 3 patients underwent additional MRI scan because of unclear diagnosis. In one patient, positron emission tomography-computed tomography (PET/CT) scan was performed. In 3 patients, cyst and HCC were found in the liver as a single lesion. In 4 cases both a hydatid cyst and HCC were

***Table 1.*** *Showing demographic features and underlying liver disease*

| Author | Age | Sex | Cirrhosis | Viral Hepatitis | Symptoms | Alcoholism | Imaging test |
|---|---|---|---|---|---|---|---|
| Kóbeck M et al | 45 | m | no | no | Weight loss, fever | no | CT |
| Kato T et al | | | | | | | |
| 76 | f | yes | Yes, B | Abdominal pain, weight loss | no | CT, MRI | |
| Kostov D et al | 64 | f | yes | Yes, B | Weight loss, abdominal pain | no | CT, MRI |
| Sevdegul K et al | | | | | | | |
| | 64 | m | yes | Yes, delta | Nausea,weight loss | yes | CT |
| Li H et al | | | | | | | |
| | 27 | f | no | no | Abdominal pain | unknown | PET CT |
| Zold et al | 66 | m | yes | unknown | Abdominal pain | unknown | unknown |
| Chien L et al | 61 | m | yes | Yes, B and C | Weight loss | - | CT, MRI |
| Our case | 65 | f | no | no | Weight loss, fever | no | CT, MRI |

***Table 2.*** *Showing features of lesions, treatment method and outcome*

| Author | Type | Single Lesion | Location | Cyst size (cm) | HCC size (cm) | Treatment method | Outcome |
|---|---|---|---|---|---|---|---|
| Kóbeck M et al | Cystic | yes | Right lobe | 6 | 3.7 | Liver resection | Recurrence within 6 months |
| Kato T et al | Alveolar | no | Right lobe (both) | 9.2 | 4.4 | Antihelmintic + liver resection | Unknown |
| Kostov D et al | Cystic | yes | Left lobe extending to 4. segment | 10.1 | 4.6 | Liver resection + mebendazole | Unknown |
| Sevdegul K et al | Cystic | no | Cyst in left, HCC in right lobe | 14.7 | 6.5 | Albendazole + sorafenib | Death within 3 months |
| Li H et al | Cystic | | Cyst in the right, HCC in the left lobe | 9.3 | Unknown | Albendazole, removal of the cyst, chemotherapy | Death after 1 year |
| Zold et al | Cystic | | Unknown | 6.7 | Unknown | Unknown | Unknown |
| Chien L et al | Cystic | no | Right lobe (both) | 9 | 5 | Liver resection | Unknown |
| Our case | Cystic | no | Right lobe (both) | 9.2 | 11 | Mebendazole + liver resection | No recurrence in a 1 year |

found to be in the right lobe, in 1 case the left lobe was involved and in one case, the cyst was in the left lobe and the HCC was in the right one. The average size of the cyst was 9.6 cm, and 5.6 cm for HCC. Only in one case, HCC was larger than the cyst at the time of diagnosis.

All patients had history of weight loss, 3 of them had abdominal pain, and two of them had fever of unknown origin as an initial symptom. Jaundice was not reported in any case as the initial symptom of the disease.

Four patients were treated with anthelmintic therapy with mebendazole or albendazole followed by surgical resection. In one patient, 2 weeks after beginning of anthelmintic therapy, needle aspiration of echinococcal cyst was performed prior to surgical procedure. One patient was treated with anthelmintic and chemotherapy only since HCC was considered inoperable, this patient died within 3 months after starting treatment. One patient underwent palliative intraarterial chemotherapy for HCC after cyst removal. This patient died for metastases of hepatic carcinoma after one year. In one patient, recurrence of HCC was found 5 months after surgical resection, for the other 4 patients, there was no data about long-term outcome, but in these cases, surgical resection was described as to be curative.

## *Case presentation*

A 65 years old women presented with a history of abdominal pain persisting for 4 months, weight loss, excessive swelling and intermittent-moderate (38-39) grade fevers. Pain was mostly located in the upper right abdominal quadrant. The patient also had enlarged cervical lymph nodes for 1 year of unknown cause. Abdominal computed tomography (CT) scan and magnetic resonance (MRI) scan were done which showed an expansive liver lesion involving the entire $6^{th}$, $7^{th}$, and partially $8^{th}$ liver segment measuring 9.5 x 7.3 cm with star like middle lesions which were of low T1 intensity and was suspicious of focal nodular hyperplasia. Also, in the eighth liver segment, an elongated, septated and calcificated liver lesion measuring 11 x 4 cm was found which was suspicious of an echinococcal cyst (*Fig. 1*). These 2 lesions were not in contact. There was no sign of liver cirrhosis on CT scan. Laboratory findings showed elevated liver enzymes, eosinophilia and alpha-fetal protein of 512 ng/L. Serology for echinococcosis was positive. Viral hepatitis markers were all negative, there was no history of alcoholism, congenital or autoimmune liver diseases.

