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Imaging Characteristics and Diagnostic Challenges of Alveolar Hydatid Disease in The Liver: A Comprehensive Analysis

Maria Wani[1], Aala Muzamil[1], Ayaan Altaf[2]* and Feroze A. Shaheen[1]

[1]Department of Radiodiagnosis, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India;
[2]Department of General Medicine, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India

E-mail/Orcid Id:

MW, altafwani1958@gmail.com; *AM*, ailazmuzamil@gmail.com;
AA, haltafwani@gmail.com; drayanaltaf@gmail.com https://orcid.org/0009-0003-2473-9467; *FAS*, ferozeshaheen@gmail.com

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Abstract: Alveolar Hydatid Disease (AHD) of the liver, primarily caused by the parasitic infection *Echinococcus multilocularis*, presents a formidable diagnostic challenge. This disease mimics a range of hepatic conditions, complicating accurate identification and timely treatment. Our study aimed to delineate the distinct imaging characteristics of AHD, facilitating better diagnostic accuracy. In this prospective study, we analysed the imaging results from thirty-five patients with confirmed AHD, either through pathology or serology. Utilizing contrast-enhanced Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), we thoroughly evaluated the radiological signatures specific to AHD. The findings demonstrated that amorphous calcifications, a hallmark of AHD, were consistently present across all patients in CT scans. MRI revealed a predominant pattern of large solid lesions accompanied by significant cystic or necrotic components. These imaging traits are critical in differentiating AHD from other hepatic diseases, such as hepatocellular carcinoma or metastatic liver disease, which often present with similar symptoms but require vastly different treatment approaches. Our study underscores the necessity of recognizing these specific imaging patterns early in the diagnostic process, a step that is crucial for the implementation of effective treatment strategies. In conclusion, this study provides valuable insights into the imaging characteristics of AHD, highlighting the role of advanced imaging techniques in improving diagnostic accuracy. These findings are a significant contribution to the medical field, especially for radiologists and clinicians dealing with hepatic diseases, enhancing patient outcomes through precise diagnosis and timely intervention.

Introduction

Alveolar Hydatid Disease (AHD) of the liver, a parasitic infection caused by *Echinococcus multilocularis*, presents significant diagnostic and therapeutic challenges (Bhatia et al., 2016). Predominantly found in the northern hemisphere, including North America, Central Europe, and Asia, the life cycle of the parasite involves small rodents as intermediate hosts and canids as definitive hosts (Bhatia et al., 2016; Torgerson et al., 2010). Humans become accidental hosts through the ingestion of parasite eggs, leading to AHD development (Mortele et al., 2017). This disease mimics malignant tumors in their slow and invasive growth pattern, contributing to the complexity of its clinical and radiological presentations (Alshoabi et al., 2023). Patients may exhibit symptoms ranging from mild abdominal discomfort to severe hepatic failure. This symptom variability often leads to delayed or misdiagnosis, negatively impacting prognosis (Maddah et al., 2016; Nunnari et al., 2012). AHD's ability to mimic other hepatic conditions, such as hepatocellular carcinoma, metastatic liver disease, and other cystic hepatic lesions, further complicates the diagnosis (Bhatia et al., 2016; Chouhan, Wiley et al., 2019). Traditional diagnostic approaches, including serology, are limited in sensitivity and specificity, increasing reliance on imaging techniques for accurate diagnosis (Sarkari and Rezaei, 2015).

***Corresponding Author:** haltafwani@gmail.com/drayanaltaf@gmail.com

Imaging modalities, particularly computed tomography (CT) and magnetic resonance imaging (MRI), are critical in diagnosing AHD (Abbasi et al., 2021; Mehta et al., 2016). These techniques provide a detailed visualization of the liver, allowing for a more accurate assessment of the lesion extent and nature (Abbasi et al., 2021; Mehta et al., 2016; Paul and Sadhukhan, 2023). Typical imaging findings include heterogeneous, multivesicular lesions with calcifications and a propensity for local invasion (Parry et al., 2020; Srinivas et al., 2016). However, despite advancements in imaging technology, there is a need for in-depth studies to better understand AHD's specific imaging characteristics (Parry et al., 2020; Srinivas et al., 2016). In addition to imaging, recent advancements in molecular techniques offer promise for more sensitive and specific diagnosis (Knapp et al., 2022). Polymerase chain reaction (PCR) and other molecular methods are being explored to detect E. multilocularis DNA in clinical samples, providing a more definitive diagnosis (Knapp et al., 2022). This molecular approach could supplement traditional methods, improving diagnostic accuracy, especially in the early stages of the disease. The management of AHD remains challenging due to its aggressive nature. Surgical resection is often considered the most effective treatment, aiming to remove all the parasitic tissue (Christodoulidis et al., 2021; Kern, 2010). However, due to the invasive nature of the disease, complete resection is not always possible. In such cases, long-term administration of antiparasitic drugs, such as albendazole, is required to control the infection (Kern, 2010).

