Abdominal Imaging PICTORIAL ESSAY

MRI findings of autoimmune hepatitis and brief review of the literature

Charalampos Maskalidis[1], Alexandros Tsitouridis[2], Maria Sousanova[1], Nona Iordanidou[1], Christina Manika[1], Eleni P Kariki[3]

[1]*Radiology department, "St. Paul" General Hospital of Thessaloniki*

[2]*"St. Demetrius" General Hospital of Thessaloniki*

[3]*Division of Informatics, Imaging & Data Sciences, School of Health Science, The University of Manchester & Manchester University NHS Foundation Trust.*

SUBMISSION: 28/12/2021 - ACCEPTANCE: 26/5/2022

ABSTRACT

Autoimmune hepatitis is a form of chronic hepatitis of unknown aetiology. Imaging is not included in the diagnostic criteria of the disease, but it may play a role in histopathologic correlation and monitoring of these patients. Certain nonspecific imaging patterns of autoimmune hepatitis may be associated with inflammation or fibrosis. Our purpose is to review the magnetic resonance imaging findings of autoimmune hepatitis, any possible correlation with histopathology and their role in assessing the follow up of these patients.

KEY WORDS: Autoimmune hepatitis; Inflammation; Fibrosis; Patchy enhancement; Reticular pattern; Periportal pattern

Introduction

Autoimmune hepatitis (AIH) is an immune mediated chronic hepatitis of unknown aetiology [1,2,3,4]. It is hypothesized that genetic predisposition associated with class II DRB1 alleles and environmental trigger factors such as drugs, herbs or infection are responsible for a T-cell mediated autoimmune reaction against the liver parenchyma leading to necroinflammation and fibrosis [1,2,3,5]. There is no specific feature or test for the diagnosis of this entity.

Nonspecific biochemical, immunological, histopathological and clinical criteria could point towards this disease and help us exclude other forms of chronic hepatitis

CORRESPONDING AUTHOR, GUARANTOR: Charalampos Maskalidis, Radiology department, "St. Paul" General Hospital of Thessaloniki, 161 Ethnikis Antistaseos Avenue, 55134, Thessaloniki, Greece, phone: +302313 304400

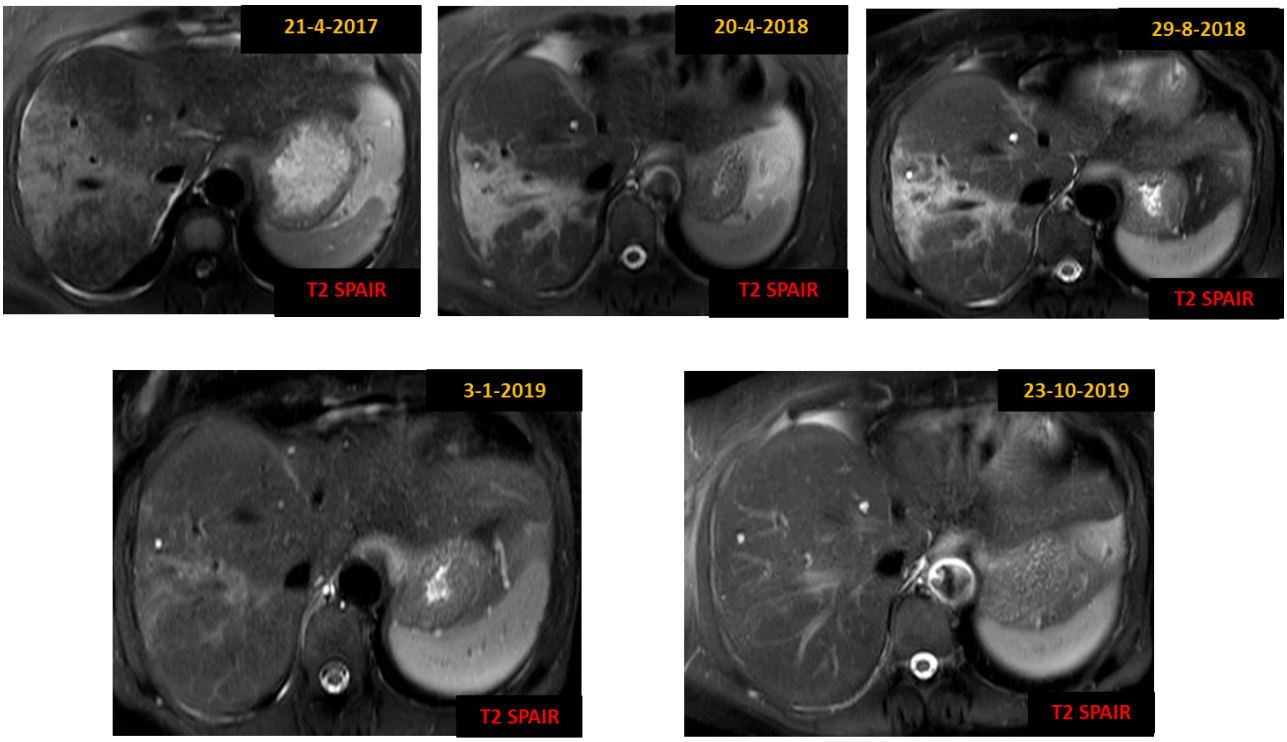

Fig. 1. *Fat-saturated T2WI in a 48-year-old patient with autoimmune hepatitis proven on biopsy. Consecutive MRI exams at approximately the same level of the right liver lobe show a wedge-shaped area of high signal intensity without any mass effect. Vessels cross the area without any distortion. There is gradual reduction of the lesion's size followed by complete remission.*