After a 4 week course of albendazole, a liver resection was

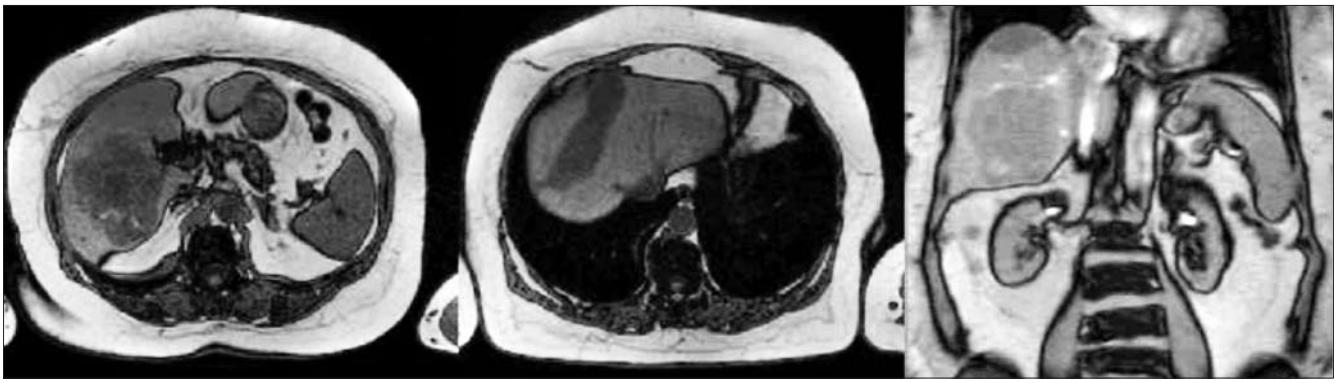

***Figure 1.*** *MRI images showing expansive liver lesion involving whole 6th, 7th, and partially 8th liver segment measuring 9.5 x 7.3 cm with star like middle lesion with low T1 intensity; an elongated, septated and calcified liver lesion measuring 11 x 4 cm in eighth liver segment. Image of the resected right liver lobe*

indicated. Intraoperatively, there was a tumor infiltrating segment 8 and cystic lesions in the 6th and 7th segment as was described on prior imaging tests. No signs of extrahepatic disease or diffuse liver disease were found so a right hepatectomy was performed. Pathohistological analysis confirmed an echinococcal cyst and hepatocellular carcinoma which were separated in the right liver lobe. The patient had an uneventful postoperative recovery and was discharged from the hospital after 12 days. At 1 year follow up, the patient is free of symptoms and no signs of recurrence have been detected. (*Fig. 2*)

## Discussion

Two groups of authors (Kübeck M et all, Li H et all) assume that cysts may induce chronic parenchymal liver disease which could lead to the development of liver carcinoma. (15,18) This is explained by chronic inflammatory reaction of liver tissue around the cyst which may lead to increased risk of HCC development.

We consider that there is not enough scientific evidence to confirm this thesis since there is a low number of relevant cases (only 7 reported cases) for analyzing the relation between these 2 focal liver lesions. Moreover, when we see that in 5 of 7 previously published cases there was liver cirrhosis as an underlying cause of HCC, it then indicates that the presence of concomitant cysts and HCC is more likely to be just a coincidence. There is also a lack of experimental research about the effect of hydatid cysts on surrounding liver tissue. It is known that the cyst consists of a central necrotic cavity filled with a white amorphous mass. There are 3 layers in a cyst wall: innermost layer contains nuclei and gives rise to brood capsules attached by short stalk in infectious cysts; second layer is an avascular laminated membrane, while third outer layer is dense fibrovascular tissue with chronic inflammatory cells and calcifications which occur after several years of untreated disease. Host tissue is directly invaded by extension of the proliferating cyst wall which is causing a pressure necrosis of the surrounding liver tissue. (20) From the beginning of infection there is a significant inflammatory and fibrous tissue reaction that surrounds the larval mass. This acellular fibrosis isolates the parasitic lesions from the host but also compresses and obstructs major vessels and bile ducts. Cyst infection and secondary liver abscesses may occur if the necrosis of the cyst is superinfected by bacteria. Carcinogenesis of HCC is a multistep process in which genetic and epigenetic changes are involved. Acquired factors are chronic infections with the hepatitis B (HBV) or C (HCV) virus, and exposure to dietary Aflatoxin B or alcohol consumption. These carcinogenic factors cause damage of the DNA and mutate cancer-related genes. Recent studies show different genetic and molecular mechanisms of carcinosgenesis in HCC within cirrhosis and HCC in NCL. In first case alterations in p53 patways are key for cancer development while in latter, cell cyle regulators have main role. (21)