Prevention strategies focus on breaking the lifecycle of *E. multilocularis*. Public health measures include deworming of domestic dogs in endemic areas, public education on the risks of eating contaminated food, and improved sanitation to reduce environmental contamination with parasite eggs (Torgerson et al., 2010). AHD of the liver poses a significant health challenge due to its complex lifecycle, varied clinical presentation, and difficulty in achieving an early and accurate diagnosis (Wazir et al., 2023). While imaging techniques have improved diagnosis, there is a need for further research into specific imaging characteristics and molecular diagnostics. Management strategies must balance surgical and pharmacological approaches, underlined by effective public health measures to prevent transmission (Horkaew et al., 2023). Continued research and awareness are crucial in improving outcomes for individuals affected by this rare but severe parasitic infection (Horkaew et al., 2023). Despite advancements in imaging technology, there remains a need for in-depth studies to understand the specific imaging characteristics of AHD better (Horkaew et al., 2023; Vernuccio et al., 2021). This study aims to bridge this gap by providing a detailed analysis of the CT and MRI findings in confirmed cases of AHD. By focusing on the unique imaging patterns, the study endeavours to enhance the diagnostic accuracy for AHD, contributing to improved clinical outcomes. Through a comprehensive analysis of imaging findings and a review of current literature, this study aims to provide a clearer understanding of the radiological aspects of AHD. The ultimate goal is to aid in differentiating AHD from other hepatic pathologies, ensuring timely and appropriate treatment of affected patients.

Methodology

This study was conducted at the Sher-I-Kashmir Institute of Medical Sciences over a span of two years (2021-2023). The primary objective was to investigate the imaging characteristics of Alveolar Hydatid Disease (AHD) of the liver using both Computed Tomography (CT) and Magnetic Resonance Imaging (MRI).

Ethical Approval

The present study was exempted from ethical clearance for the following reasons:

The study was retrospective and non-interventional, utilizing existing imaging data without directly involving patients or affecting their treatment course. The data used in the study was anonymized, ensuring patient confidentiality and privacy were maintained, which was in line with ethical research practices. The primary focus was on the analysis of imaging characteristics, which is a standard and established practice in radiological research, typically not requiring specific ethical approval when using anonymized data.

Patient Selection

A total of thirty-five treatment naive patients with pathologically or serologically confirmed AHD of the liver were included in this study. The inclusion criteria were based on a definitive diagnosis of AHD, either through pathological examination (Figure 1) or serological testing. Apart from a single patient who presented with a positive serology and the classical imaging characteristics, all the rest were confirmed using histopathological examination. Patients who had resorted to any form of treatment or else had any contraindications to MRI, such as implanted medical devices not compatible with MRI or severe claustrophobia, were excluded from the study.

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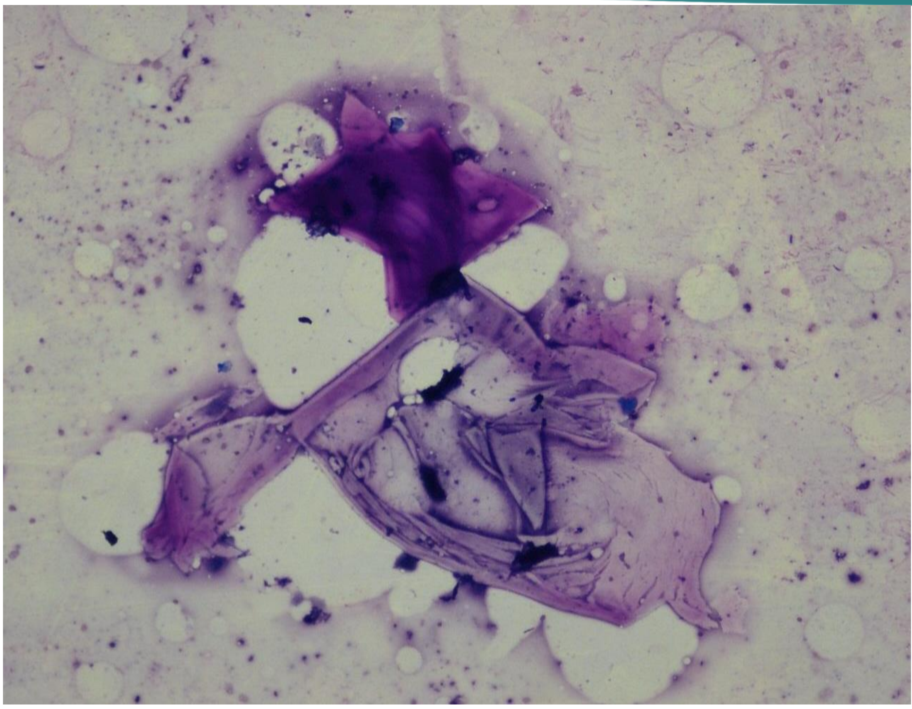

