

# Imaging spectrum of Alveolar Hydatid as per PNM Classification.

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## Abstract

**Introduction:** There are two forms of infestation by Echinococcus: the unilocular cystic form caused by E. granulosus is much more common than the rare multilocular alveolar form caused by E. multilocularis. Without early diagnosis and treatment, disease has poor prognosis. Death eventually results from hepatobiliary complications like cholangitis or secondary biliary cirrhosis; bleeding from esophageal or duodenal varices due to portal hypertension, Budd-Chiari disease, or obstruction of the vena cava; or complications related to heart, lung, or brain involvement.

**Materials and Method:** This was an observational study where a cohort of 24 patients with avascular hepatic mass on ultrasound were subjected to triple phase contrast computerized tomography over a span of two years from December 2020 to November 2022 in GMC, Srinagar.

**Aim:** The aim of the study was to present the Imaging spectrum of alveolar Hydatid on CECT as per PNM classification and to assess characteristics of alveolar hydatid on contrast enhanced computed Tomography.

**Results:** The most common form of alveolar hydatid in liver was an infiltrating non enhancing heterogeneous mass lesion with irregular margins with internal calcifications (75%) cases. Calcification was seen in 22(91.6%) out of 24 cases (P value < 0.001). All of the masses were non enhancing with peripheral rim enhancement in only 5 cases (20.8%). P2N0M0 was the most common stage found on CECT as per PNM classification in 14(58.3%) patients followed by P1N0M0 in about 4 patients (16.6%). P3 and P4 stage was found in 3 patients (12.5%) each. N1 stage was found in 2 patients (8.3%). M1 stage was found in 3(12.5%) patients with metastasis to lung in two cases and Brain in one case.

**Conclusion:** CECT has a very important role to suggest diagnosis of Alveolar Echinococcosis since MRI take long acquisition times. Radiologists especially those residing in endemic region must be aware of imaging findings of Alveolar Echinococcosis so that they can direct clinicians to take proper therapeutic decision.

**Keywords:** Echinococcosis Multilocularis, Alveolar Hydatid, Non Contrast Computed tomography (NCCT), Contrast Enhanced Computed tomography (CECT), Magnetic Resonance Imaging (MRI), Intrahepatic Biliary Radical and Periodic acid Schiff (PAS).

## Introduction

Echinococcosis is the name given to zoonotic infections caused by tapeworms (cestodes). There are two forms of infestation: the unilocular cystic form caused by E. granulosus is much more common than the rare multilocular alveolar form caused by E. multilocularis <sup>[1]</sup>. The life cycle of this parasite involves

a definitive host and natural intermediate host. The definitive hosts are red foxes, and rodents are the intermediate hosts. Humans are accidentally infected by the parasite [2]. The invasion of different organs by metacestodes, primarily the liver and lungs, causes severe problems in the intermediate hosts or accidental hosts [2, 3]. The metacestodes of *Echinococcus multilocularis* invade different organs in humans and produce slowly progressive infiltrating mass mimicking neoplastic processes. The metacestode of *E. multilocularis* is not usually demarcated by fibrous capsule at its outer margins. The larval mass proliferates peripherally, and, at the same time, regressive changes occur centrally; thus, *E. multilocularis* may appear as a progressively enlarging infiltrating mass with central necrotic areas with a relatively thin zone of viable proliferating tissue [3]. Diagnostic difficulties are encountered since it is not a common disease, particularly in nonendemic regions [4]. Early diagnosis as well as appropriate treatment and follow up is very important in improving the patient's quality of life. Imaging plays an important role in the diagnosis, follow up and management of disease.

**Materials and Method:** This was an observational study where a cohort of 24 patients with avascular hepatic mass on ultrasound were subjected to triple phase contrast enhanced computerized tomography on 256 slice CT over a span of one year from December 2020 to November 2021, in government medical college, Srinagar. Non contrast and Contrast-enhanced CT scans (reconstruction section thickness, 5 mm; reconstruction intervals, 5 mm) were obtained at 30 seconds (arterial), 55 seconds (portal) and 90-120 seconds (venous) after IV injection of 100 mL of iohexol (Omnipaque 350), injected at a rate of 3.0 mL/s, using a mechanical power injector. The aim of the study was to present the Imaging spectrum of alveolar Hydatid on CECT as per PNM classification and to assess characteristics of alveolar hydatid on contrast enhanced Computed Tomography. Final diagnosis in all cases was confirmed by histopathological biopsy. Exclusion criteria: 1. Patients with history of contrast allergy.  
2. Refusal to participate in the study.  
3. Patients with elevated creatinine (1.5 mg/dl) levels.

