

Nerve Infiltrating *Echinococcus Multilocularis* (Alveolar Hydatid Disease) Masquerading as Malignancy

Echinococcus Multilocularis (EM) causes Alveolar Hydatid disease. Humans are accidental hosts of the parasite. The parasite always affects the liver and forms large masses mimicking malignancy. These masses are however slow growing and well marginated. Involvement of vascular structures has been reported. We herein report the first known case of EM causing nerve infiltration.

Case Report

We report a case of a 24 year old female resident of Kyrgyzstan who was a known case of hydatid liver disease involving both lobes of the liver and vascular structures. Abdominal Multislice Spiral CT performed in her native country revealed lesions in the right and left liver lobes with involvement of the right and left hepatic arteries, hepatic veins, portal vein and hepatic segment of the inferior venacava. Portal hypertension was noted.

She underwent laparotomy for the same. However, due to extensive involvement of vessels and the inferior venacava, the mass was deemed inoperable and the patient was referred for liver transplantation

She underwent living donor liver transplant, and the native liver was sent for histopathological examination.

Grossly the explanted liver weighed 1659 gm, measuring 22x17x11 cm. The liver was soft in consistency with the external surface being a smooth brown color. The left lobe capsule appears thickened and whitish. Serial slicing of the specimen revealed two large lesions one in each lobe of the liver with a creamy yellow cut surface. The right measured 11x11x7 cm and the left, 8x5.6x5.5 cm. **(Figure 1a,b)** The firm cream coloured lesion showed central areas of cystic change filled with brown grumous debris. The lesion in the right lobe was seen extending upto the porta hepatis. The gall bladder was adherent to the liver bed measuring 5x2 cm.

Light microscopy of the section examined from the firm cream colored mass with adjacent liver interface showed abundant granulomatous reaction around the laminated Periodic acid-Schiff (PAS) positive parasitic membranes. The granulomatous reaction was seen creeping into adjacent liver tissue and destroying the hepatocytes. The inflammatory infiltrate was predominantly comprised of eosinophils, lymphocytes and epithelioid cells. Only periphery of the lesion showed viable inflammatory cells. The remaining central area of the mass showed coagulative necrosis with interspersed laminated membranes. Foci of calcification were noted. Section from the porta hepatis showed infiltration by similar granulomatous reaction. There was a prominent peri and intraneural inflammatory infiltrate at the porta **(Figure 1c)**. Section from adherent gall bladder showed necrosis and parasitic remnants in wall tissue **(Figure 1d)**. Immunohistochemistry of the nerve infiltration stained positive for S100, CD56 and calretinin **(Figure 2)**. The parasitic membranes were PAS positive and acid fast negative, with Masson's trichrome stain showing two tone appearance **(Figure 3)**.

The patient was diagnosed to have had alveolar hydatid disease with parasitic infiltration of the liver

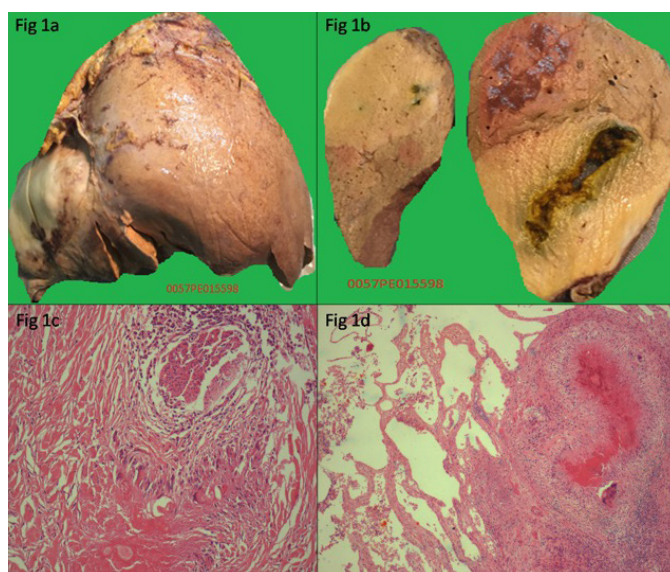


Figure 1(a,b): Explant liver showing large cream colored masses in both lobes of the liver; **(c):** Light microscopy showing nerve fibre infiltration (H&EX10); **(d):** Light microscopy showing gall bladder infiltration (H&EX 10).