Figure 1. Shows fine needle aspiration smear with bits of acellular laminated membrane of hydatid cyst in a proteinaceous background (Giemsa, 40X).

Imaging Protocols

CT Imaging

Contrast-Enhanced CT (CECT) scans were performed using a 16-slice Siemens scanner. The protocol involved acquiring non-contrast, arterial, and venous phase images following the intravenous administration of 100 ml of Iohexol. This comprehensive approach was designed to capture the various phases of liver enhancement, which is crucial in identifying and characterizing liver lesions.

MRI Imaging

MRI scans were obtained using a 1.5 Tesla Avanto Magnetom Siemens scanner. The same patients underwent MRI scans to correlate with CT findings and provide a comprehensive imaging assessment. The MRI sequences deployed were:

Axial T2 Turbo Spin Echo (TSE) with TR 4240ms, TE 90ms, Flip angle 15^o.

Axial and coronal Half-Fourier Acquisition Single-shot Turbo spin Echo (HASTE) with TR 900ms, TE 80ms, Flip angle 15^o.

Axial T1 Turbo Spin Echo (TSE) with TR 450ms, TE 10ms, Flip angle 15^o

T1 post-contrast Volumetric Interpolated Breath-hold Examination (VIBE) with TE 1.97, TR 4.33

Diffusion Weighted Imaging (DWI) at b values of 100, 500, and 900 s/mm^2.

These sequences were selected to provide detailed information on the lesion's morphology, signal characteristics, and enhancement patterns, essential for accurate diagnosis and characterization of AHD.

Data Analysis

All imaging was reviewed and analysed by the same experienced radiologists to maintain consistency in the interpretation of the findings. The focus was on identifying typical and atypical imaging characteristics of AHD, such as calcifications, lesion size, and the presence of cystic or necrotic components. For the analysis of the collected data, SPSS version 23.0 (SPSS Inc., Chicago, IL, USA) was utilized. The statistical tests were performed at a significance level (alpha) of 0.05. This threshold is standard in medical research, indicating that results with a p-value less than 0.05 are considered statistically significant. The use of SPSS enabled the application of various statistical methods to analyze the imaging findings from the CT and MRI scans. The tests likely included descriptive statistics to summarize the data, such as mean and standard deviation for continuous variables (e.g., size of lesions, age of patients) and frequencies and percentages for categorical variables (e.g., prevalence of specific imaging characteristics). Additionally, inferential statistical tests might have been used to examine the relationships between different variables or to compare subgroups within the study population. The choice of specific statistical tests would have been based on the nature of the data and the specific research questions or hypotheses being tested. This comprehensive approach ensures that the findings are not only scientifically valid but also relevant to the clinical management of Alveolar Hydatid Disease of the liver.