**Statistics:** Categorical variables were described in terms of frequency and percentage. Continuous variables were described in terms of mean. The value of  $P < 0.05$  indicated a statistically significant in the Chi-square test.

**Results:** There were 14 male patients and 10 female patients. The mean age of patients in our study was 42.5 years with youngest patient being 28 years and oldest patient being 57 years. All the patients were immuno competent with no underlying comorbidity. Most of the patients were cattle and sheep rearing belonging to hilly areas. The histopathology of biopsy specimen showed darkly stained laminar membranes with PAS staining and echinococcus vesicles

The most common clinical presentation was right hypochondrium pain (62.5%) followed by jaundice (29.1%). Clinical presentation in one patient with cerebral hydatid was headache followed by vomiting. The most common form of alveolar hydatid in liver was an infiltrating non enhancing heterogeneous mass lesion with irregular margins with internal calcifications. Central lesion involving both right and left lobe was seen in 17 patients. Biliary radicle dilatation adjacent to mass was seen in 8 patients likely suggesting biliary infiltration. Calcification was seen in 22 (91.6%) out of 24 cases ( $p$  value  $< 0.001$ ). Peripheral calcification were seen in 5 patients and central calcifications were seen in 17 patients. There were small

peripheral microcysts in 6 patients. All of the masses were non enhancing with peripheral rim enhancement in only 5 cases (20.8%).

The Chest radiography (PA view) and non contrast CT scan of the brain were also done to look for the dissemination or metastasis.

P2N0M0 was the most common stage found on Contrast Enhanced Computerized Tomography as per PNM classification in 14(58.3%) patients followed by P1N0M0 in about 4 patients (16.6%). P3 and P4 stage was found in 3 patients (12.5%) each. N1 stage was found in 2 patients (8.3%) with infiltration into right adrenal gland in one case and anterior abdominal wall in other case. M1 stage was found in 3(12.5%) patients with metastasis to lung in two cases and Brain in one case.

The average size of lesion was 7 cm. Ten patients underwent surgery; resection of lobe. Whereas other 14 were put on medical therapy (albendazole) for a period of two years. The disease progression was arrested however the size of the lesion did not decrease significantly. Two patients died during the course of follow up, and were belonged to category of P2N0M0 and P2N0M1.

### **Discussion:**

*Echinococcus multilocularis*, the causative agent of alveolar hydatid disease, is a rare occurrence in humans and has a considerably lower prevalence compared to *Echinococcus granulosus*-induced hydatid disease. Infection by the metacestode stage of this pathogen primarily affects the liver, giving rise to a tumor-like growth that can be mistakenly identified as a malignancy. Distinguishing between alveolar hydatid disease and hepatic malignancy poses significant clinical challenges. The disease follows a chronic and afebrile course and is frequently fatal. It often remains asymptomatic for extended periods and occasionally gets incidentally detected. Timely diagnosis is crucial, as delayed detection can lead to dire consequences. Previously, histological examination of biopsy specimens served as the primary diagnostic approach for alveolar hydatid disease. However, radiographic imaging has proven beneficial in certain cases, particularly when peculiar calcification patterns are observed within the mass.

At least two of the four following criteria have to be present for diagnosis of the disease: (I) characteristic lesions shown by imaging; (II) specific serum antibodies to *Echinococcus* antigens detected on laboratory tests; (III) pathologic verification of *E. multilocularis* metacestodes; (IV) identification of parasite nucleic acids in clinical specimens <sup>[4]</sup>.

Commonly used modalities for diagnosis and follow up include ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI).

