Review

Diagnostic imaging modalities in the study of hepatic alveolar echinococcosis: A review of literature

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Abstract

Objective: This review article aims to summarize the main imaging modalities employed in the diagnosis of hepatic alveolar echinococcosis (HAE) and provide radiologists with an overview of the most relevant diagnostic approaches. **Methods**: A literature review was conducted, selecting the most relevant articles from the past 5–10 years. The search was performed in PubMed, MDPI, Scopus, Web of Science eLIBRARY.RU, using the keywords alveococcosis, hepatic alveolar echinococcosis, echinococcus multilocularis, liver, metastasis, USG, CT, MRI, positron-emission tomography, imaging, diagnosis. Illustrative materials presented in the article originate from the authors' personal archive.

Results: Hepatic alveolar echinococcosis (HAE) is a chronic parasitic disease characterized by an infiltrative growth pattern, often mimicking malignant liver tumors. Its ability to invade adjacent structures and disseminate to distant organs necessitates a comprehensive imaging approach for accurate diagnosis and staging.

Ultrasound (US) serves as the primary screening tool for HAE, particularly in remote endemic regions where advanced imaging modalities may be unavailable. Its accessibility and real-time imaging capabilities allow for the initial detection of hepatic lesions. However, due to its limited ability to assess vascular and biliary involvement, further imaging is required for precise disease evaluation.

Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are the cornerstone imaging techniques for assessing both hepatic and extrahepatic disease extension. CT provides detailed anatomical visualization of the liver parenchyma and is essential for evaluating lesion size, vascular encroachment, and potential metastatic spread. MRI, particularly magnetic resonance cholangiopancreatography (MRCP), is superior in delineating biliary tree involvement, facilitating preoperative planning and surgical decision-making.

To standardize disease staging, the World Health Organization (WHO) has introduced the PNM classification system, which parallels the oncological TNM framework. This classification system enables a systematic assessment of the parasite burden within the liver (P), its invasion of adjacent structures (N), and the presence of distant metastases (M), thereby guiding therapeutic strategies.

Conclusion: Radiologists should be aware of the specific imaging features of HAE to avoid misdiagnosis as a malignancy. A multimodal imaging approach is recommended to ensure accurate diagnosis and staging.

Key words: Alveococcosis, hepatic alveolar echinococcosis, Echinococcus multilocularis, liver, metastasis, ultrasonography, computed tomography, magnetic resonance imaging, positron-emission tomography

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Introduction

Hepatic alveolar echinococcosis (HAE) is a chronic zoonotic infection caused by the pseudo-tumoral intrahepatic development of the larval stage of the tapeworm *Echinococcus multilocularis*, which mainly affects the liver (1, 2). Until the 19th century, the disease was described as one of the forms of liver

tumors, and only in 1856, R. Virchow disclosed its true nature (3).

The natural reservoirs for alveococcus are mainly found in Europe (Poland, Germany, Austria, Switzerland), Russia, Asia (Kyrgyzstan, Kazakhstan, China, Japan), and North America (4, 5).

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Graphical abstract



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Every year around 11 400 to 29 600 people are infected with HAE, with a fatal outcome in 17 000 people (6). According to the World Health Organization (WHO), it causes 19,300 deaths annually (6).

Alveococcosis is defined as 'parasitic cancer', because of its infiltrating nature (7). This is actually appropriate given that the disease has an infiltrating growth pattern and dissemination of larvae from the primary focus to surrounding tissues and organs (8). After a parasitic node grows to a substantial size, it affects the bile and lymphatic ducts or blood vessels, which is a characteristic of malignancy (9-11). Metastases doi: 10.24969/hvt.2025.558

occur when the parasites spread via a hematogenous or lymphatic route secondary to the liver, known as intrahepatic metastases, or when they disseminate to the regional and retroperitoneal lymph nodes, referred to as extrahepatic metastases(10-13). They can expand into neighboring tissues and organs (kidney, bones, diaphragm, further into the pleural cavity and lung, resulting in broncho-biliary fistula), and give distant metastases to the lungs (4.7-20%), brain (1-3.3%), bones, peritoneum, and other organs (14-16). According to studies published, distant metastases of patients range from 6.3% to 34% of cases (17- 22). The spread of the alveolar node through the diaphragm and vascular bed, primarily through the inferior vena cava, can reach the pleural cavity, mediastinum, right side of the heart, and muscles as well (23). With the addition of secondary infection, cholangitis, liver abscesses, suppuration and disintegration of nodes occur (24. 25).