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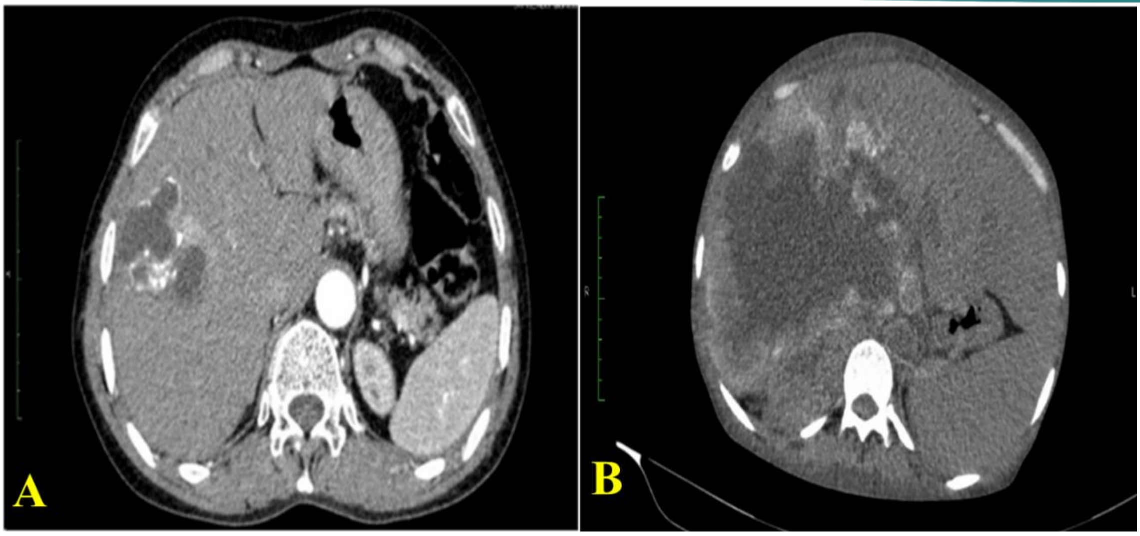

Figure 2. Illustrates the varied calcification patterns in Alveolar Hydatid Disease of the liver: Panel (A) displays clustered nodular and interrupted rim calcifications along the lesion's periphery, while Panel (B) demonstrates the widespread distribution of amorphous calcifications at the lesion's fringe.

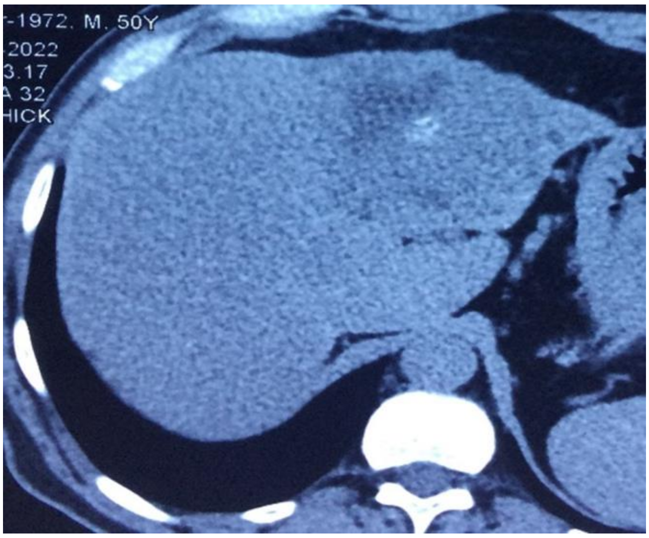

Figure 3. It depicts a notable case of central calcification within an alveolar hybrid disease lesion, as clearly visualized in non-contrast computed tomography (NCCT) images.

Results

Our study observed a variable appearance of liver lesions on cross-sectional imaging. Contrast-Enhanced Computed Tomography (CECT) revealed three different morphological types of the lesion. These included thick-walled lesions with central necrotic or cystic components, multiloculated cystic lesions with irregular walls, and predominantly solid lesions. Notably, these lesions appeared as aggressive-looking masses, which could potentially mimic tumors due to their indistinct morphology, as noted in similar studies. The average size of the lesions was 8cm (range 5-13cm) with an average of involvement of 4 hepatic segments. The right lobe of the liver was more commonly involved (88%, $p<0.05$). Regarding the calcification patterns, all lesions exhibited calcifications. The lesions predominantly showed amorphous calcifications, with focal and clustered nodular calcifications observed in 62% of the cases, interrupted rim calcifications seen in 32% of the cases and both in 8% (Figure 2A and B; $p<0.05$). The distribution of these calcifications was mainly peripheral in almost all the lesions, except for two cases where central calcification was observed **(**Figure 3). In terms of enhancement patterns, 96% of the lesions showed minimal patchy peripheral enhancement on both arterial and venous phases, with no significant enhancement within the lesions themselves ($p<0.05$). This peripheral enhancement could most likely reflect a reactive inflammatory response.