[1,2,3,5,6]. These features include polyclonal hypergammaglobulinemia and autoantibodies such as antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA) and anti-liver-kidney microsomal antibody (anti-LKM) [2,3,4,6,7]. Liver biopsy can exclude other aetiologies and determine disease severity [6,7,8]. Biopsy specimens show nonspecific interface hepatitis (piecemeal necrosis) with a predominant portal and periportal lymphoplasmacytic cell infiltrate as well as lobular inflammation and damage [1,2,3,5,6,7,8]. Necro-inflammatory changes are followed by fibrosis, which is present in all, but the mildest forms of autoimmune hepatitis [2]. Bile ducts are generally spared [3]. Clinical presentation varies significantly and these patients at the time of diagnosis may be asymptomatic, present with cirrhosis or even, demonstrate fulminant hepatic failure [1,2,3,5,6]. Evidence of cirrhosis at diagnosis is seen in 28-34% of patients [9,10,11,12]. An additional number of patients ranging between 10-20% develops cirrhosis within a period of 4-7 years after the establishment of diagnosis [9,10,11].

The absence of specific imaging findings and the great variability of imaging appearances in these patients limits the diagnostic value of imaging [5,13].

Nevertheless, imaging may show a positive correlation with the histological stage of the disease, especially fibrosis. It is also very useful for monitoring these individuals for treatment efficacy, disease progression and identification of chronic liver disease complications [5,13].

The purpose of our study is to review the MRI findings of autoimmune hepatitis, any possible correlation with histopathology and their impact on patient monitoring.

MR Imaging

The two major histopathologic characteristics of any chronic hepatitis, including autoimmune hepatitis, are inflammation and fibrosis [14]. Positive correlation with MRI may exist in certain cases, although imaging features are not part of the diagnostic criteria of the disease [13].

Inflammation has been associated with early patchy enhancement [13,14,15,16], **(Fig. 1, 2, 3)** and early periportal linear enhancement [17,18], **(Fig. 4, 5)** which appear on late arterial or portal venous phase post-contrast images.

Fibrosis demonstrates a reticular or confluent pattern with delayed enhancement appearing on portal venous

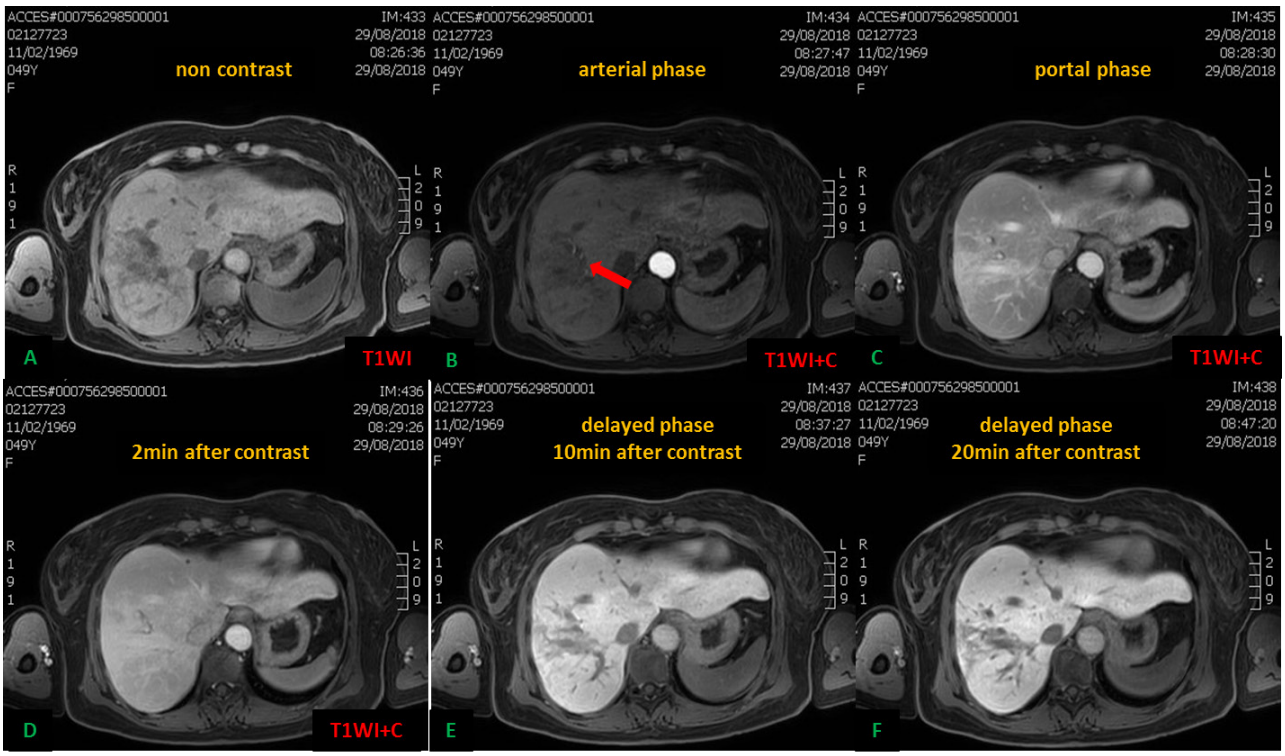

Fig. 2. *Dynamic contrast MRI of the previous lesion with the use of a hepatobiliary contrast agent. A. Fat-saturated, non-contrast T1WI shows a wedge-shaped area of low signal intensity in the right liver lobe. B. There is no contrast enhancement on the early arterial phase. Notice the small arterial branches within the lesion (red arrow). C,D. Enhancement of the region on the portal venous phase and maintained 2min after contrast enhancement. E.F. Wash out, that is no enhancement of the lesion on the delayed phase 10min and 20min after contrast enhancement. Biopsy showed inflammatory cell infiltrates and hepatocellular necrosis indicating active inflammation.*