Ultrasound is a cheap, easily available, dynamic and radiation free modality, US can be used as a fast diagnostic modality in endemic areas populations as a screening tool <sup>[5, 6]</sup>. Most common pattern of involvement is mixed heterogeneous echogenic pattern with ill-defined margins with internal cystic necrotic areas and multiple calcific foci. Other patterns of involvement include pseudocyst with a large central necrotic area with peripheral irregular rind of hyperechogenicity representing fibrous tissue. Less typical sonographic appearance is the hailstorm pattern with multiple hyperechoic solid nodules or a pseudocyst with massive necrosis mimicking cystadenoma, cystadenocarcinoma <sup>[7-9]</sup>. Color Doppler shows absence of vascularity within lesion. USG can be used for assessing distortion and displacement of the hepatic veins, portal vein, and biliary tree resulting from mass effect or their invasion and secondary biliary duct involvement and intrahepatic biliary duct dilatation.

Computerized tomography is the workhorse for anatomic localization and morphologic characterization of alveolar echinococcosis lesions and best depicts the characteristic pattern of calcification <sup>[10]</sup>. It also

helps determine the number, size, and location of lesions in the liver and allows assessment of relation of lesion to adjacent vascular structures and bile ducts. Extrahepatic extension or organ involvement as well as staging as per PNM classification can be done with CT <sup>[11,12]</sup>. Triad of heterogeneity, calcification, and absence of contrast enhancement in a hepatic lesion are highly suggestive of alveolar echinococcosis. Most common pattern of involvement is an infiltrating non enhancing tumor like hepatic mass with irregular margins and heterogeneous contents with including scattered hyperattenuating calcifications and hypoattenuating areas corresponding to necrosis and parasitic tissue; these are characteristic findings of alveolar echinococcosis. Mild enhancement in the peripheral fibro-inflammatory tissue on delayed phase can be seen. Extrahepatic primary organ involvement is very rare. The lungs are the most commonly involved organs with secondary AE <sup>[13]</sup>. They are seen as low-density masses with lobular contours on CT. Calcifications as well as cavitation can be detected inside the lesions <sup>[14]</sup>. Invasions of the diaphragm, perirenal region, abdominal lymph nodes, peritoneum, mesenteric tissues, spleen, pancreas, adrenal glands, kidneys, gallbladder, retroperitoneum, abdominal wall, and the stomach have been reported <sup>[9, 14, 15-17]</sup>. The spleen is the most commonly invaded intra-abdominal organ by metastasis.

The characteristic CT findings with positive serology could diagnose liver hydatid with significant accuracy avoiding biopsy. In our study three patients were having metastatic lesions in lung and brain. Five patients were showing infiltration into portal vein and IVC. All the patients with distal metastasis were having vascular infiltration.

To provide an international benchmark for evaluating measures of diagnostic performance and therapeutic outcomes, the World Health Organization Informal Working Group on Echinococcosis established a “PNM” classification system <sup>[11,19]</sup>. The PNM classification system describes the presence of a hepatic parasitic mass (P), involvement of neighboring organs (N), and involvement of distant sites (M) (Table 1) <sup>[14]</sup>. The purpose of PNM classification is to improve the quality of treatment and allow uniform evaluation of outcomes across healthcare institutions <sup>[8]</sup>.

Table 1

PNM Classification of Alveolar Echinococcosis	
P	Primary lesion localized to the liver
P0	No detectable hepatic lesion
P1	Peripheral hepatic lesion with no proximal hepatic vascular or biliary involvement
P2	Central hepatic lesion with proximal involvement of vessels or biliary ducts in one lobe
P3	Central hepatic lesion with involvement of hilar vessels or biliary ducts in both lobes or with involvement of two hepatic veins
P4	Hepatic lesion with extension along the vessels† and biliary tree
N	Extrahepatic involvement of neighboring organs or tissues (diaphragm, lung, pleura, pericardium, heart, gastric or duodenal wall, adrenal gland, peritoneum, retroperitoneum, parietal wall [muscles, skin, bone], pancreas, regional lymph nodes, hepatic ligaments, kidney)
NX	Cannot be evaluated
N0	No regional involvement
N1	Regional involvement of contiguous organs or tissues

M	Absence or presence of distant metastasis (in lung, distant lymph nodes, spleen, central nervous system, orbits, bone, skin, muscle, kidney, distant peritoneum, and retroperitoneum)
MX	Not completely evaluated
M0	No metastasis <sup>‡</sup>
M1	Metastases
†Vessels include the inferior vena cava, portal vein, and arteries	
‡Absence of metastases is considered to be indicated by negative findings at chest radiography and CT of the brain.	