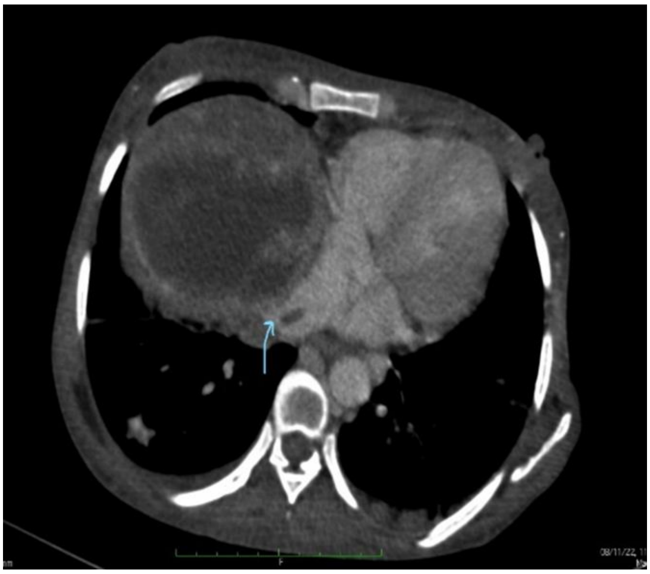

Figure 4. Represents the rare and significant extension of an Alveolar Hydatid Disease lesion into the Inferior Vena Cava (IVC), as indicated by the curved arrow, highlighting a critical aspect of the disease's aggressive nature and its potential for vascular involvement.

The study also revealed associated complications. Approximately 30% of the subjects had occlusion of a first or second-degree branch of the portal vein ($p<0.05$), with the former being more common. Additionally, two cases presented with occlusion of one or more hepatic veins and the inferior vena cava (IVC), with one of these cases showing extension of the lesion into the IVC and right atrium (Figure 4). One case involved the rupture of the lesion, extending beyond the anatomical confines of the liver. Dilatation of intrahepatic biliary radicles was noted to be focal in most cases, observed in only 26% of the cases ($p<0.05$). The CT images could not conclusively establish the presence or absence of communication with the biliary radicles. MRI findings were found to be very similar to those of CECT. The typical signal characteristics included T1 isointense to hypointense signals, with the solid parts of the lesion showing a corresponding isointense signal on T2-weighted images and the cystic components exhibiting a bright signal. Notably, the lesions often displayed scattered areas hypointense to the paraspinal musculature, indicative of calcifications.

The morphology of the lesions, when analysed via MRI, allowed for a better appreciation of the cystic components and could be categorized into broader types (Table 1). According to the classification model suggested by Kodama et al. (2003) there are five types of lesions. In our study, the majority were type 3 lesions, consisting of a solid component surrounding a large pseudocyst with multiple small cysts, followed closely by type 2 lesions comprising multiple small cysts with a solid component (Figure 5; $p<0.05$). The margins of most of the lesions (92%) were irregular, with some lesions (5%) illustrating an infiltrative margin. Well-circumscribed margins were seldom noted (3%).

Table 1. Showing the percentage incidence of the various morphological patterns of alveolar hydatid disease in our study.

Morphology of lesion	% incidence
Kodama type 1	2
Kodama type 2	40
Kodama type 3	52
Kodama type 4	6
Kodama type 5	0

With regard to the diffusion-weighted imaging, most lesions did not show any diffusion restriction. However, approximately 20% of the lesions exhibited central restriction on DWI, suggestive of a likely superadded infection. Contrast enhancement patterns on MRI mirrored those observed on CECT, with most lesions showing a peripheral rim of enhancement (Figure 6). Furthermore, MRI proved effective in establishing communication with the biliary radicles when present. However, in most cases, the biliary ductal dilatation appeared more as a consequence of the mass effect rather than direct communication with the lesion. There were a few atypical cases with the lesion showing infiltrative morphology with ill-defined borders and no cystic components on MRI. In these cases, the diagnosis was suggested by CT imaging, which manifested the calcifications (Figure 7). We followed the patients over a variable span of time who resorted to medical or surgical treatment. The patients put on Albendazole didn't seem to respond to the treatment, with some patients showing serial increase in the size of the lesion despite the drug administration ($p<0.05$). The only definitive treatment option for such patients has been lobar or segmental resection of the liver, depending on the extent of the lesion. The post-operative course wasn't uneventful either. While a few cases developed perihepatic collections (Figure 8), some even developed biliary strictures, thereby requiring percutaneous transhepatic biliary drainage procedures.

