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Hepatocellular Carcinoma Combined with Underlying Alveolar Echinococcosis. Clinical Case Report

Semenkov AV[1*], Poddubskaya EV[2], Yurichenko YY[3], Sorokin MI[4,5], Buzdin AA[4,5], Kogan Y[6], Nekrasova TP[6], Lerner YV[6], Ippolitov LI[3] and Shchekoturov IO[7]

[1]Department of oncology, radiotherapy and plastic surgery of the University Clinical Hospital №1, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[2]The Scientific-research department of the Center of personalized oncology, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[3]Department of oncological surgery №1 of the University clinical hospital №1, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[4]Laboratory of Clinical and Genomic Bioinformatics, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[5]Moscow Institute of Physics and Technology, Dolgoprudny, Moscow Region, Russia

[6]Department of anatomic pathology named after Academician A.I. Strukhov, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[7]Radiology department of I.M. Sechenov First Moscow State Medical University, Moscow, Russia

[*]Corresponding author:

Alexey Vladimirovich Semenkov, Department of oncology, radiotherapy and plastic surgery, University Clinical Hospital №1 I.M. Sechenov First Moscow State Medical University, Moscow, 119435, Russia, Tel: +7(903)212-12-14, E-mail: semenkov@inbox.ru

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Semenkov AV, Poddubskaya EV, Yurichenko YY, Sorokin MI4, Buzdin AA, Kogan Y, Nekrasova TP, Lerner YV, Ippolitov LI, Shchekoturov IO and these authors are contributed equally to this work.

1. Abstract

The aim of the present article was to demonstrate the clinical case of a quite rare combination of hepatocellular carcinoma and liver alveolar echinococcosis. The literature review showed that the combination of these nosological forms of the liver damage was extremely rare. The present clinical case describes a diagnosed liver alveolar echinococcosis that was based on the combination of the data obtained by the instrumental methods of diagnostics and pre-operative morphological verification of the material. Combined hepatocellular carcinoma was accidentally revealed during the histological examination of the specimen obtained during the second surgery. The possibility of combining these nosological forms of liver damage determines the necessity of performing the full range of diagnostic tests for the differentiated diagnostics in patients with liver tumors even during the primary morphological verification of liver echinococcosis.

2. Introduction

Alveolar Echinococcosis (AE) is a parasitic disease caused by a larval stage of Echinococcus multilocularis which is widespread in the majority of the countries of the Northern hemisphere [1-3]. The main parasite hosts are dogs, foxes, or related species whose feces spread the parasite eggs. Therefore, humans can accidentally become intermediate hosts in the living cycle of E. multilocularis [1, 2]. Larva actively penetrates the intestinal mucosa and gets into the portal vein system via venous vessels [1, 4]. Generally, the damage is caused to the liver where the parasitic tumor begins to grow [1, 5]. The dis-

ease is characterized by a long-term symptomless development due to the extremely slow growth of the echinococcus cysts. The diagnostics data of AE is obtained by ultrasound imaging (USI), computed tomography (CT), Magnetic Resonance Tomography (MRT), endoscopic ultrasound imaging (endo-USI), and serological testing [1, 6, 7]. At the same time these diagnostic methods do not always provide for differentiated diagnostics among other liver neoplasms [1, 5, 6]. Alveolar echinococcosis usually develops without any symptoms and the clinical picture depends on damage size and area [1, 5]. Sometimes this disease is difficult to differentiate from malignant neoplasms in the liver, especially in the non-endemic regions [1, 5, 6]. The slow growth of the parasitic focus (approximately 1-3 cm per year) has been noted, and that can also be encountered in cases of hepatic tumors [1, 5, 6]. There is a limited number of reports on a combined parasitic and tumor damage of the liver [1, 8-14]. The present study describes a clinical case of a biphenotypical liver damage found in the case of a patient with hepatocellular cancer revealed during a histological study of a dissected hepatic lobe and liver alveolar echinococcosis.