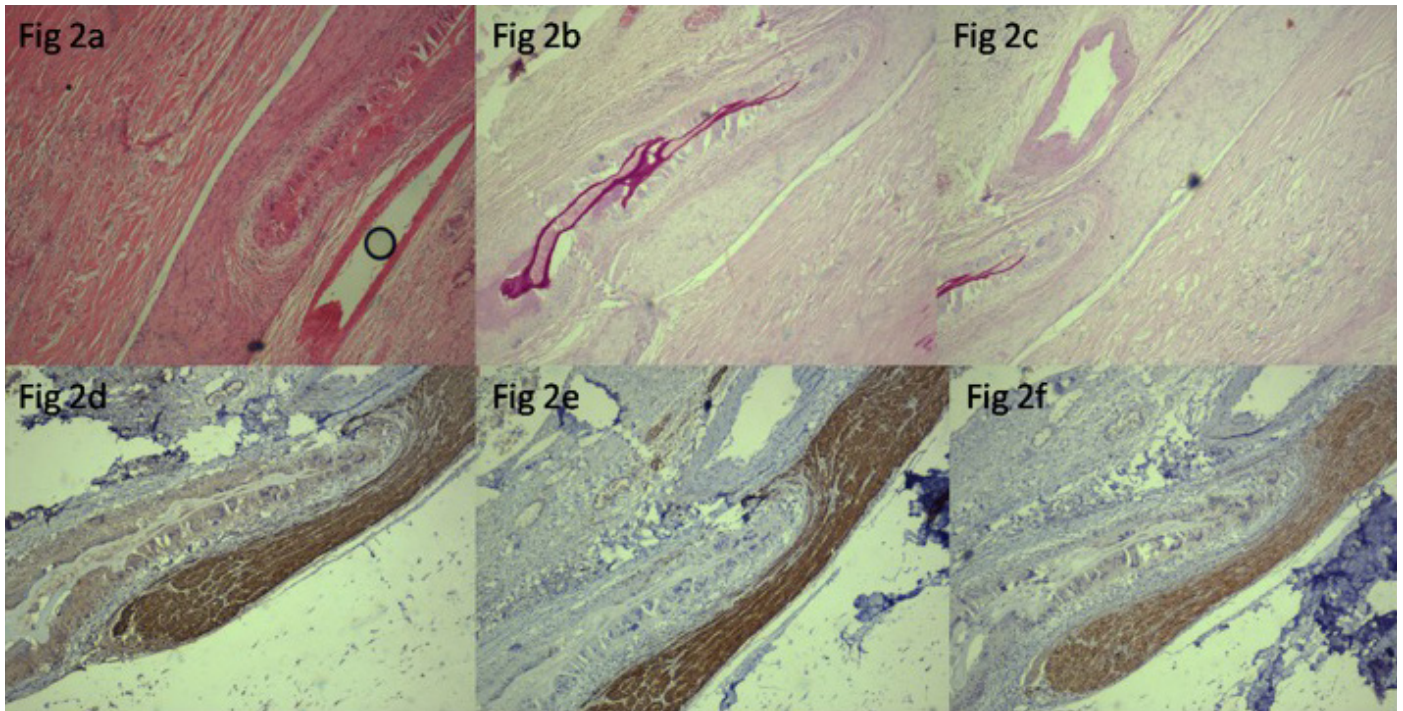


Figure 2(a,b,c): Parasite seen infiltrating the nerve bundle at porta hepatis (H&EX10); (d,e,f): Immunohistochemistry CD 56, S100 and Calretinin positive staining by the nerve bundles.