Discussion

The variable appearance of liver lesions in Alveolar Hydatid Disease (AHD) as observed in our study through cross-sectional imaging,, enriches the current understanding of this complex parasitic infection. The types of lesions identified through Contrast-Enhanced Computed Tomography (CECT), including thick-walled lesions with central necrotic or cystic components, multiloculated cystic lesions with irregular walls, and predominantly solid lesions, align with the previous descriptions of AHD as aggressive-looking masses that closely mimic tumors (Mavilia et al., 2018). This mimicking is particularly challenging for differential diagnosis, as also noted in the studies by (Bulakci et al., 2016; Kantarci et al., 2012). These similarities to malignant tumors underscore the need for radiologists and clinicians to maintain a high degree of suspicion for AHD in patients presenting with such liver lesions, especially in regions where *Echinococcus multilocularis* is endemic (Graeter et al., 2016; Kovac et al., 2022). The

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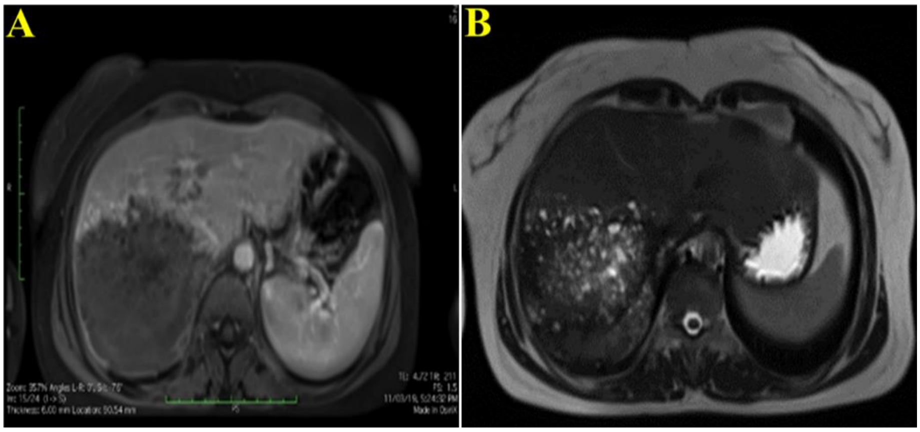

Figure 5. Demonstrates the classification of Alveolar Hydatid Disease lesions according to Kodama et al.'s model: Panel (a) illustrates a post contrast T1 weighted image with Type 3 lesion, characterized by a solid component surrounding a large non-enhancing pseudocyst with multiple small cysts at the periphery, and Panel (b) depicts an axial T2 weighted image with Type 2 lesion, marked by multiple small cysts with a solid component.

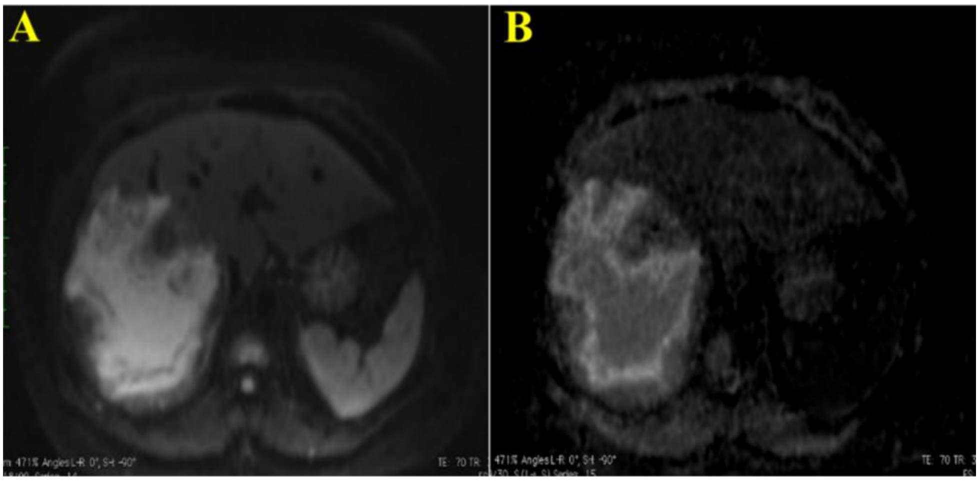

Figure 6. Displays Diffusion Weighted Imaging (DWI) and corresponding Apparent Diffusion Coefficient (ADC) maps, revealing central restriction in a known case of Alveolar Hydatid Disease, particularly in a patient presenting with fever, thereby illustrating the potential complexity in diagnosis due to overlapping symptoms with other conditions.