Ultrasound (US) serves as the primary screening tool for HAE, particularly in remote endemic regions where advanced imaging modalities may be unavailable (26). Computed tomography (CT) with bolus contrast is essential for all patients with hepatic alveococcosis, as it provides valuable diagnostic information (27, 28). Implementing CT volumetry is highly recommended for accurately determining the residual volume of the liver parenchyma (29). Magnetic resonance imaging (MRI) is an excellent tool for evaluating vascular and biliary tract involvement (30). Currently, MR cholangiopancreatography has largely replaced percutaneous cholangiography in assessing the relationship between HAE lesions and the biliary tree (31). Without appropriate treatment, parasitic infection leads to death in 95% of cases, typically from hepatic failure or cachexia within 5 to 10 years (32). HAE is diagnosed based on an epidemiological history, physical examination, radiological examination, laboratory tests, and histopathological examination (33, 34). In 1996, based on radiation imaging methods, the WHO Informal Working Group of Experts on Echinococcosis (WHO-IWGE) developed a clinical classification known as the PNM system (P -Parasite, N – Neighboring organs, M – Metastasis), similar to the TNM oncological classification (T -Tumor, N – Nodes, M – Metastasis), to describe the anatomical distribution of the parasitic process (1). In the PNM system, category P evaluates the dissemination of parasites in the liver and the involvement of its tubular structures. Category N accesses the involvement of adjacent organs and anatomical structures. Category M assesses the presence of distant metastases (Table 1) (35).

Table 1. PNM classification of human hepatic alveolar echinococcosis		
Classified according to the data received		
P: Hepatic localization of the primary lesion		
РХ	Primary lesion cannot be assessed	
P0	No detectable liver lesions	
P1	Peripheral lesions without proximal vascular and/or biliary involvement	
P2	Central lesions with proximal vascular and/or biliary involvement of one lobe	
Р3	Central lesions with hilar vascular and biliary involvement of both lobes and/or with involvement of two hepatic veins	
P4	Any lesion with extension along large vessels (IVC, portal vein, hepatic veins, hepatic arteries) and the biliary tree	
N: Extra hepatic involvement of neighboring organs or tissues involving diaphragm, pleura, lungs, pericardium, heart, adrenal glands, kidneys, pancreas, liver ligaments, regional lymph nodes, abdominal walls, muscles, skin, bones		
NX	Cannot be evaluated	
N0	No regional involvement	
N1	Regional involvement of contiguous organs or tissues	
M: Absence or presence of distant metastases (lungs, non-regional lymph nodes, CNS, orbits, bones, skin, muscles, kidneys, abdomen, retroperitoneum)		
MX	Distant organ metastases not completely evaluated	
M0	No distant metastases.	
M1	Distant metastases present	
CNS- central nervous system, PNM – parasite, node, metastasis		
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TabLe 2. Staging of alveolar echinococcosis based on PNM classification			
Stage of alveolar echinococcosis	PNM classification		
Stage I	P1 N0 M0		
Stage II	P2 N0 M0		
Stage IIIa	P3 N0 M0		
Stage IIIb	P1– 3 N1 M0		
Stage IIID	P4 N0 M0		
	P4 N1 M0		
Stage IV	Any P Any N and/or M1		
PNM – parasite, node, metastasis			
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For staging of alveolar echinococcosis, the PNM classification is used (Table 2).

The accurate diagnosis of hepatic alveolar echinococcosis (HAE) is crucial for determining the appropriate treatment strategy and avoiding misdiagnosis as a malignant liver tumor (36). Since HAE exhibits an infiltrative growth pattern and can spread beyond the liver, the selection of imaging modalities must be carefully considered to ensure a comprehensive assessment of the disease (37).