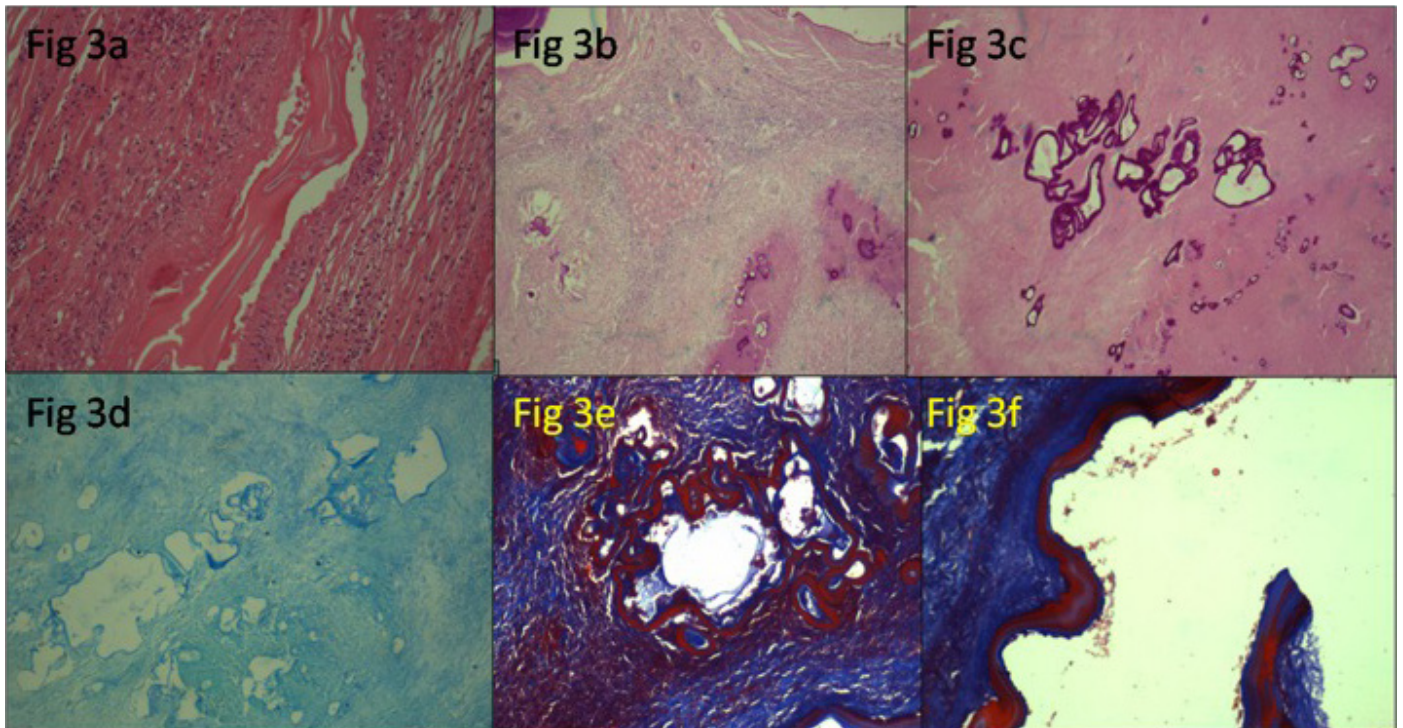


Figure 3(a): Light microscopy showing parasitic membranes; (b,c): PAS positive membranes; (d): Ziehl Neelsen stain showing AFB negative parasitic membrane; (e,f): Masson's trichrome stain showing two tone appearance of parasitic membranes.

and gall bladder demonstrating mass effect along with involvement of the portal vein and nerve bundles at the porta hepatis.