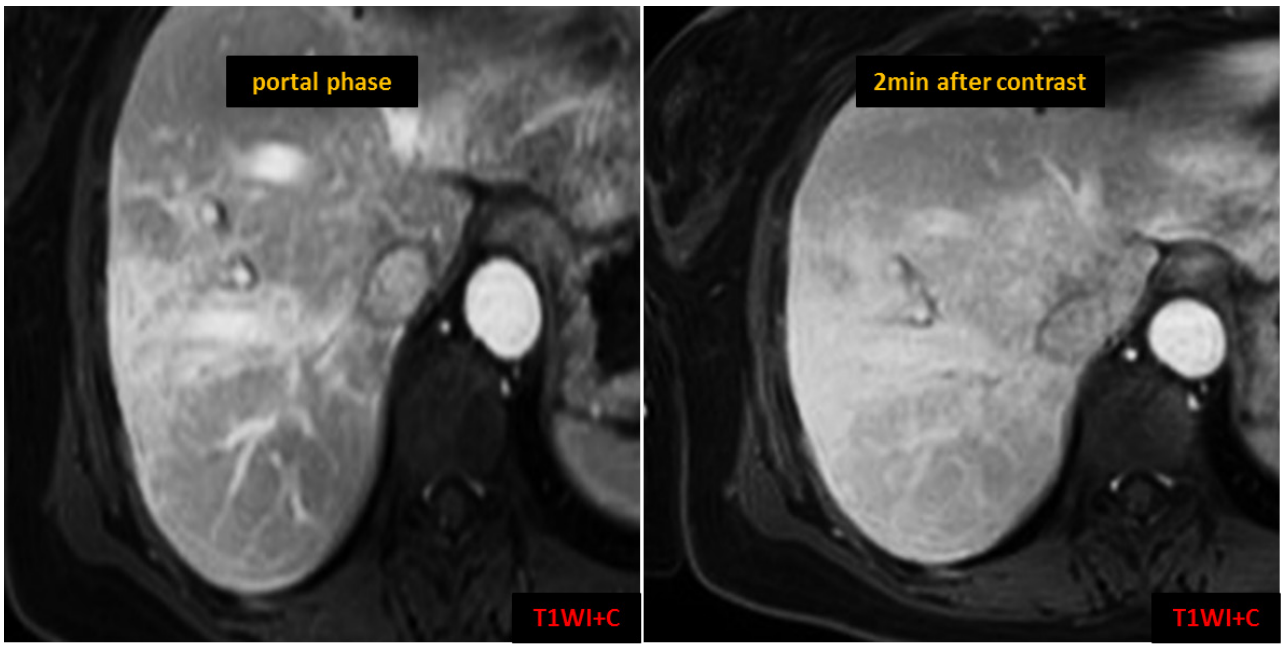

Fig. 3. *Enlarged postcontrast images of the patient in figure 1 & 2 showing the wedge-shaped heterogeneous enhancement of the liver.*