MR imaging is the best modality for characterizing the components of parasitic lesions <sup>[2]</sup> and depicting vascular or biliary tree involvement and extrahepatic extension. Characteristic MR imaging features of alveolar echinococcosis include a heterogeneous infiltrative mass with irregular margins and a necrotic center that exhibits low to intermediate signal intensity on T1-weighted images and heterogeneous signal intensity (areas of low and high signal intensity) on T2-weighted images <sup>[7]</sup>. Areas of high T2 signal intensity correspond to small cystic or necrotic components, whereas areas of low T2 signal intensity correspond to fibrotic or collagenous components. T2-weighted images are useful for detecting small hepatic cysts and extrahepatic cysts. Presence of fat and hemorrhage is not seen in alveolar hydatid. Delayed enhancement of the peripheral fibroinflammatory component is observed in some alveolar echinococcosis lesions on contrast enhanced images. Kodama et al. <sup>[18]</sup>, proposed an MRI classification for liver AE lesions, with five types: type 1 (4%), multiple small round cysts without a solid component; type 2 (40%), multiple small round cysts with a solid component; type 3 (46%), a solid component surrounding a large and/or irregular pseudocyst with multiple small round cysts; type 4 (4%), a solid component without cysts; type 5 (6%), a large cyst without a solid component. In their series, small parasitic cysts were detected in 96% of lesions.

Upcoming modalities include PET-CT and contrast enhanced ultrasound. FDG uptake is positive in the peripheral zones of the parasitic lesions, no uptake is present in the central necrotic tissue <sup>[21]</sup>. <sup>18</sup>F-FDG PET-CT has been considered as a reliable method for differentiation between inactive and active AE lesions <sup>[22]</sup>. It has especially been proposed for the medical treatment planning of alveolar hydatid disease <sup>[22,23]</sup>.

Kashmir is a highly endemic region for Echinococcosis Multilocularis. Both males and Females are equally susceptible to this parasitic infection. Since liver is the most Organ involved by it, most common presentation of right upper quadrant pain can be explained by anatomic localization of liver. Jaundice was due to biliary infiltration by alveolar hydatid. P2N0M0 was the most common stage found in our study on Contrast enhanced computerized tomography. This may be explained by the fact Alveolar echinococcosis is a chronic disease with a latent stage that may last years before signs and symptoms develop. Hence, P1N0M0 stage is less often seen on CECT than P1. Adrenal gland and anterior abdominal wall were the two neighboring structures involved by Alveolar Echinococcosis. Adrenal gland involvement in AE is very rare. Kamishima et al. <sup>[24]</sup> first reported it in a 77-year-old patient monitored for hypertension who



was found to have primary right adrenal gland involvement. According to our study, both calcification and heterogeneity were characteristic of Alveolar Echinococcosis. Heterogeneity was described as presence of both hyper and hypoattenuating areas within the lesion. Till date there haven't been any studies describing universal computerized Tomography features of alveolar Echinococcosis.