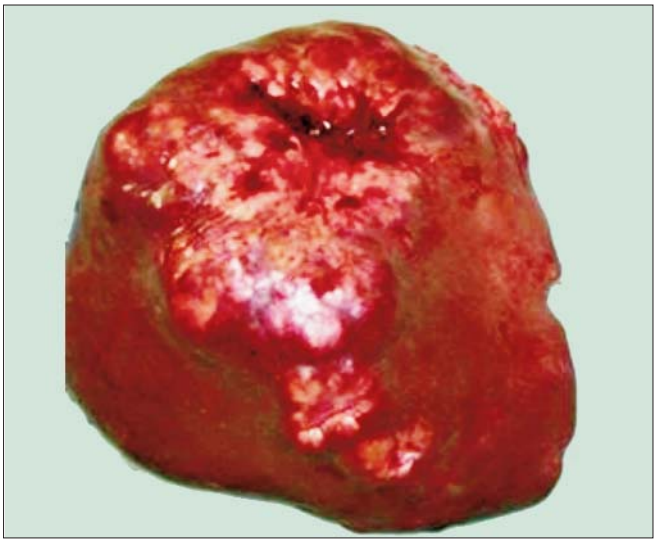

***Figure 2.*** *Surgical specimen after right hepatectomy*

We did not find any strong evidence in scientific literature supporting that the cyst presence could lead to the mutation within hepatocytes' DNA and consequently carcinogenesis as is seen in liver cirrhosis or chronic viral infection. The only reliable molecular study about possible relation between HCC and Echinococcal cyst was done by Stadelmann B at al that

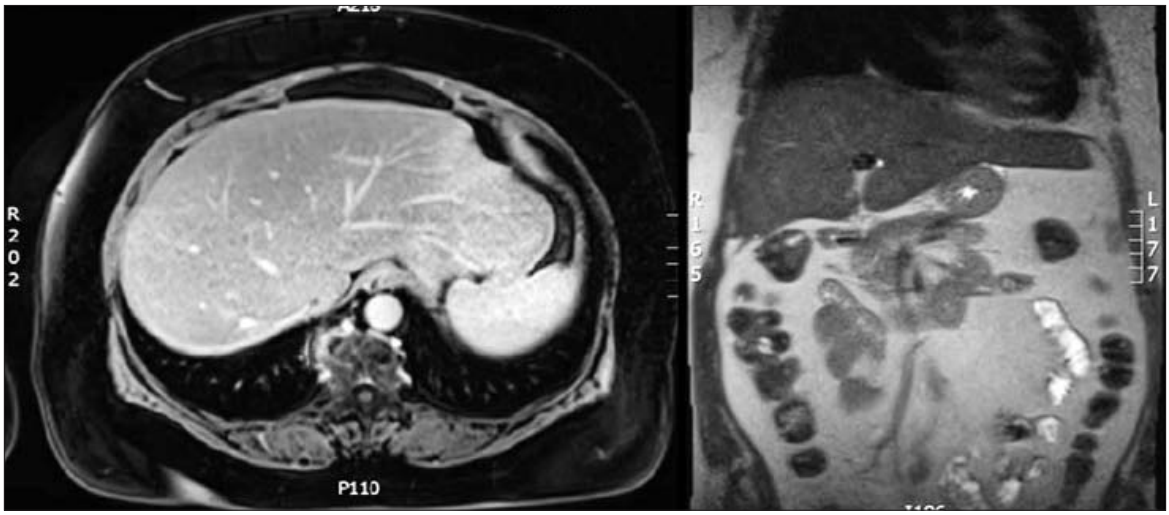


***Figure 3.*** *MRI images in the same patient one year after surgery showing no focal liver lesions with significant hypertrophy of liver remnant (left lobe)*

suggests the E. multilocularis phosphoglucose isomerase (EmPGI), shows a sequence similarity of 86% with human PGI at the terms of animo acid sequence, and this enzyme is a multi-functional protein which can act as a growth factor and may play a role in tumorogenesis. (22) Some authors speculate about effect of parasitic cyst on humman immune system which coud lead to increased risk for malignant diseases but according to our knowledge there is no scientific support for this thesis. (18)