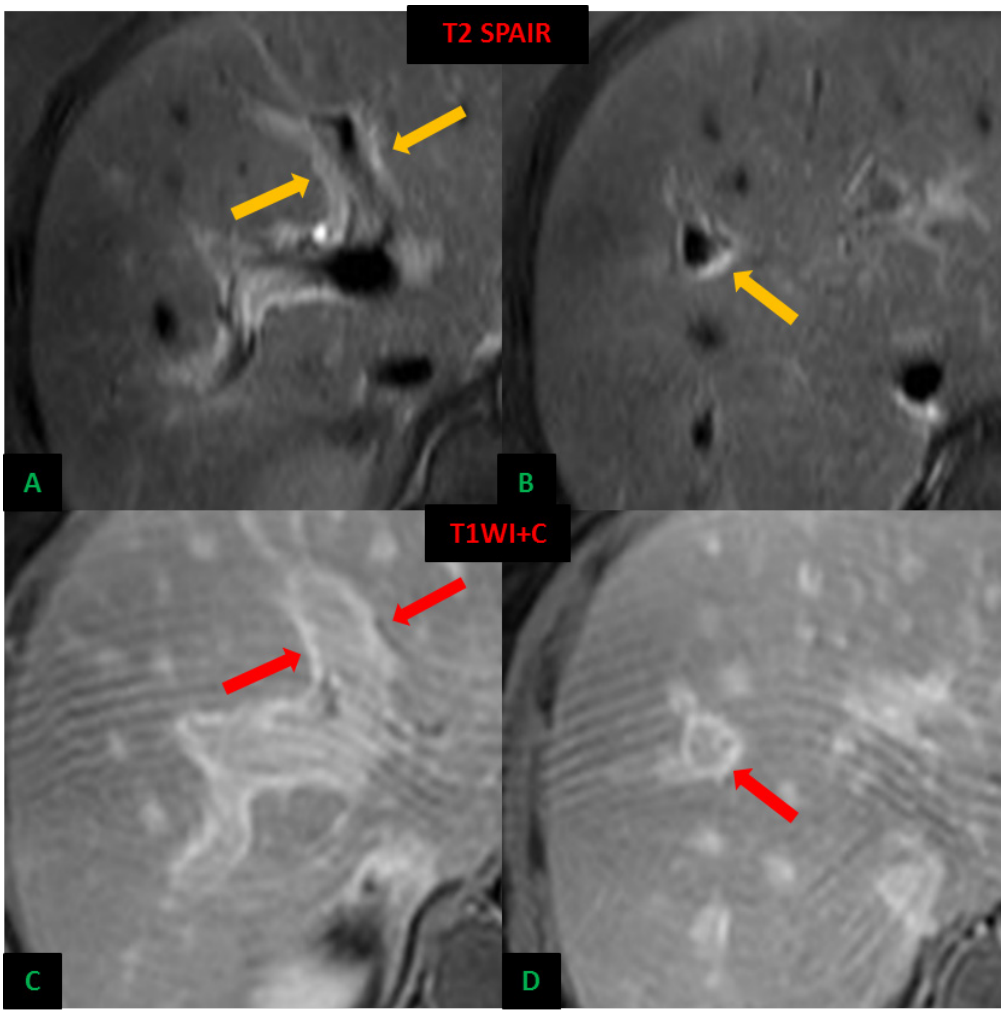

Fig. 4. *Periportal halo hyperintensity on fat-saturated T2WI (yellow arrows in A,B) and periportal linear enhancement on fat-saturated post-contrast T1WI (red arrows in C,D) in a 50-year old woman with known autoimmune hepatitis.*

phase or delayed phase post-contrast images [13,15,16], **(Fig. 6, 7, 8)**.

Liver morphologic changes and intrahepatic biliary dilatation should be evaluated in these patients, mainly, to exclude coexistent primary sclerosing cholangitis (PSC), [15,19].

The incidence of early heterogeneous enhancement without an underlying lesion or mass effect has been recorded in 31% of patients with autoimmune hepatitis. This finding is usually associated with acute inflammation, that is inflammatory cellular infiltrates and recent hepatocellular damage or necrosis [13,14,15,16], **(Fig. 1, 2, 3)**. It is seen on arterial-phase or portal-phase post-contrast CT/MRI and may resolve on the delayed phase [13], **(Fig. 2, 3)**. The areas of enhancement usually correspond to increased signal intensity on T2-weighted images (T2WI) and better visualized on fat-suppressed T2-weighted images (fat-sat T2WI), **(Fig. 1, 2, 3)**. Reversibility after treatment has been also reported [13], **(Fig. 1)**.

Linear periportal T2WI and DWI hyperintensity followed by linear periportal enhancement on post-contrast images is an imaging pattern reflecting active inflammation in cases of autoimmune hepatitis [17], **(Fig. 4, 5)**. This periportal hyperintensity on T2WI and DWI is associated with a pathologic process in Glisson capsule, the layer of loose connective tissue that surrounds portal veins [18]. This may be due to periportal edema, periportal lymphedema, fibrosis, inflammation, infection as well as malignant infiltration [18]. Periportal lymphedema is indicated when T2WI hyperintensity is not followed by corresponding enhancement [18]. The presence of arterial-phase or portal venous enhancement may be associated with infection,