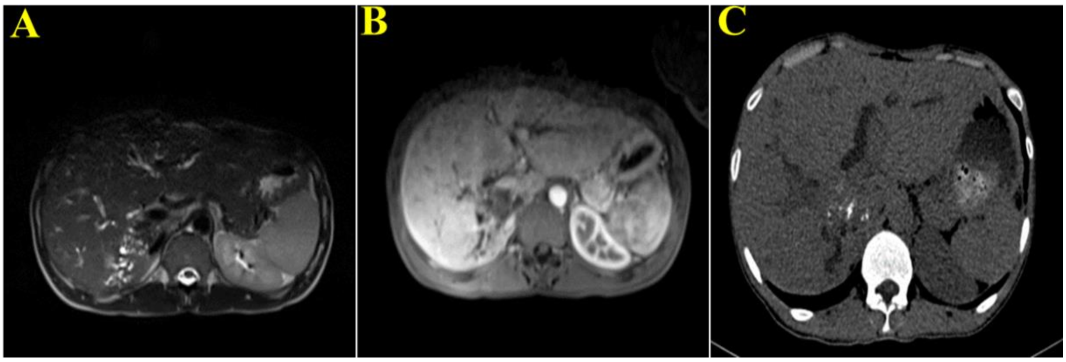

Figure 7. Axial T2 weighted image shows a hypointense lesion in segment seven of liver with proximal dilatation of biliary radicles with no definite intralesional cystic component (a) and no definite enhancement on axial T1 post-contrast imaging(b). Axial NCCT revealed nodular calcifications in the lesion(c).

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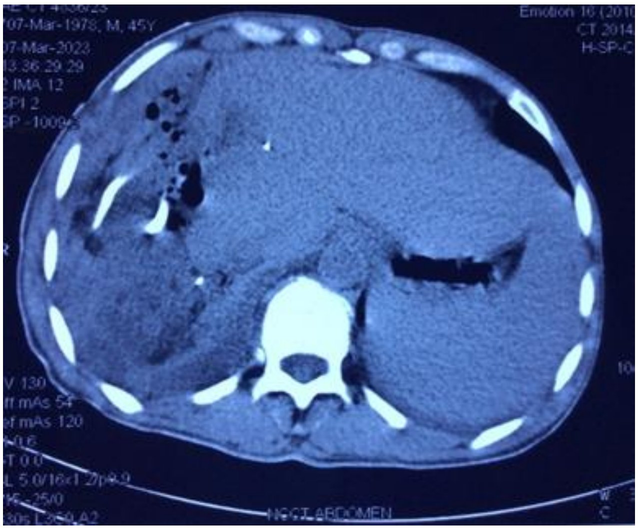

Figure 8. Showing post-operative air containing collection following resection of right lobe of liver for alveolar hydatid.

morphology of these lesions, particularly the thick-walled appearance with central necrosis, is intriguing. This characteristic can be misleading, as similar features are often observed in hepatocellular carcinoma or metastatic liver disease (Kim et al., 2019). The clinical implications of this are significant; a misdiagnosis can lead to inappropriate treatment strategies, potentially worsening patient outcomes (Khullar et al., 2015; Kim et al., 2019). Therefore, understanding the subtleties in these imaging characteristics is crucial for accurate diagnosis and appropriate management (Khullar et al., 2015; Kim et al., 2019).