3. Case Presentation

A 46-year old woman was examined because of the complaints on the feeling of weight and the occurrence of a palpated dense neoplasm in the right subcostal area. A multiphasic multidetector computed tomography with contrast enhancement demonstrates a mass in the right liver lobe (Figure 1a-d). Computed tomography (CT) scans show an invasion of the right and the middle hepatic veins and the right branch of a portal vein (Figure 2a-b). The left liver lobe, the portal vein trunk, the left portal branch, and the left hepatic vein were not affected by the lesion. The retrohepatic segment of the inferior vena cava was involved within 5 cm (Figure 2c). The authors performed a differentiated diagnostic between the hemangioma (with atypical contracting), alveococcosis of the liver, and hepatocellular carcinoma. The patient underwent such surgical manipulations as diagnostic laparoscopy, revision of the abdominal cavity, and excision biopsy of the neoplasm in the liver. The morphological study of the obtained material revealed the classical picture of the liver alveococcosis. A patient was treated by albendazole and she was directed to the surgery department of the University hospital. The patient did not have any chronic liver diseases other than echinococcosis. The markers of viral hepatitis (HbsAg, anti HCV (Cor, NS)) were negative. Anthropometry: height - 156 cm; weight - 57 kg, body mass index - 23.4 kg / m2, the absence of excess body weight. No history of diabetes. Bad habits: smoking, alcohol and drugs - denied. No clinical and laboratory signs of nonalcoholic fatty liver disease were noted.

The evaluation of the resectability was performed in accordance with the criteria of resectability approved by the Expert consensus of the WHO working group for the diagnosis and treatment of cystic and alveolar echinococcosis in humans [15]. The main criterion for the choice of treatment was the evaluation of the resectability in R0 volume. The patient was performed an extended right-sided hemihepatectomy with a prosthetic repair of the inferior vena cava with a synthetical frame-mounted graft with its further implantation into the left hepatic vein prosthesis in the conditions of veno-venous by-pass. In the cut surface (Figure 2D) the largest part is occupied by a parasitic node with small fragments of chitinous membrane residues with a diffuse growth pattern on the periphery (Figure 2D). The macroscopic picture of alveococcosis of the right lobe of the liver with the invasion into the inferior vena cava (Supplementary File 1, Figure S1) was performed.

The histological study of the resected liver revealed that the lobular and lamellar structure of the liver was damaged because of a great number of small and medium merging epithelioid cellular granulomas with centrally located elements of alveococci with foci of necrosis and single micro calcifications. The infiltration contained lymphocytes, macrophages, a lot of eosinophils, plasma cells, multinuclear giant cells of foreign body. There were expressed hepatic tissue atrophy, lipofuscinosis of hepatocytes, and fields of granulation tissue in between the inflammatory foci. The adjacent hepatic tissue contained small non-caseous epithelioid-cell granulomas, focal fatty changes of the hepatocytes, uneven blood filling of the sinusoids and extravasation of erythrocytes, foci of ischemic damage of hepatocytes. The portal tracts contained moderate polymorphic cellular infiltration - chronic productive inflammation (Supplementary File 1, Figure S2). The intrahepatic segment of the inferior vena cava contained foci of alveococci invasion with productive perifocal inflammation (Supplementary File 1, Figure S3). Histological examination revealed several lesions located within liver parenchyma and represent small hepatocellular areas appear to be cobblestone appearance which indicates regeneration of hepatic parenchyma, that macroscopically did not differ from liver parenchima (Supplementary File 1, Figure S4. A). At the periphery of the removed liver segments there was the one, largest lesion, about 2,3 centimeters in the largest diameter, represents histologically as hepatocellular carcinoma (Supplementary File 1, Figure S4. B). The tumor cells have eosinophilic cytoplasm and increase in nuclear: cytoplasmic ratio, with the formation of trabecular cords up to six cells thick (appreciated with reticulin stain) lined by flattened endothelial cells. The mitotic figures were noted, including single atypical (tri-polar) (Supplementary File 1, Figure S4.C). Glypican-3 and Anti-Human Hepatocyte show strong positive cytoplasmic staining of tumor cells (Supplementary File 1, Figure S5.). Some other markers, such as HSP70, glutamine synthetase and p53 were also positive. After Ki67 staining mitotic index was detected as 30%. These investigations indicated the morphological picture of hepatocellular carcinoma, trabecular variant, G1.