**Figures:**

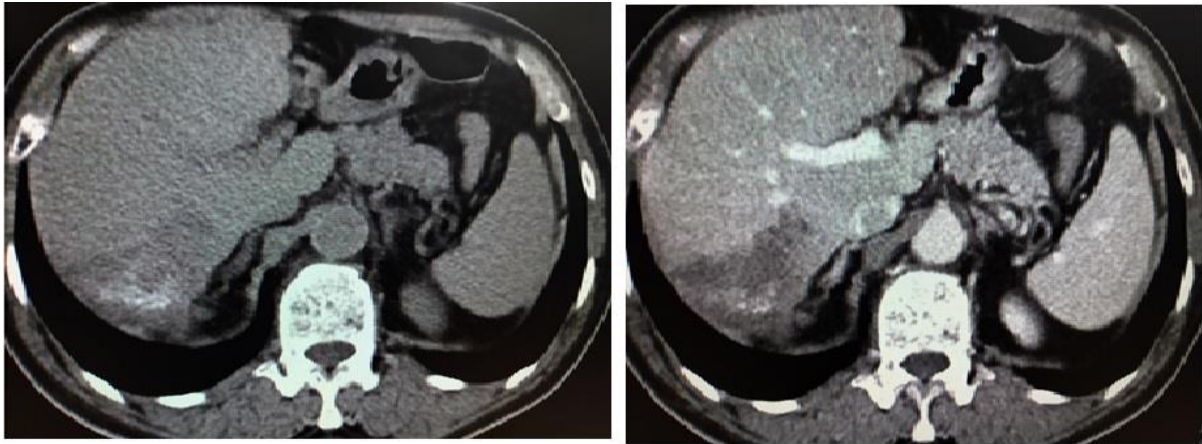


Fig 1: Non contrast and Contrast enhanced computerized tomography revealing evidence of peripheral heterogeneous ill-defined non enhancing mass in segment VII with internal calcifications. Lesion is not infiltrating into any proximal vessel although it's abutting right hepatic vein. There is no evidence of any Intrahepatic Biliary dilatation consistent with stage P1.