Our study's observation of calcification patterns in AHD lesions adds another layer to the diagnostic puzzle. The predominance of amorphous-type calcifications in all lesions and the presence of focal and clustered nodular calcifications in a majority of cases is consistent with the findings of Kodama and co-workers (Kodama et al., 2003)**.** Furthermore, the peripheral interrupted rim calcifications seen in a substantial portion of our cases align with the earlier research (Eckert and Deplazes, 2004; McManus et al., 2003). These patterns are not only characteristic of AHD but are also critical in differentiating it from other hepatic lesions, such as simple cysts or haemangiomas, which typically do not exhibit such calcification patterns (Mavilia et al., 2018). The presence of these specific calcification types is thus a key diagnostic marker in AHD and can guide clinicians towards more targeted and effective treatment strategies. The enhancement patterns observed in the present study, characterized by minimal patchy peripheral enhancement and a lack of definitive enhancement within the lesion, are particularly noteworthy. This pattern contrasts with that seen in other hepatic pathologies, where lesions often show more pronounced internal and peripheral enhancement (Kwee and Kwee, 2019). The peripheral enhancement observed in AHD is likely indicative of a reactive inflammatory response, supporting the hypothesis suggested by Bulakçı et al. (2016). Recognizing this pattern is crucial for radiologists, as it aids in differentiating AHD from other hepatic malignancies and infections, thereby preventing misdiagnosis (Zhang et al., 2022). Our study also sheds light on the complications associated with AHD, a crucial aspect of the disease's clinical profile. The portal vein branch occlusion observed in approximately 30% of our subjects reflects the aggressive nature of AHD and its propensity to invade vascular structures (Quarrie and Stawicki, 2018). This finding is consistent with the clinical complexities described by McManus et al. (2003). The identification of such vascular involvement has important implications for the surgical management of AHD, as it may necessitate more complex and high-risk procedures (Mulroy et al., 2021). Additionally, the occurrence of hepatic vein and inferior vena cava (IVC) occlusion, as well as lesion rupture beyond the liver's anatomical confines, further highlights the aggressive behaviour of AHD. These complications are not only indicative of advanced disease but also pose significant challenges in terms of surgical respectability and long-term management (Okuda, 2002). They also underscore the importance of early diagnosis and intervention to prevent disease progression to such advanced stages (Okuda, 2002). Another significant aspect of our findings is the involvement of the biliary system in AHD. The focal biliary dilatation observed in a quarter of our cases is a noteworthy observation. As suggested by Kantarci and colleagues, the involvement of the biliary system in AHD is likely more attributable to mass effect rather than direct invasion by the disease (Kantarci et al., 2012). This distinction has important surgical implications, as it affects the approach to managing biliary complications in AHD. For instance, if biliary involvement is due to mass effect, surgical decompression may be sufficient. In contrast, direct invasion by the disease may require more extensive surgical intervention, including possible resection of affected biliary tracts (Machado, 2011; Matsukuma et al., 2019).

In light of these observations, our study not only corroborates the existing literature but also provides new insights into the imaging characteristics of AHD. By offering a comprehensive analysis of lesion appearance, calcification patterns, enhancement characteristics, and associated complications, we enhance the understanding of AHD's radiological profile. This is crucial for guiding clinicians in making accurate diagnoses and formulating

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effective management plans (Horkaew et al., 2023; Khullar et al., 2015; Kumar et al., 2023; Mehta et al., 2016). Our findings underscore the importance of considering AHD in the differential diagnosis of liver lesions, particularly in endemic areas. Additionally, they highlight the role of advanced imaging techniques in the early detection and characterization of AHD, which is essential for timely intervention and improved patient outcomes. Furthermore, our study contributes significantly to the body of knowledge on AHD. It emphasizes the importance of recognizing specific imaging patterns in its diagnosis and management. This is vital for improving patient outcomes, as early and accurate diagnosis allows for timely and appropriate treatment, potentially preventing complications associated with advanced disease (Liu et al., 2014; Sadr et al., 2023). The detailed analysis provided by our study offers valuable insights for both radiologists and clinicians in their approach to patients with suspected AHD, reaffirming the pivotal role of imaging in the diagnosis and management of this challenging condition.

Conclusion and Future Prospects

Our comprehensive study on the imaging characteristics of Alveolar Hydatid Disease (AHD) significantly contributes to the existing body of knowledge in the field of parasitic infections. By meticulously analysing the variable appearance of liver lesions in AHD through cross-sectional imaging, particularly Contrast-Enhanced Computed Tomography (CECT), we have provided a deeper understanding of the disease's radiological profile. The detailed examination of lesion types, calcification patterns, enhancement characteristics, and associated complications enriches the diagnostic process for this complex condition. The findings from our study underscore the importance of considering AHD in the differential diagnosis of liver lesions, particularly in endemic areas. The ability to differentiate AHD from malignant tumors and other hepatic pathologies through specific imaging patterns is crucial. This differentiation is not only pivotal in guiding clinicians towards accurate diagnosis but also in formulating effective management strategies. Our research highlights the necessity for heightened awareness and expertise among radiologists and clinicians in recognizing the subtle imaging nuances of AHD. Our study paves the way for future research and development in the diagnosis and management of Alveolar Hydatid Disease. Continued exploration in this field is essential for advancing our understanding of AHD, improving diagnostic accuracy, and enhancing patient care and outcomes. As we expand our knowledge and capabilities, we move closer to more effective management and, ultimately, the eradication of this challenging parasitic disease.

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Conflict of interest

The authors declare no conflicts of interest.

Ethical approval

The present study was exempted from ethical clearance due to its retrospective nature.

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