Methods

A systematic literature search was conducted using the databases PubMed, Scopus, Web of Science. The search covered articles published between 2013–2023 and included studies in English and Russian. The following keywords were used: "hepatic alveolar echinococcosis", "metastasis", "imaging modalities", "CT", "MRI", "WHO classification". Studies that did not provide imaging findings or were unrelated to hepatic alveolar echinococcosis were excluded.

Imaging modalities in hepatic alveolar echinococcosis

Some commonly used imaging modalities for the diagnosis and follow-up of HAE include ultrasonography (USG), CT, and MRI (38).

Ultrasound

Ultrasonography is the most effective method for the initial diagnosis and dynamic monitoring of alveococcosis (39, 40). Its main advantage is accessibility, which allows its use in endemic 'hot spots,' significantly reducing the time for primary diagnosis and enabling earlier treatment (41). However, specific details regarding the ultrasonographic semiotics of HAE are scarce in the literature and are found in only limited sources due to the peculiarities of the geographical endemicity of the infection (42, 43). Thus, in B-mode ultrasound (Brightness mode), five types of parasitic nodes are classified (EMUC-US: Echinococcus multilocularis sonomorphological classification): hailstorm, pseudocystic, hemangioma-like, ossification, and metastasis-like (44). Each of these five types has its own characteristic ultrasound patterns (45).

Type 1. Hailstorm is characterized by the presence of hyperechoic structures with/without dorsal acoustic shadowing, indistinct uneven contours, and heterogeneous structure (Fig. 1).

Type 2. Pseudocystic are mainly characterized by a pseudo-cystic pattern with no clear contours, a hypoor an-echoic heterogeneous structure, often with heterogeneous central zone due to hyperechoic inclusions, with a hyperechoic halo (rim), avascular in power or color Doppler imaging. These lesions may be larger than 10 mm. They can develop from the primary hailstorm type, and during initial presentation and scanning of asymptomatic patients, the first two types can be detected simultaneously, forming the "typical pattern of HAE". Sometimes, sizes that can already occupy the entire lobe of the liver (Fig. 2).

Type 3. Hemangiomas-like: these lesions are difficult to distinguish from atypical hemangiomas (eg, that are partially thrombosed); they often create a major diagnostic dilemma. The lesions are characterized by increased echogenicity, and range from indistinct/clearly defined tumors of a heterogeneous structure, relatively echogenic in relation to the liver parenchyma to a pronounced hyperechoic pattern of a homogeneous structure (Fig. 3).

Type 4 Ossification: this pattern is mostly single or multifocal hyperechoic structure with strong dorsal acoustic shadowing. In the differential diagnosis, it is often difficult to distinguish from inflammatory structures or metastases of various carcinomas. Large foci are rare (Fig. 4).

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Figure 3. Hemangiomas-like: Hyperechoic formation (arrow) with unclear, uneven contours with a dorsal acoustic shadowing (star)

Figure 4. Ossification: A single hyperechoic structure (arrow) with a strong dorsal acoustic shadowing (star)

Type 5. Metastasis-like: lesions appear as typical structures of liver metastases (for example, colorectal cancer). However, in general, these are hypoechoic solid structures that do not have a typical rim, unlike metastases, and in the center, there is a hyperechoic heterogeneous scar-type pattern (Fig 5, 6).

USG evaluates the size of the liver, the location and segmentation of the parasitic tumor, as well as the extent of involvement of the tubular structures of the liver (46). It also assesses the relationship of the tumor with the inferior vena cava. It describes the ultrasound characteristics of the node (edges, structure, echogenicity, the presence or absence of calcified inclusions and decay cavities) (47). To assess the blood flow, linear blood flow velocity, volumetric

blood flow velocity, and resistive indices are determined (48). The criteria for invasion are the uneven contour of the vessel wall, its fragmentary hyper echogenicity, turbulent blood flow, and invasion into the lumen (49). Unlike cystic echinococcosis, there are no cysts in alveolar echinococcosis, so to make diagnosis with an ultrasound is often a difficult task for clinicians and radiologists, especially for those who are unfamiliar with this disease (50).

The use of intravenous contrast in ultrasound examination of the liver can provide important additional data to accurately determine the structure of the parasitic node and assess the local spread of the process (51).



It also provides information about the viability and activity of alveococcosis, which helps suggest the prognosis (49).