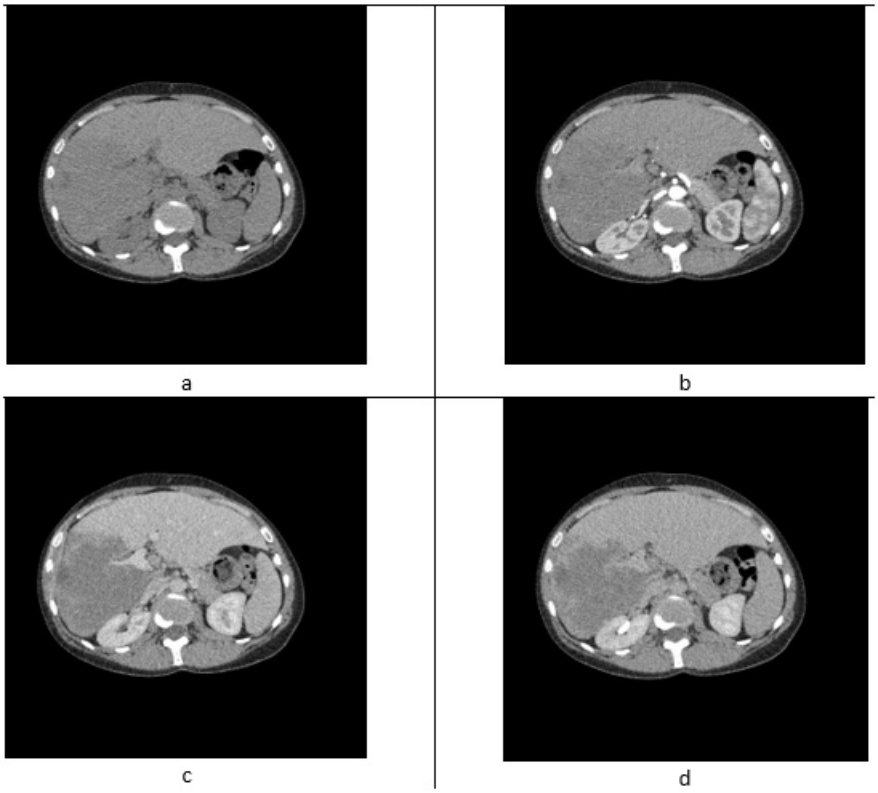

Figure 1: Axial multiphasic CT scans obtained during the (a) precontrast, (b) arterial, (c) venous, and (d) delayed phases show an hypodense mass in the right liver lobe. The lesion shows hypoattenuation in the precontrast phase and no no evidence of contrast enhancement after intravenous contrast injection.