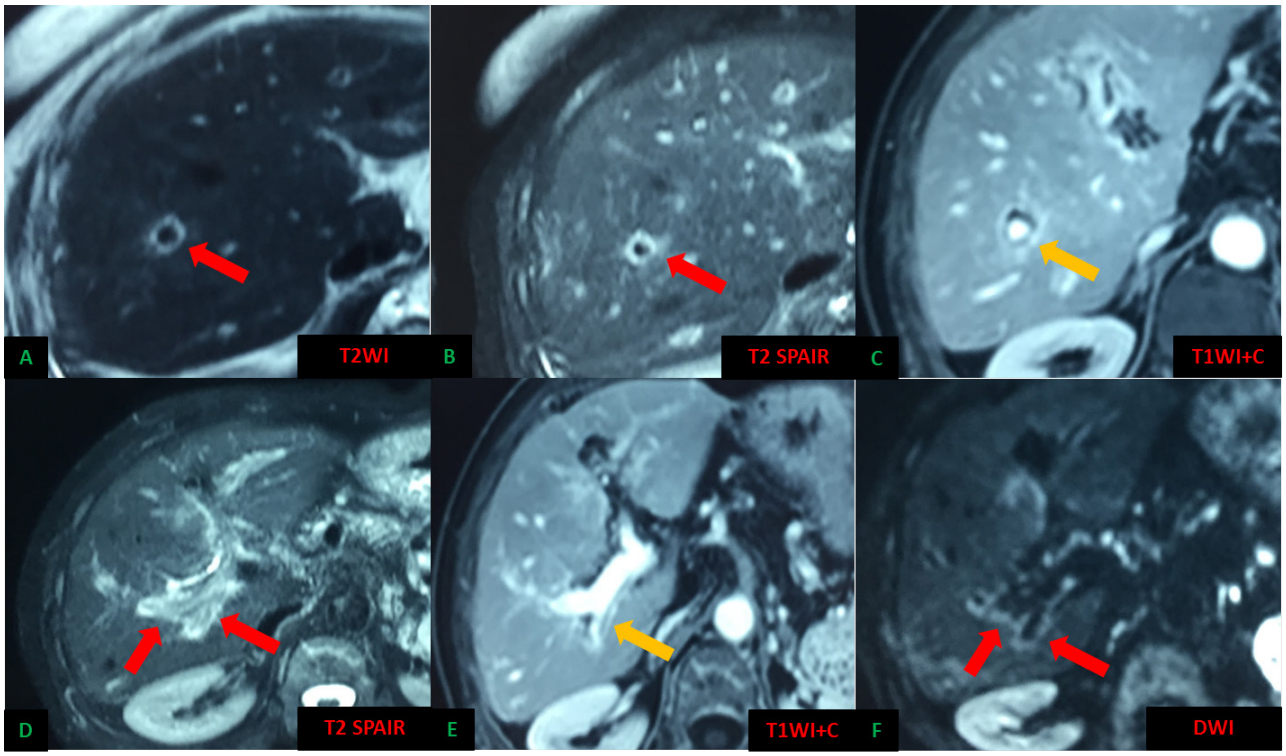

Fig. 5. *Periportal halo hyperintensity on T2WI, fat-saturated T2WI and DWI (red arrows in A, B, D and F images respectively) and linear periportal enhancement on post-contrast T1WI in a 75-year old woman with autoimmune hepatitis (yellow arrows in C and E).*

inflammation or malignancy. Delayed enhancement may be due to expanded periportal loose connective tissue, fibrosis or malignancy such as cholangiocarcinoma, when it is associated with its fibrotic component [17,18]. The fine linear nature of this finding is inconsistent with malignancy.

Fibrosis is a common finding in patients with autoimmune hepatitis. It represents a fundamental factor in liver cirrhosis [15]. It may be reticular, confluent or both. The presence of fibrosis varies among different studies. The most common reticular pattern ranges from 41,7% [13] to 94% [15], while the confluent pattern has been reported in 20% [15] to 50% [4].

Reticular or bridging fibrosis has been described as a network of fine linear abnormalities, that show low signal intensity on T1WI, high signal intensity on T2WI, especially on fat-suppressed T2WI, and late progressive enhancement on portal-phase or delayed-phase post-contrast T1WI [8,13,14,15,16], **(Fig. 6, 7, 8)**. Thickness of these fibrotic bands and the presence or absence of surface nodularity are used to stage reticular fibrosis **(Table 1)** [13,15].

Confluent fibrosis has been defined as an irregular region of fibrosis greater than 2cm in diameter displaying the same MRI signal intensity characteristics as reticular fibrosis [13,14,15,16]. Confluent fibrosis is usually located at the level of interlobar and intersegmental fissures, as these areas have terminal territory perfusion [16]. It has a geometrical or wedge-shaped appearance with its apex pointing towards the hepatic hilum and the base oriented towards the hepatic capsule [5,16]. Volume loss and capsular retraction or capsular flattening may also be present [5,16]. However, a wedge-shaped area of early instead of delayed enhancement and no atrophic changes is more consistent with inflammation than confluent fibrosis **(Fig 1, 2, 3)**.

Magnetic resonance elastography is emerging as a method not only for staging liver fibrosis but for detecting fibrosis in normal appearing liver as well [5].

Surface nodularity has been described in 62-66,7% of autoimmune hepatitis patients [13,15]. It has been associated with moderate and severe reticular fibrosis, where fibrotic bands surround small regenerative nodules as a consistent part of liver cirrhosis [13,15,16], **(Fig. 7)**. It has been suggested that this nodularity in autoimmune hepa-