The prognosis of synchronous HCC and hydatid cyst cannot be relevantly calculated, but from data it can be seen that only one case was inoperable. It could indicate that in patients with hydatid cysts, it is more likely that HCC will be discovered in an earlier phase of disease due to earlier clinical investigation of liver related symptoms. Both lesions may cause symptoms such as weight loss, pain, fever, jaundice or lymphadenopathy, so these synchronous lesions can make those symptoms to be more prominent. Although, in all cases, HCC size was significant at the time of diagnosis so tumor progression was probably the main reason for medical attention, especially if we know that cysts have a long time incubation and may be asymptomatic for years, even decades.

Presence of cyst increases the necessity for more extensive liver resection but in reported cases, postoperative liver failure was not detected.

### *Classification proposal*

There is an interesting number of studies about concomitant hepatocellular carcinoma and echinoccocal disease. We found 12 such cases in scientific literature by pubmed research and 8 of them had enough data that could be included in out review. Some authors suggest possible relation between HCC and hydatid cyst due to possible carcinogenic effect of the cyst to surrounding liver tissue. Standard treatment protocol for liver hydatid cysts is well established, and in most cases include antihelmintic 4 weeks therapy followed by liver resection. On the other side, HCC treatment requires multidisciplinary approach, and firstly, resectability must be determined. In case of inoperability, chemotherapy or locoregional palliation is considered. But the questionis, what would be the most appropriate diagnostic algorithm and treatment of concommitant

***Table 3.*** *Romic classification of concomitant HCC and hydatid cyst*

| | | |
|---|---|---|
| Type 1 | Both lesions in the right lobe | a) Single<br>b) Separated |
| Type 2 | Both lesions in the left liver lobe | a) Single<br>b) Separated |
| Type 3 | HCC in the right and cyst in left lobe | a) Without extending to the contralateral lobes<br>b) HCC extending to the contralateral lobe<br>c) Cyst extending to the contralateral lobe |
| Type 4 | HCC in the left and cyst in the right lobe | a) Without extending to the contralateral lobes<br>b) HCC extending to the contralateral lobe<br>c) Cyst extending to the contralateral lobe |
| Type 5 | Both lesions extending to the both lobes | |

*In cases of multicentric HCC, we suggest to add letter "m" to HCC (mHCC)

hcc and hydatic cyst.

To help with this question, we suggest classification system for concomitant HCC and hydatid cyst which would clarify treatment algorithms and categorization of this clinical scenario. (*Table 3*)

HCC and hydatide cysts can be located in both liver lobes, in same lobes or in different lobes. When occur synchronously, these lesions may be present in liver as separated or as a "single lesion". Considering this, we propose next classification based on anatomical location of the cyst and liver tumor.

Type 1: Both cyst and HCC in the right liver lobe
- a) Separated lesions
- b) Single lesion

Type 2: Both cyst and the HCC in the left liver lobe
- a) Separated lesions
- b) Single lesion

Type 3: HCC in right and cyst in left lobe
- a) Without extending to the contralateral lobes
- b) HCC extending to the contralateral lobe
- c) Cyst extending to the contralateral lobe

Type 4: HCC in the left and cyst in the right lobe
- a) Without extending to the contralateral lobes
- b) HCC extending to the contralateral lobe
- c) Cyst extending to the contralateral lobe

Type 5: Both lesions extending to the both lobes

In cases of multicentric HCC, we suggest to add letter "m" to HCC (mHCC).

The example of type 1a HCC/hydatid lesion is seen in our case report where two separated liver masses are present in the right lobe (*Fig. 1*). The example of type 3a HCC/hydatid lesion is seen on in another patient on *Fig. 4*.