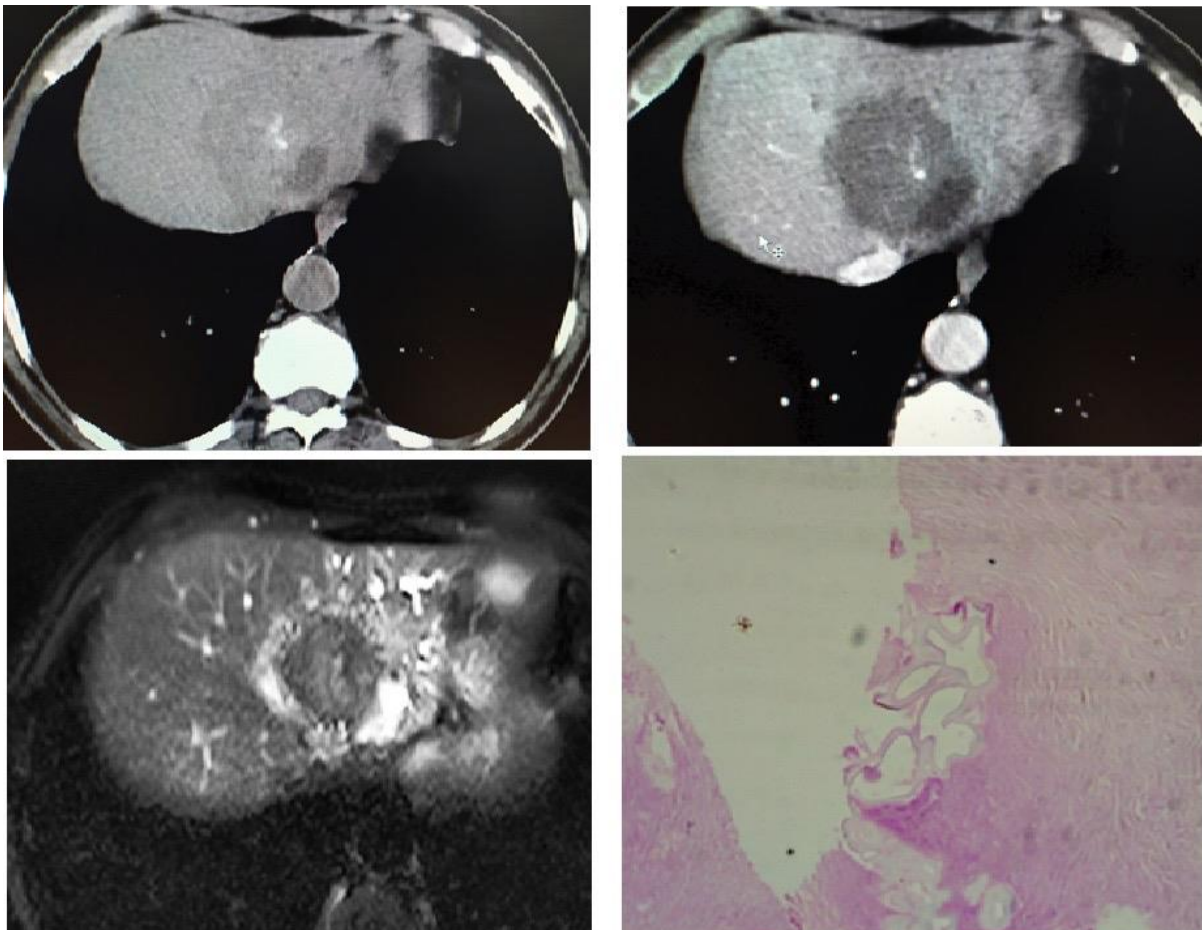


Fig 2: Non contrast computerized tomography reveal evidence of heterogeneous predominantly hyperattenuating ill defined lesion with coarse calcification and internal hypoattenuating area in segment II of liver. Post contrast CT reveals no enhancement of lesion with conspicuous internal cystic area and peripherally small linear hypoattenuating areas consistent with dilated intrahepatic Biliary radicals consistent with P2 stage. T2 weighted MRI image reveals evidence of hypointense lesion with internal T2 hyperintense area with surrounding edematous changes and dilated linear hyperintense areas consistent with IHBRs. Photomicrograph (periodic acid–Schiff stain) shows deranged liver architecture with liver parenchyma infiltrated by multiple irregular cysts with stained laminar membranes.

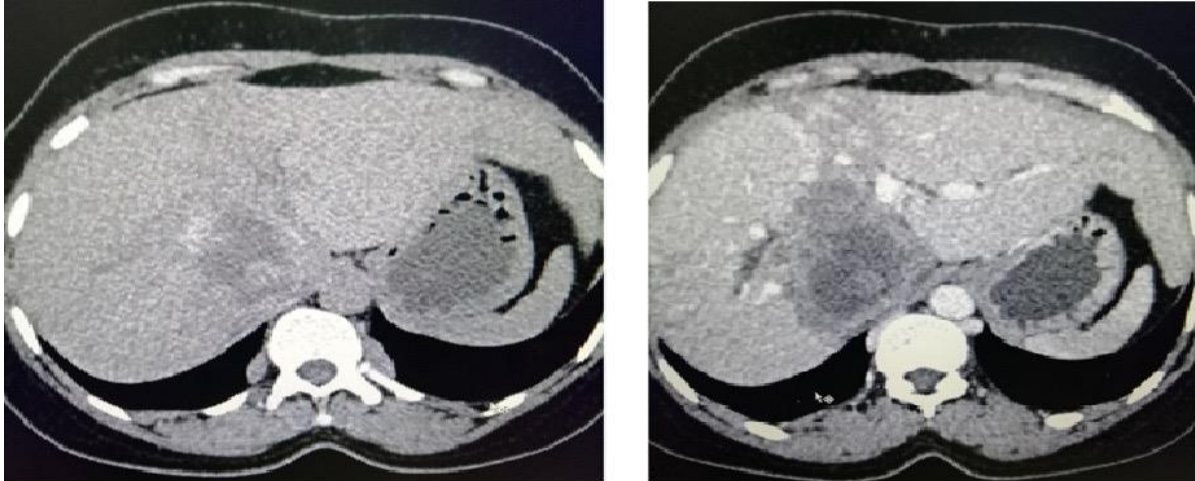


Fig 3: Non contrast and contrast enhanced computerized tomography revealing evidence of centrally based ill defined heterogeneous lesion involving both right and left lobe with internal calcification infiltrating into inferior vena cava and portal vein mimicking leiomyosarcoma of IVC. There is evidence of intrahepatic venous collaterals and dilated IHBR consistent with P3 stage.



Fig 4: Axial Non contrast and contrast enhanced CT revealing evidence of large heterogeneous infiltrating non enhancing mass with internal calcification predominately in right lobe of liver with extension into left lobe. Sagittal CECT confirms extension into both lobes. Mass is infiltrating into right and middle hepatic vein (which are not seen), portal vein and biliary radicals.





Fig 5: contrast enhanced CT revealing evidence of ill defined, soft tissue lesion infiltrating along porta hepatis( portal vein, hepatic artery and common biliary duct) consistent with stage P4. There is evidence of dilated Intrahepatic biliary radical in right lobe. Patient had drain for aspirating contents of alveolar hydatid. This was one of the patients without any calcification in hepatic mass



Fig 6: Ultrasound of the same patient revealing heterogeneous mass. Axial Non contrast and Coronal contrast enhanced CT reveals evidence of ill defined hepatic lesion infiltrating into right adrenal gland. Hyperattenuating areas within lesion were due to calcification. This represents N1 stage as per PNM classification.