This method has significant disadvantages, including its dependence on the device and operator, as well as difficulties in detecting small lesions (52). During preoperative preparation, it is essential to complement the obtained data with MRI and multislice CT interpretations to choose the best treatment options (53).

Elastography

Compression elastography and shear wave elastography are used to assess the 'stiffness' and 'elasticity' of pathological liver lesions (54). Alveococcal nodes typically show a high 'stiffness' score when assessed using shear wave elastography (Acoustic Radiation Force Impulse, ARFI). In ARFI VShear (Virtual Touch Quantification Shear Wave) study, the shear wave velocity (SWV) of the pathological node reaches 12.7 m/sec, while the density of the surrounding parenchyma is 2.67 m/sec (or 487 kilopascals (kPa)/22.6 kPa, respectively) (55).

Computed tomography

CT of the abdominal cavity reveals the entire morphological aspect of alveococcal lesions (56). It is one of the primary methods for the objective visualization of parasitic lesions in the liver, allowing for a complete assessment of the anatomical and structural characteristics of the disease (36). It is the best diagnostic method for identifying typical calcified inclusions within lesions, and is especially useful for highly calcified nodules that are difficult to delineate with ultrasound and MRI (57). The use of spiral CT allows determination of the size, number, and location of parasitic foci. It also assesses the degree of invasion into the tubular structures of the liver, which is extremely important for evaluating the extent and resectability of the disease (58). A typical image reveals a tumor-like lesion in the liver with uneven edges and heterogeneous contents (59). These often include calcified inclusions, cysts of various sizes, and areas of necrosis (60).

The generalized primary morphological-tomographic classification of alveolar echinococcosis, known as AEUC (Alveolar Echinococcosis Ulm Classification), developed by T. Graeter, includes five types of foci (61). The AEUC classification, based on computed tomography findings, distinguishes the following five types of alveolar echinococcosis:

Type 1 – Small cystic/metastasis-like: characterized by irregular, homogeneous nodules with minimal signs of degeneration, without calcification or with central calcification (Fig. 7);

Type 2 – Diffuse-infiltrative: features indistinct, irregular contours, an oval or branching shape, may contain cystic inclusions (fluid necrosis), delicate small focal and linear calcifications (Fig. 8);

Type 3 – Predominantly circumscribed, tumor-like: has fairly distinct contours, a convex shape, may contain large cystic areas and focal calcifications (Fig. 9);

Type 4 – Predominantly cystic: has fairly clear contours, medium to large size, oval or round shape with a dominant cystic component (necrosis), pronounced diffuse calcification (Fig. 10);

Type 5 – Predominantly calcified: the dominant part of the lesion consists of calcified tissue with small areas of necrotic tissue (Fig. 11).

Primary morphology

I Diffuse infiltrating (Fig. 7) With cystoid portion Without cystoid portion II Primarily circumscribed tumor-like With cystoid portion Without cystoid portion (Fig. 8) III (a) Primarily cystoid - intermediate (approximately 3-8 cm) With more solid portions at the edge Without more solid portions at the edge (b) Primarily cystoid - widespread (approximately > 8 cm) With more solid portions at the edge Without more solid portions at the edge (Fig. 9) IV Small-cystoid/metastatic (approximately < 3 cm) (Fig. 10) V Mainly calcified







Figure 9. III- Primarily cystoid. Native phase: The formation has a large central cavity (star) with thick walls containing layered and finely focal calcification, small cystic inclusions.



III- Primarily cystoid. Venous phase: Contrast does not accumulate.



According to Beate Grüner et al., ultrasound classification (EMUC-US) and CT classification of alveococcal nodules of the liver are poorly comparable to each other (62). However, both modalities have superior information value for the diagnosis and differential diagnosis of HAE (63).

Abdominal CT with intravenous bolus contrast is useful for preoperative assessment of vascular invasion, spread of parasitic tumor to adjacent organs and tissues like diaphragm, lungs, stomach, spleen, right kidney, and right adrenal gland (30, 64). CT scans of the chest and brain are recommended before any radical surgery, especially prior to liver transplantation (65).