Principle of treatment in reported cases was antihelmintic therapy followed by major liver resection. In 6/8 cases this was hepatectomy or extended hepatectomy while in other 2 cases, nonanatomical resections or segmentectomies were performed. We recommend antihelmintic therapy in all cases. In types 1 and 2 we suggest hepatectomies/extended hepatectomies (irrespective of size of the lesions) which would provide complete removal of both lesions with clear oncological benefit and sufficient future liver remnant. Less radical liver resections for types 1 and 2, especially for separated lesions, would increase the risk for iatrogenic cyst perforation or incomplete tumor resection. For types 3 and 4 and multicentric HCCs, surgical therapy may be more complex since it is more difficult to achieve adequate future liver remnant so the therapy should be planned individually. In most cases, hepatectomy and pericystectomy can be safely performed and in selected patients with solitary HCCs, small HCCs, or HCCs fulfilling the Milan criteria, it may be sufficient to perform anatomic subsegmentectomy or nonanatomic minor hepatectomy. In such patients, hepatectomy may be even performed on the side where the cyst is located (if cyst $>10$ cm), but adequate healthy liver parenchyma should be preserved. For more extensive lesions, if both larger than 10 cm, additional procedures for promoting liver hypertrophy, such as portal vein ligation/embolization can be considered. Type 5 would be late stage of the disease and the treatment should include combination of chemotherapy, locoregional therapy and liver resection if possible. Liver transplantation may be option in selected patients, however we did not find case in which transplantation was done.

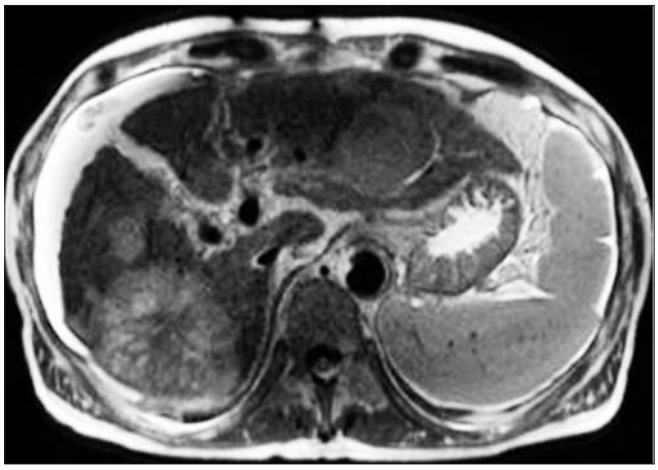

***Figure 4.*** *An example of type 3a HCC/hydatid lesion where HCC is located in the right lobe and hydatid cyst in the left lobe with no extending of lesions to contralateral lobe*

## Conclusion

There is no specific clinical peculiarity for hydatid cyst so these are found mainly in patients with suspected nonspecific focal liver lesions. In such patients, beside imaging and liver functions tests, tumor markers and specific echinococcal serologic tests should be part or routine work up so that in cases of hydatid cyst presence, appropriate preoperative antihelmintic therapy can be administered. (23,24,25) We performed literature review of all reported of synchronous HCC and hydatid cyst in scientific literature- Pathogenesis for HCC in cirrhosis is well known but relation between HCC and hydatid cyst, and the effect of pericystic inflammatory process on surrounding liver tissue is not investigated due to lack of clinical cases. We propose anatomical classification of this rare entity and hope that together with future fundamental studies on hydatid cyst and similar clinical cases, it may help us to understand possible relation between these 2 liver lesions, identify diagnostic features of these lesions and choose the most appropriate type of treatment.

### *Conflict of interest*

Authors declare that they have no conflict of interest.

## References

1. Singal AG, El-Serag HB. Hepatocellular Carcinoma from Epidemiology to Prevention: Translating Knowledge into Practice. Clin Gastroenterol Hepatol. 2015;13(12):2140-51. doi: 10.1016/j.cgh.2015.08.014. Epub 2015 Aug 15.
2. El-Serag HB, Marrero JA, Rudolph L, Reddy KR. Diagnosis