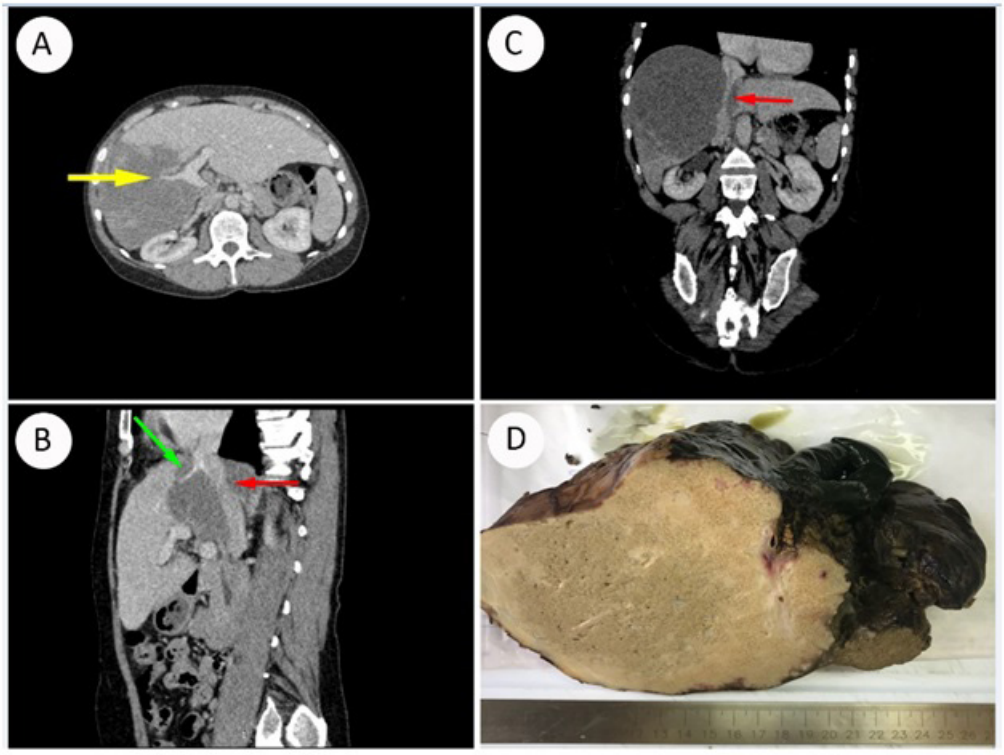

Figure 2: Enhanced multiphasic axial (a), sagittal (b) and coronal (c) CT scans obtained in venous phase shows right branch of portal vein invasion (yellow arrow) and circular invasion of vena cava inferior (red arrows) and middle hepatic vein (green arrow). (d) Macroscopic picture of alveococcosis of the right lobe of the liver.

Supplementary File 1: Macroscopic view of alveococcosis invasion into the inferior vena cava and histological slides

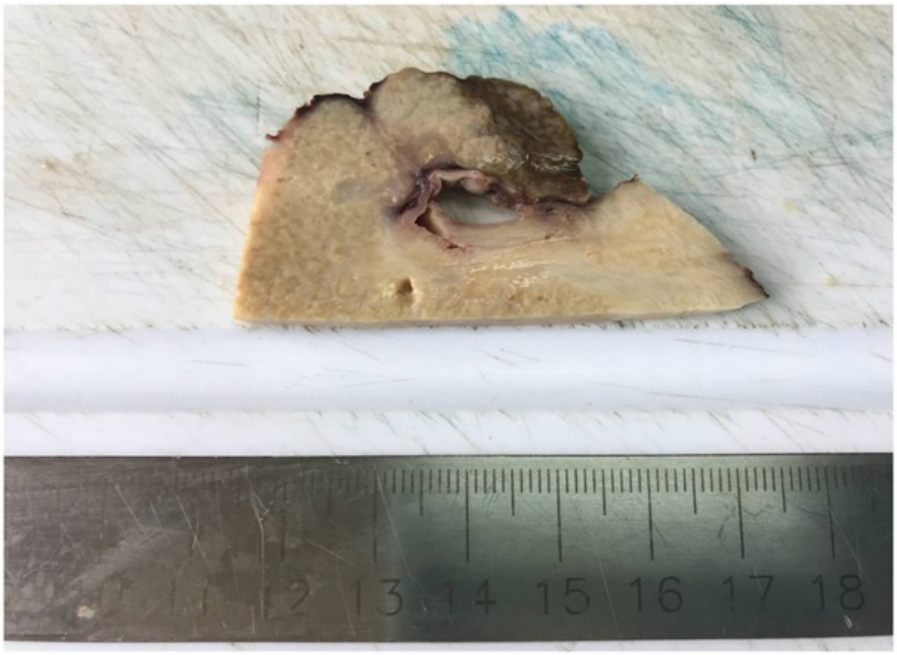

Figure S1: Gross specimen. A section of the liver with a fragment of the lower hollow vein, which is located within the node.