The 'gold standard' for determining the volume of the postoperative liver remnant (FRL or FRL–V, future remnant liver volume) is volumetry (66).



The technique involves determining the total liver volume by calculating the average density values and the number of voxels (67). Then, the liver is segmented according to its vascular architecture, and a virtual 'resection' is performed to calculate the FRL (68). The minimum FRL value is set at 25-30% of the total liver parenchyma volume; however, in cases of morphofunctional disorders (e.g., after chemotherapy), an FRL–V of more than 40% is required. 3D reconstructions and liver segmentation are essential for planning surgical interventions (69).

Post-hepatectomy liver failure is the main complication after liver resection (70). To increase the volume of the future remnant liver, surgical interventions are performed in stages using various regenerative techniques, such as portal vein embolization, associating liver partition and portal vein ligation for staged hepatectomy, and liver venous deprivation (71). Before each step, volumetry is performed to assess FLR hypertrophy and the feasibility of liver resection (72).

CT and positron emission tomography (PET)/CT with labeled fluorodeoxyglucose-18 (18F-FDG) are key methods for diagnosing liver lesions (73). High metabolic activity in alveolar echinococcosis lesions is observed with FDG-PET/CT, especially in areas of microcalcification accumulation (pinnate calcifications or calcifications less than 3 mm) (74). FDG-PET allows indirect identification of parasitic activity and can be used as a tool for further observation (75). PET/CT can detect active lesions even in the absence of clinical symptoms (76). Alveococcal nodes do not have their own circulatory system and are not perfused, so metabolic activity in the marginal zone is associated with inflammatory activity in perifocal tissues (76). It is important to note that a lack of activity on PET does not always indicate the death of the parasite, especially in immunocompromised patients (77). Rather, it reflects the suppression of peri-parasitic inflammation (78). Additionally, at the beginning of treatment with albendazole, inflammatory activity may increase (79).

Magnetic resonance imaging

MRI is a highly sensitive method for differentiating small cystic lesions of hepatic and extrahepatic localization (74). In cases of HAE, MRI reveals a microcystic structure with a solid component, sometimes described as a 'bunch of grapes' or 'honeycomb' (80). The cysts can vary in size—small, medium, or large—and may exhibit a diffuse or uneven distribution at the periphery of the lesion (81). When describing MRI findings of cystic lesions in HAE (Fig. 12, 13), the Kodama classification based on T2weighted imaging, is commonly used. This classification includes five types (82):

Type 1: Multiple small round cysts without a solid component;

Type 2: Multiple small round cysts with a solid component;

Type 3: A solid component surrounding large and/or irregular cysts, with multiple small round cysts resembling a pseudocyst;

Type 4: A solid component without cysts; Type 5: A large cyst without a solid component.



Figure 12. Hepatic alveococcosis. Axial and coronary T2 WI reveal an area of increased heterogenicity in the MR signal (stars), with high diffusion on ADC maps due to the cystic component (arrow head). ADC - apparent diffusion coefficient, MR- magnetic resonance, T2WI - T2-weighted imaging



Figure 13. Hepatic alvecoccosis. In the right lobe of the liver, a large zone of heterogeneous changes in the MR signal is detected with the presence of small cysts along the periphery, with a high-intensity MR signal on T2 WI (star). Invasion into the portal vein (arrow head) and inferior vena cava is noted (arrow). The left lobe of the liver is hypertrophied. On ADC maps, diffusion is higher than in unchanged liver parenchyma (dotted line)

ADC - apparent diffusion coefficient, MR- magnetic resonance

However, over time, it has been recognized that some lesions do not fit into this classification, especially those that

do not contain microcysts. In 2021, a modified Kodama-XUUB (Kodama Xining and Urumqi in China, Ulm in Germany, and Besanßcon in France consortium) classification was proposed to address these limitations. In this new system, type III was divided into subtypes IIIa and IIIb (83).