and treatment of hepatocellular carcinoma. Gastroenterology. 2008;134(6):1752-63.
3. Bresson-Hadni S, Laplante J J, Lenys D, Rohmer P, Gottstein B, Jacquier P. et al. Seroepidemiologic screening of Echinococcus multilocularis infection in a European area endemic for alveolar echinococcosis. Am J Trop Med Hyg. 1994;51:837-46.
4. Filice C, Brunetti E. Use of PAIR in human cystic echinococcosis. Acta Trop. 1997;64(1-2):95-107.
5. Noureddin M, Rinella ME. Nonalcoholic Fatty liver disease, diabetes, obesity, and hepatocellular carcinoma. Clin Liver Dis. 2015;19(2):361-79.
6. Chen MS, Li JQ, Zheng Y, Guo RP, Liang HH, Zhang YQ, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg. 2006 Mar;243(3):321-8.
7. Guidelines for treatment of cystic and alveolar echinococcosis in humans. WHO Informal Working Group on Echinococcosis. Bull World Health Organ. 1996;74(3):231-42. English, French
8. Lantinga MA, Gevers TJ, Drenth JP. Evaluation of hepatic cystic lesions.World J Gastroenterol. 2013 Jun 21;19(23):3543-54. doi: 10.3748/wjg.v19.i23.3543.
9. Parija S C. A review of some simple immunoassays in the serodiagnosis of cystic hydatid disease. Acta Trop.(1998);70:17–24.
10. Filippou D, Tselepis D, Filippou G, Papadopoulos V. Advances in liver echinococcosis: diagnosis and treatment. Clin Gastroenterol Hepatol. 2007;5(2):152-9.
11. Rinaldi F, Brunetti E, Neumayr A, Maestri M, Goblirsch S, Tamarozzi F. Cystic echinococcosis of the liver: A primer for hepatologists. World J Hepatol. 2014;6(5):293-305. doi: 10.4254/wjh.v6.i5.293.
12. Karadas S, Dulger AC, Gonullu H, Bulut G, Beyazal M. Coexistence of hepatocelluler carcinoma and cyst hydatid disease of the liver. J Pak Med Assoc. 2014;64(9):1075-7.
13. Kostov D, Dragnev N, Patanov R, Kobakov G. Hepatocellular carcinoma complicated with echinococcal cyst of the liver. Khirurgiia (Sofiia). 2010;(4-5):49-50.
14. Kato T, Seino Y, Takada K, Maruya M, Okubo S, Nakamura H et al. A resectable case of hepatocellular carcinoma complicated with hepatic alveolar echinococcosis]. Nihon Shokakibyo Gakkai Zasshi. 2003 May;100(5):587-92. Japanese
15. Kübeck M, Stöckl V, Stainer W, Schermaier T, Preisinger J, Schauer W et al. Cystic echinococcosis and hepatocellular carcinoma--a coincidence? A case report. Z Gastroenterol. 2014;52(7):657-62. doi: 10.1055/s-0034-1366528. Epub 2014 Jul 15. German
16. Kohlenberg A, Wüsten O, Dierkes C, Discher T, Tappe D. Education and Imaging. Hepatobiliary and pancreatic: alveolar echinococcosis mimicking hepatocellular carcinoma. J Gastroenterol Hepatol. 2010;25(10):1712.
17. Zöld E, Barta Z, Zeher M. Hydatid disease of the liver and associated hepatocellular carcinoma. Clin Gastroenterol Hepatol. 2005;3(8):xxxv.
18. Li H, Song T, Shao Y, Wen H. Cystic echinococcosis accompanied by hepatocellular carcinoma in a female herdsman. Int J Clin Exp Med. 2015;8(2):2985-8.
19. Komisarof JA, Olthoff K, Siegelman ES, Lawton TJ, Furth EE. Focal nodular hyperplasia contiguous with an echinococcal cyst. Am J Gastroenterol. 2000;95(4):1078-81.
20. Mistrello G, Gentili M, Falagiani P, Roncarolo D, Riva G, Tinelli et al. Immunobinding assay as a new diagnostic test for human hydatid disease. Immunol Lett. (1995);47:79-85.
21. Thorgeirsson SS, Grisham JW. Molecular pathogenesis of human hepatocellular carcinoma. Nat Genet. 2002;31(4):339-46.
22. Stadelmann B, Spiliotis M, Müller J, Scholl S, Müller N, Gottstein B, et al. Echinococcus multilocularis phosphoglucose isomerase (EmPGI): a glycolytic enzyme involved in metacestode growth and parasite-host cell interactions. Int J Parasitol. 2010;40(13):1563-74. doi: 10.1016/j.ijpara.2010.05.009. Epub 2010 Jun 30.
23. Guidelines for treatment of cystic and alveolar echinococcosis in humans. Bull World Health Organ. 1996;74(3):231-42. English, French
24. Men S, Hekimoğlu B, Yücesoy C, Arda IS, Baran I. Percutaneous treatment of hepatic hydatid cysts: an alternative to surgery. AJR Am J Roentgenol. 1999;172(1):83-9.
25. Horton RJ. Albendazole in treatment of human cystic echinococcosis: 12 years of experience. Acta Trop. 1997;64(1-2):79-93.