Discussion

Alveolar hydatid disease is a disease of the Northern Hemisphere commonly seen in Russia, Central Asia, China, Northern Japan, Central-Western Europe, Eastern Europe, Turkey, and Alaska. The disease is caused by *Echinococcus multilocularis*. Foxes, and occasionally dogs and cats are the definitive hosts with rodents and other small mammals serving as intermediate hosts. The eggs produced by the adult parasite are released into the environment by the fox and the cycle continues with digestion of contaminated food by the intermediate host. The eggs penetrate the bowel wall and invade the lymphatic and portal systems, and from there they spread to multiple organs. The parasite matures into its metacestode stage in natural intermediate hosts and in humans who are accidental hosts.¹⁻³ The metacestode stage almost always occurs in the liver. Within the liver they cause formation of infiltrative mass lesions with no distinct demarcation from adjacent hepatic parenchymal tissue. Over time these masses undergo diffuse fibrosis with calcific foci and necrotic areas. Rarely the parasite can undergo lymphovascular invasion and is disseminated to other intra-abdominal organs.⁴⁻⁶ However, to our knowledge there has been no reported case of nerve infiltration by *Echinococcus multilocularis*.

Most cases are seen between the age of 50 and 70 years. The natural course of the disease consists of approximately 5-15 years of an asymptomatic incubation period followed by a chronic period.^{1,2} Clinical features are non specific including pain, abdominal lump, fever, jaundice or portal hypertension.

Radiologically, features may mimic a primary or metastatic liver tumour. CT is the best imaging modality for diagnosis. Imaging shows a heterogeneous non enhancing well marginated lesion with both central & peripheral calcification.⁷

Hepatic lobectomy with a prolonged course of chemotherapy is suggested. Liver transplantation is the final resort for incurable symptomatic biliary alveolar

hydatid disease cases.^{8,9} In conclusion, alveolar echinococcus forms a slow growing infiltrative solid cystic lesion in the liver with the potential to cause obstruction of the bile duct, portal vein, hepatic vein or inferior vena cava. The disease is highly fatal if left untreated and can cause lymphovascular dissemination with delayed recurrence. This feature of vascular dissemination and widespread infiltration, including nerves, shows resemblance to a malignant tumour.

NALINI BANSAL¹

VIVEK VIJ²

MANAV WADHAWAN³

¹*Department of Histopathology,*

SRL Ltd Fortis Escorts Heart Institute, Okhla, New Delhi

²*Department of Liver Transplant and Hepatobiliary Surgery,*

Fortis Escorts Heart Institute, Okhla, New Delhi

³*Department of Hepatology,*

Fortis Escorts Heart Institute, Okhla, New Delhi

Corresponding Author: Dr Nalini Bansal

Email: drnalinibansal@yahoo.com

References

1. Eckert J, Deplazes P. Biological, epidemiological, and clinical aspects of echinococcosis, a zoonosis of increasing concern. *Clin Microbiol Rev.* 2004;17(1):107–35.
2. McManus DP, Zhang W, Li J, Bartley PB. Echinococcosis. *Lancet.* 2003 18;362(9392):1295–304.
3. Kantarci M, Bayraktutan U, Karabulut N, Aydinli B, Ogul H, Yuce I, et al. Alveolar echinococcosis: spectrum of findings at cross-sectional imaging. *Radiographics.* 2012;32(7):2053–70.
4. Bulakci M, Yilmaz E, Cengel F, Gocmez A, Kartal MG, Isik EG, et al. Disseminated Alveolar Hydatid Disease Resembling a Metastatic Malignancy: A Diagnostic Challenge - A Report of Two Cases. *Case Rep Radiol [Internet].* 2014 [cited 2018 Feb 8];2014. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206930/>
5. Piotin M, Cattin F, Kantelip B, Miralbès S, Godard J, Bonneville JF. Disseminated intracerebral alveolar echinococcosis: CT and MRI. *Neuroradiology.* 1997;39(6):431–3.
6. Demir MK, Kilicoğlu G, Akinci O. Alveolar hydatid disease of the liver: brief review and spectrum of adjacent