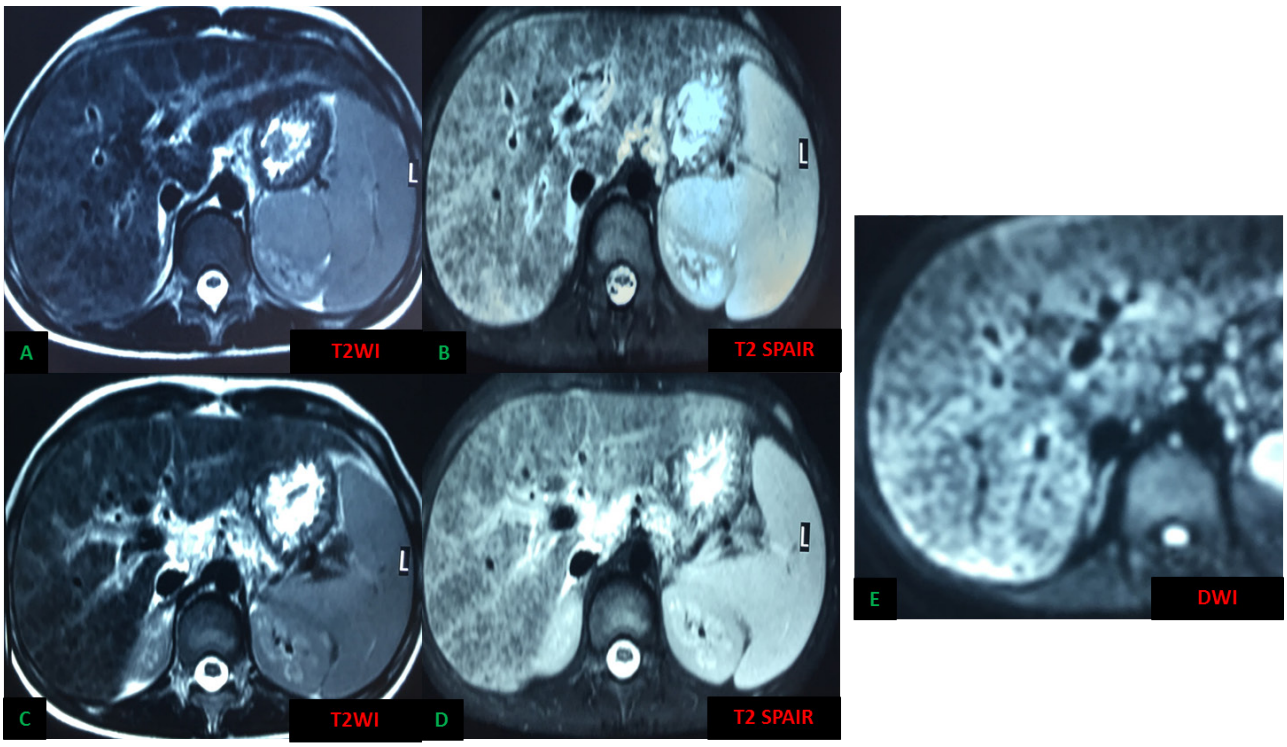

Fig. 6. *Bridging fibrosis in a 13-year-old patient with autoimmune hepatitis. Reticular hyperintensity throughout the liver parenchyma on T2WI (A, C), fat-saturated T2WI (B, D) and DWI (E).*

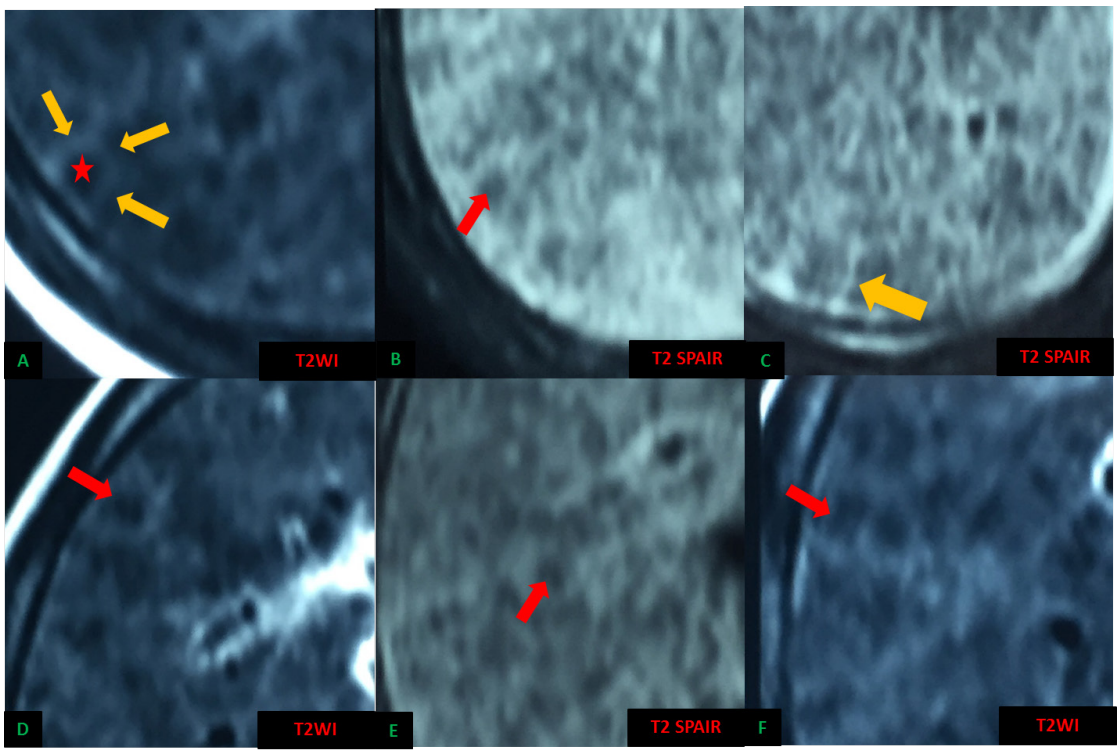

Fig. 7. *Bridging fibrosis. Enlarged images of the previous patient show isointense regenerative nodules (red star, red arrows) surrounded by bridging fibrous septa of high signal intensity (yellow arrows) on T2WI (A, D, F) and fat-saturated T2WI (B, C, E).*