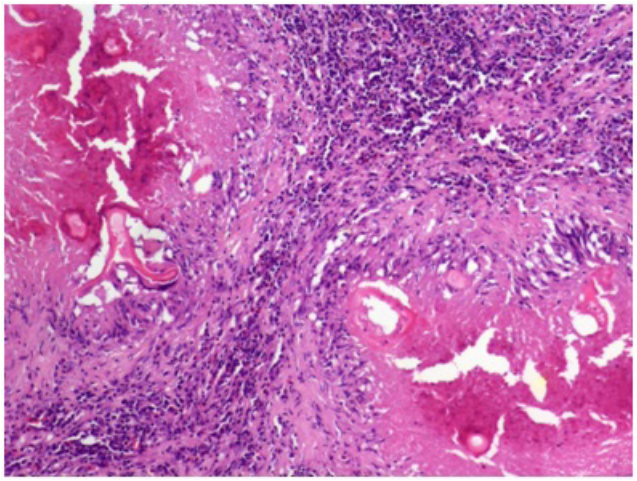

Figure S2: Photomicrography. (A) elements of alveococci and chitinous coating; (N) areas of necrosis; (I) infiltrate, consisting of lymphocytes, macrophages, plasma cells, and single multinuclear giant cells of foreign body. (Hematoxylin-eosin, x200).

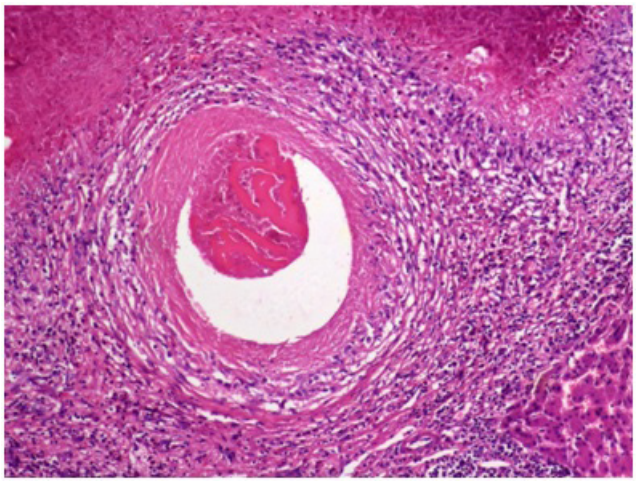

Figure S3: Photomicrography. (A) a wall of a venous vessel with the focus of invasion of the parasitic elements; (N) necrotic areas in the liver; (L) Intact hepatic tissue. (Hematoxylin-eosin, x200).

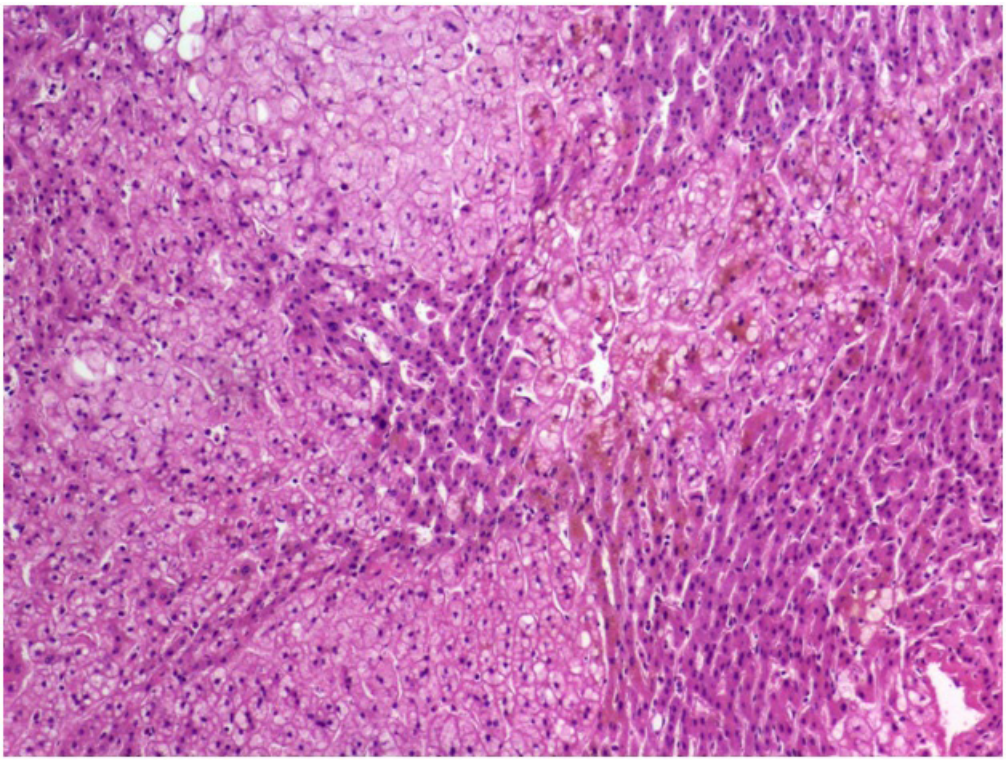

Figure S4A: Cobblestone appearance (RN) due to areas of regeneration of the hepatic parenchyma.