Tumor-like formations in the liver on MRI images typically show a low signal on T1-weighted imaging, sometimes with an isointense component. On T2weighted imaging, the signal is usually heterogeneous (84). Areas of necrosis show a high-intensity signal, while some regions exhibit a low signal (85). Diffusionweighted imaging allows for the differentiation of parasitic nodules from malignant tumors by assessing tissue diffusion and average values on apparent diffusion coefficient maps (86). To assess the involvement of the biliary tract structures, magnetic resonance cholangiopancreatography (MRCP) is highly effective (87). It provides a complete picture of the relationship between the parasitic process and biliary involvement (88). The informational value of MRCP is comparable to invasive procedures such as percutaneous transhepatic cholangiography and endoscopic retrograde cholangiopancreatography, but it does not require the administration of contrast agents (30). Therefore, MRI should be included in the preoperative evaluation, especially for patients undergoing major liver resection or transplantation (89).

In the study of distant metastases of alveococcosis in the brain, MRI is the preferred method (14). Metastases are usually multiple but can also be singular (90). On T2 and FLAIR-weighted imaging, alveococcal lesions in the brain show a weak signal with multiple small vesicles inside, along with perifocal edema at the periphery (91). On postcontrast T1-weighted images, there is an increased signal from the peripheral parts of the lesion (92).

The final diagnosis of alveococcosis is always based on the results of a morphological study (93). The measured size of the alveococcus cestode, a parasitic larva, usually consists of a conglomerate of multiple microcysts containing excretory capsules, scolexes, and hooks, all bound together by connective tissue (94).

Future directions and challenges

significant advancements in Despite imaging modalities for HAE, several challenges remain in achieving early detection, accurate staging, and optimal treatment planning. Future research should focus on enhancing imaging techniques, improving diagnostic algorithms in endemic regions, and integrating artificial intelligence (AI) into image analysis. Contrast-enhanced ultrasound has shown promise in differentiating HAE lesions from malignant tumors by assessing microvascularization patterns in real time. It is a cost-effective and widely available tool that can be particularly useful in low-resource endemic regions. PET/CT, particularly with 18F-FDG, can provide valuable metabolic information about parasitic viability and treatment response. This modality may help in assessing occult metastases and residual disease activity, potentially influencing longterm management strategies.

Improving Diagnostic Algorithms in Endemic Regions Many endemic areas lack access to advanced imaging modalities like CT and MRI, leading to delays in diagnosis and treatment. To address this issue: •Efforts should be made to develop standardized ultrasound-based diagnostic protocols, enabling primary healthcare providers to detect HAE at an early stage.

•Portable ultrasound devices combined with telemedicine solutions could improve access to diagnostic services in rural areas.

•Enhancing medical training programs for radiologists and general practitioners in endemic regions will facilitate earlier detection and referral for specialized imaging.

The Role of Machine Learning in HAE Imaging

The integration of AI and machine learning (ML) into radiology is expected to revolutionize the diagnosis of HAE. AI-driven image analysis algorithms could help automate the detection of HAE lesions on ultrasound, CT, and MRI scans, improving diagnostic accuracy and reducing human error. Deep learning models trained on large datasets of echinococcosis cases could assist in differentiating HAE from malignant liver tumors and other hepatic lesions. AI applications in radiomics and texture analysis may provide insights into disease progression, treatment response, and prognosis, enabling personalized patient management (95).

Conclusion

The global epidemiological situation regarding the prevalence of human alveococcosis has remained consistently tense over the past decades. HAE has a distinct radiological appearance, but the parasitic process is often mistakenly diagnosed as a malignant liver tumor. Among diagnostic modalities, ultrasound remains the primary method, continuously improving with the introduction of elastography and contrastenhanced techniques. CT with bolus contrast is essential for all patients with hepatic alveococcosis, as it provides valuable diagnostic information. Implementing CT volumetry is highly recommended for accurately determining the residual volume of the liver parenchyma. MRI is an excellent tool for evaluating vascular and biliary tract involvement. Currently, MR cholangiopancreatography has largely replaced percutaneous cholangiography in assessing the relationship between HAE lesions and the biliary tree. Preoperative preparation should also include CT of the lungs and brain. To assess the effectiveness of conservative therapy, FDG-PET can be used to determine the metabolic activity of the parasite. The final diagnosis of HAE is always established based on the results of a morphological study.

The larva of the alveococcus typically consists of a conglomerate of multiple microcysts containing excretory capsules, scolexes, and hooks, all bound together by connective tissue.

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