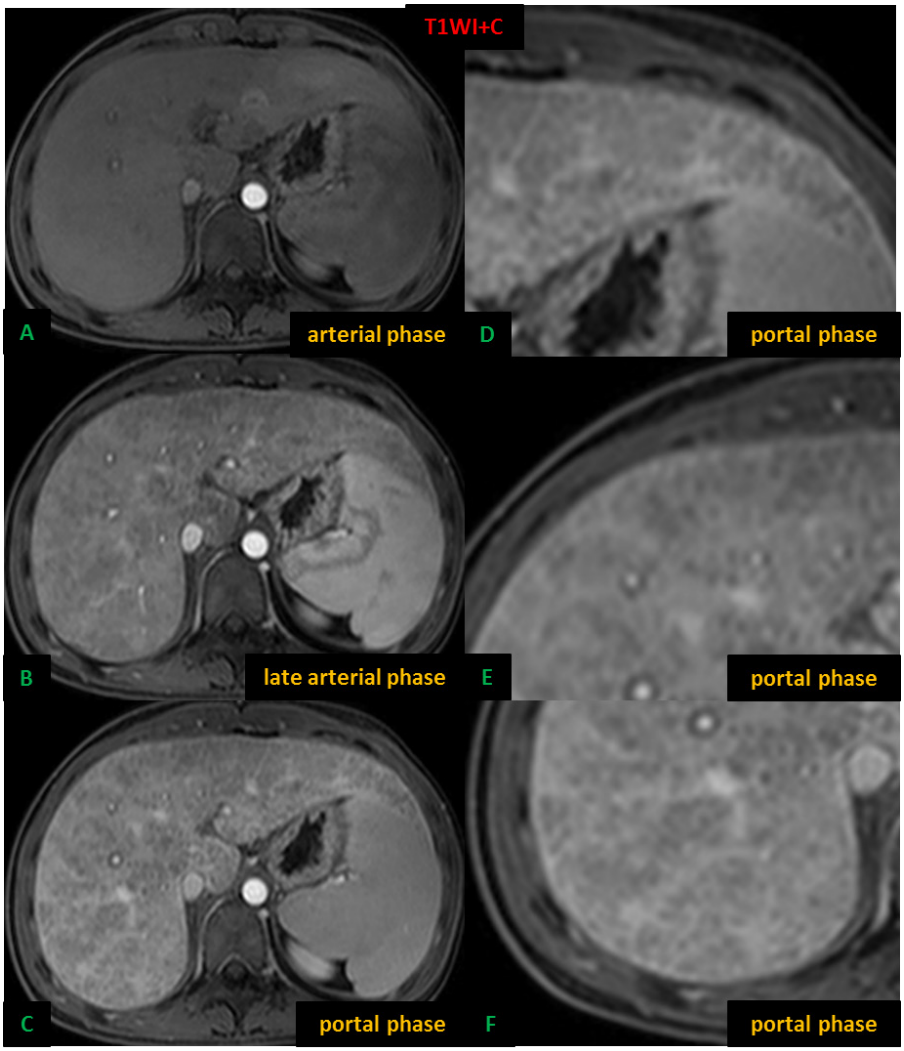

Fig. 8. *Dynamic MRI of the aforementioned case of bridging fibrosis. A reticular pattern of linear enhancement discerns in late arterial phase and becomes more conspicuous on portal venous phase (A,B,C). Enlarged images of portal venous phase (D,F,E) better depict the fine linear enhancement of fibrous septa surrounding isointense regenerative nodules.*

titis may be seen in patients without cirrhosis as a consequence of hepatic atrophy and hypertrophy rather than regeneration [1,20]. Generally, CT density and MRI intensity of regenerative nodules on pre- and post-contrast images is similar to the surrounding liver parenchyma in cirrhotic patients, including those with autoimmune hepatitis [15,21] (**Fig. 6, 7, 8**).

Another imaging pattern of regenerative nodules in autoimmune hepatitis is that of hypervascular nodules on arterial phase imaging [5,21]. Persistence of enhancement or uniform washout without a persistent hyperintense rim may be seen on portal venous phase [5,21]. Differential diagnosis should include pseudolesions and hepatocellular carcinoma despite the rarity of the latter in autoimmune hepatitis [16,21,22,23]. The incidence of hypervascular nodules has been reported in 22% of cases [15].

Caudate lobe hypertrophy is seen in only 8-13% of individuals with autoimmune hepatitis, while is far more common in other forms of cirrhosis, especially in PSC [13,15,24]. Left lateral segment enlargement has been described in 25% of the cases [15]. Liver atrophy appears more often, and manifests as left medial segment atrophy (56%) and right lobe atrophy (25%) [15]. Signs of liver atrophy, such as expanded gallbladder fossa and enlarged pre-portal space along with ascites and splenomegaly, have been positively correlated with fibrosis at histopathology [13].

Portocaval and porta hepatis lymphadenopathy in auto-

SCORING SYSTEM OF RETICULAR FIBROSIS (Bilaj et al Radiology 2005, Sahni at al Abdominal Imaging 2008)			
POINT SYSTEM	THICKNESS OF FIBROUS STRANDS	SURFACE NODULARITY	FIBROSIS-STAGE
0	absence	NO	absence
1	<2mm	NO	mild
2	2-5mm	YES	moderate
3	>5mm	YES	severe

Table 1

immune hepatitis demonstrates a relatively low incidence of 12-27% [13,15] in contrast to primary biliary cirrhosis (PBC), (62-88%) and viral hepatitises (67%) [18,1,25].

Generally, imaging is useful in the diagnosis of complications associated with chronic liver disease such as manifestations of portal hypertension and hepatocellular carcinoma, despite the latter showing lower incidence in cirrhotic patients with autoimmune hepatitis [2,5,13,22,23,26].