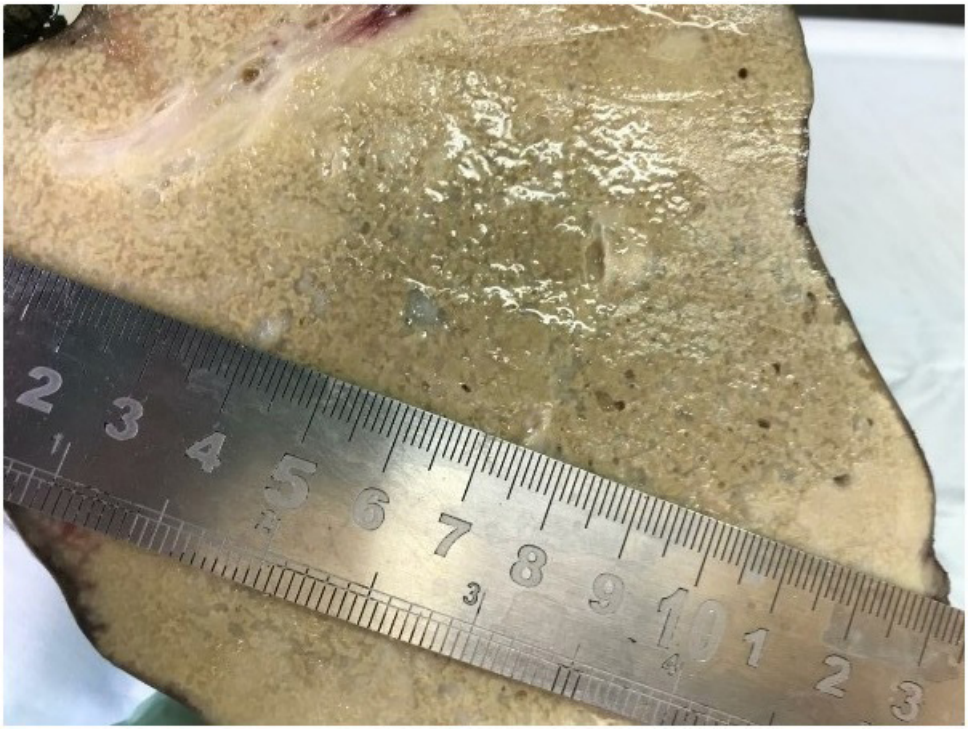

Figure S4B: Largest lesion at the periphery of the removed liver segments (arrow). Far from the alveococcal cysts.