organ invasion. *Australas Radiol.* 2007;51:346–350

7. Bulakçı M, Kartal MG, Yılmaz S, Yılmaz E, Yılmaz R, Şahin D, et al. Multimodality imaging in diagnosis and management of alveolar echinococcosis: an update. *Diagn Interv Radiol.* 2016;22(3):247–56.
8. Bresson-Hadni S, Koch S, Beurton I, et al. Primary disease recurrence after liver transplantation for alveolar echinococcosis: long-term evaluation in 15 patients. *Hepatology.* 1999;30:857–864.
9. Koch S, Bresson-Hadni S, Miguet JP, et al. Experience of liver transplantation for incurable alveolar echinococcosis: a 45 case European collaborative report. *Transplantation.* 2003;75:856–863.

Non Cirrhotic Portal Hypertension with a Large Spontaneous Splenic Abscess

In the western world, non-cirrhotic portal hypertension (NCPH) is a rare disease. However in the Indian subcontinent, it is estimated that over 30% of cases of variceal bleeds are due to NCPH or extra hepatic portal venous obstruction (EHPVO). Multiple splenic abscesses are a rare condition in clinical practice, and are seen mostly in immune-compromised patients or in those presenting following an intervention.¹ There are also reports of such spontaneous abscesses developing in the setting of enteric fever or infective endocarditis. Reports have suggested that ultrasound-guided percutaneous drainage is a safe and feasible alternative to surgery in the treatment of splenic abscesses allowing splenic preservation.² A search through available literature has shown several reports of splenic abscesses developing after splenic artery embolisation. Splenectomy is reserved for those cases where medical treatment has failed. To the best of our knowledge, the development of a spontaneous splenic abscess in a cirrhotic patient has only been described in one prior case report by Cacopardo et al.³ There are no prior descriptions of such a case in a patient with NCPF.

Case Report

We report the case of a 39 year old clerk who was diagnosed with chronic hepatitis B in 2011 and has been on tenofovir for the same. He presented to our emergency with a history of progressively worsening abdominal distension for the last 3 months and intermittent high grade fever for 2 months. He did not report hematemesis, melena or altered sensorium. He denied any prior abdominal trauma or surgery, chest pain, shortness of breath, palpitations, cough or altered bowel habits. On physical examination he was found to be pale, icteric, severely sarcopenic and had a tender massive splenomegaly, palpable 15 cm below the left hypochondrium extending up to the pelvis. He was found to have evidence of anemia, hyperbilirubinemia and hypoalbuminemia upon investigation. His INR was 2.4 and thromboelastography showed global coagulation failure requiring correction. Serum alkaline phosphatase was grossly elevated to 213 IU/l with mild elevation of other liver enzymes. CT imaging of the abdomen revealed a normal appearing liver, massive splenomegaly and a patent dilated portal venous system with multiple collaterals and a large lienorenal shunt. The spleen showed a large abscess about 15 x 21 x 10 cm in size, with no evidence of rupture (**Figure 1 and 2**). Iron studies showed elevated serum ferritin, and transferrin saturation-71.2%. Gastroduodenoscopy did not show any varices or portal hypertensive gastropathy. His transjugular liver biopsy showed evidence of chronic hepatitis, and hepatic venous portal gradient was just 4 mm Hg confirming the clinical suspicion of non cirrhotic portal hypertension (**Figure 3 and 4**). Malaria antigen test, widaltitres and viral serologies for hepatitis A, C, E, herpes simplex, cytomegalovirus and Epstein Barr virus were all negative. His HBsAg and anti HBe were reactive without detection of HBV DNA or HBeAg. Interestingly, on immuno-phenotyping of CD4 and CD8 lymphocytes, he was found to have CD4 lymphocytopenia with a CD4 count of 195 cells/ μ l. However his CD4/CD8 ratio was within normal limits and IgG was 13.1 g/l. HIV-1 and 2 and HIV 1 RNA were non-reactive and there was as no evidence of lymphoma or parasitic infections. 2D Echocardiography did not reveal any endocarditis. Bone marrow biopsy aspirate showed evidence of a reactive