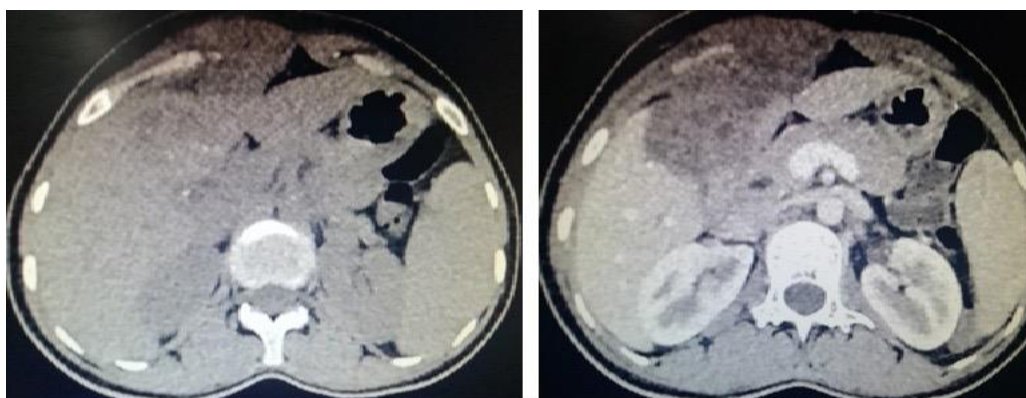


Fig 7: Non contrast and contrast enhanced CT reveals evidence of ill-defined heterogeneous lesion with internal tiny nodules(Hailstorm appearance) and tiny calcifications with no enhancement infiltrating into anterior abdominal wall. Mass had ill-defined margins with pancreas. This is consistent with N1 stage as per PNM classification.



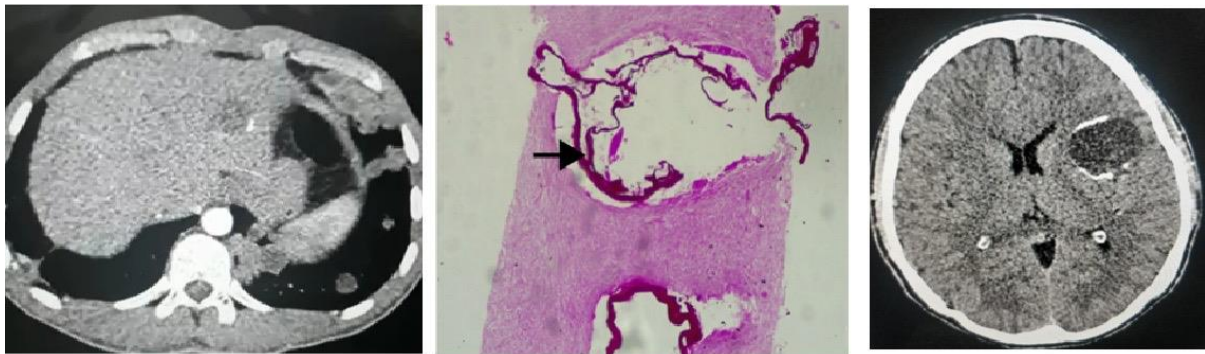


Fig 8: Contrast enhanced CT reveals evidence of hypodense lesion in Liver with calcification. There is evidence of multiple well and ill-defined hypoattenuating and heterogeneous lesions in left lung base. Biopsy from both liver and lung lesion revealed alveolar Echinococcosis. Photomicrograph (periodic acid–Schiff stain) shows darkly stained lamellar membranes (arrow). This was consistent with Stage M1 as per PNM Classification. It's important to note that different morphological forms can occur in same patient. Non contrast CT reveals hypoattenuating lesion with peripheral calcification in left cerebral hemisphere centered upon grey white junction.

### Conclusion:

Contrast enhanced computerized tomography has a very important role to suggest diagnosis of Alveolar Echinococcosis. In endemic regions like ours the characteristic CT findings with positive serology could diagnose liver hydatid with significant accuracy avoiding biopsy. In third countries like ours MRI is not accessible and affordable to most of the population and also, MRI has long acquisition times. Radiologists especially those residing in endemic region must be aware of Imaging findings of Alveolar Echinococcosis so that they can direct clinicians to take proper therapeutic decision. These lesions can be miss diagnosed as inflammatory fibroblastic tumors, leiomyosarcoma, metastasis etc.

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