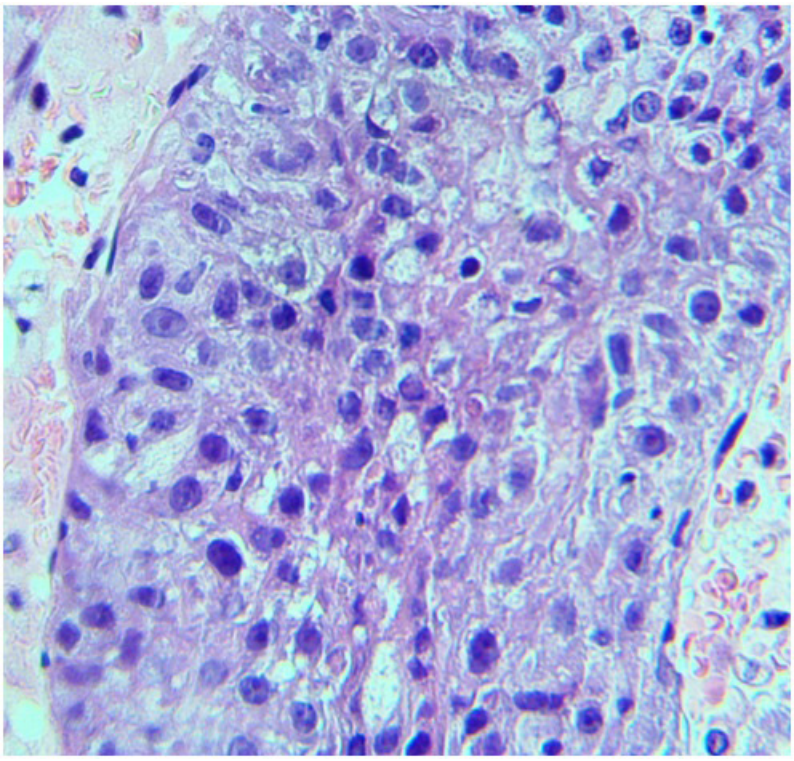

Figure S4C: Photomicrography. Area of hepatocellular carcinoma: the tumor cells have eosinophilic cytoplasm and increase in nuclear:cytoplasmic ratio, with the formation of trabecular cords up to six cells thick lined by flattened endothelial cells. Cellular atypia of tumor cells can be seen and nucler atypia is distinct in. (Hematoxylin-eosin staining, x400).

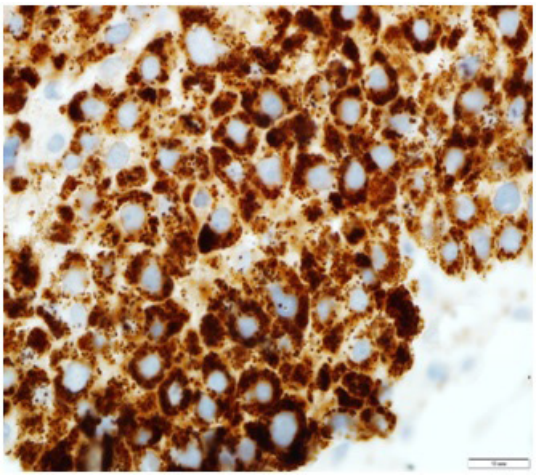

Figure S5: Photomicrography. Anti-Human Hepatocyte shows strong positive cytoplasmic staining of tumor cells. (Immunohistochemical reaction X1000).

4. Discussion

In the case of combined hepatocellular carcinoma and alveolar echinococcosis it is important to reveal both pathologies because of the further treatment and prognosis depending on the correct diagnosis [9]. In the majority of cases (85-90%) hepatocellular carcinoma develops in patients with hepatic cirrhosis caused by viral hepatitis, alcohol abuse or other diffuse liver diseases, while in 10-15% of cases it develops in the unaltered liver [9, 16, 17]. The etiology of hepatocellular carcinoma provokes discussion, but recent studies demonstrated a possible connection between metabolic syndrome and alcohol abuse [9, 16, 17]. Some authors believe that chronic inflammatory reaction around the segment of the liver affected by echinococci increases the risk of hepatocellular carcinoma development [10, 13]. Other authors believe that this hypothesis lacks scientific grounds due to a limited number of observations required for a reliable analysis. Furthermore, there are no experimental data on the association between cancerogenesis and echinococci damage of the liver [9]. According to B. Romic et al [9], the analysis of electronic database PubMed revealed only 12 published cases of the combination of these nosologies. Only three cases showed a combined tumor damage in patients who did not have a background chronic diffuse liver disease. However, a combination of hepatocellular carcinoma and alveolar echinococcosis was described only in one case [11].

In the present observation, the diagnosis of alveolar echinococcosis was based on a combination of the results of instrumental radiological diagnostics and morphological verification of the material obtained during the primary surgery performed at the patient's local hospital. The revealed combined hepatocellular carcinoma was an accidental finding during the histological study of the material obtained during the second surgery. The authors believe that the description of the present case can be useful while demonstrating the possibility of a combination of the described nosological variants of the liver damage. Even the primary morphological verification of the diagnosis of hepatic alveococcosis does not exclude the performance of the complete range of the diagnostic studies for the differentiated diagnostics with tumor damage of the liver.

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