Autoimmune hepatitis may coexist with other diseases such as PBC and more commonly, PSC [2,4,19]. The additional presence mainly, of biliary irregularities such as biliary dilatation, biliary strictures and duct beading, but also, of central macro-regenerative nodules larger than 3cm and peripheral liver atrophy in patients with autoimmune hepatitis may be associated with an AIH-PSC overlap syndrome [1,2,19]. Because of implications in management and prognosis, MRCP is indicated in patients with autoimmune hepatitis who present with cholestasis, inflammatory bowel disease or poor corticosteroid response in order to exclude concomitant PSC [1,2,3,4,5,27]. In 25% of patients, autoimmune hepatitis may show mild intrahepatic bile duct irregularities due to fibrosis, without evidence of PSC [4].

Conclusion

Nonspecific imaging patterns of autoimmune hepatitis may be associated with the histologic stage of the disease. In cases of early heterogeneous patchy enhancement or early linear periportal enhancement, MRI may point towards active inflammation. Reticular or confluent MRI patterns, on the other hand, indicate fibrosis. Magnetic resonance imaging appears to be useful in monitoring these patients and on certain occasions, MRCP is necessary to exclude an AIH-PSC syndrome. **R**

References

1. Gossard AA, Lindor KD. Autoimmune hepatitis: a review. J Gastroenterol 2012; 47:498-503.
2. Krawitt EL. Autoimmune hepatitis. N Engl J Med 2006; 354:54-66.
3. Manns MP, Czaja AJ, Gorham JD, et al. Diagnosis and management of autoimmune hepatitis. Hepatology 2010; 51(6):2193-2213.
4. Lewin M, Vilgrain V, Ozenne V, et al. Prevalence of sclerosing cholangitis in adults with autoimmune hepatitis: a prospective magnetic resonance imaging and histological study. Hepatology 2009; 50:528-537.
5. Malik N, Venkatesh SK. Imaging of autoimmune hepatitis and overlap syndromes. Abdom Radiol 2017; 42:19-27.
6. Liberal R, Grant CR, Longhi MS, et al. Diagnostic criteria of autoimmune hepatitis. Autoimmunity Reviews 2014; 13:435-440.
7. Czaja AJ, Freese DK. Diagnosis and treatment of autoimmune hepatitis. Hepatology 2002; 36(2):479-497.
8. Knowlton JQ, Taylor AJ, Reichelderfer M, Stang J. Imaging of biliary tract inflammation: an update. AJR 2008; 190:984-992.
9. Liberal R, Grant CR. Cirrhosis and autoimmune liver disease: Current understanding. World J Hepatol

2016; 8(28):1157-1168.
10. Werner M, Prytz H, Ohlsson B, et al. Epidemiology and the initial presentation of autoimmune hepatitis in Sweden: a nationwide study. Scand J Gastroenterol 2008; 43: 1232-1240
11. Verma S, Gunuwan B, Mendler M, et al. Factors predicting relapse and poor outcome in type I autoimmune hepatitis: role of cirrhosis development, patterns of transaminases during remission and plasma cell activity in the liver biopsy. Am J Gastroenterol 2004; 99: 1510-1516
12. Feld JJ, Dinh H, Arenovich T, et al. Autoimmune hepatitis: effect of symptoms and cirrhosis on natural history and outcome. Hepatology 2005; 42: 53-62
13. Sahni VA, Raghunathan G, Mearadji B, et al. Autoimmune hepatitis: CT and MR imaging features with histopathological correlation. Abdom Imaging 2010; 35:75-84.
14. Semelka RC, Chung J-J, Hussain SM, et al. Chronic hepatitis: Correlation of early patchy and late linear enhancement patterns on gadolinium-enhanced MR images with histopathology initial experience. J Magn Reson Imaging 2001; 13:385-391.
15. Bilaj F, Hyslop WB, Rivero H, et al. MR imaging findings in Autoimmune Hepatitis: Correlation with clinical staging. Radiology 2005; 236:896-902.
16. Marti-Bonmati L, Delgado F. MR imaging in liver cirrhosis: classical and new approaches. Insights Imaging 2010; 1:233-244.
17. Onishi H, Theisen D, Zachoval R, et al. Intrahepatic diffuse periportal enhancement patterns on hepatobiliary phase gadoxetate disodium-enhanced liver MR images. Do they correspond to periportal hyperintense patterns on T2-weighted images? Medicine 2019; 98:11(e14784).
18. Ly NJ, Miller FH. Periportal contrast enhancement and abnormal signal intensity on state-of-the-art MR images. AJR 2001; 176:891-897.
19. Hyslop WB, Kierans AS, Leonardou P, et al. Overlap syndrome of autoimmune chronic liver diseases: MR findings. J Magn Reson Imaging 2010; 31:383-389.
20. Dodd GD, Baron RL, Oliver JH, Federle MP. End-stage primary sclerosing cholangitis: CT findings of hepatic morphology in 36 patients. Radiology 1999; 211:357-362.
21. Qayyum A, Graser A, Westphalen A, et al. CT of benign hypervascular liver nodules in autoimmune hepatitis. AJR 2004; 183:1573-1576.
22. Park SZ, Nagorney DM, Czaja AJ. Hepatocellular carcinoma in autoimmune hepatitis. Dig Dis Sci 2000; 45:1944-1948.
23. Teufel A, Weinmann A, Centner C, et al. Hepatocellular carcinoma in patients with autoimmune hepatitis. World J Gastroenterol 2009; 15(5):578-582.
24. Bader TR, Beavers KL, Semelka RC. MR imaging features of primary sclerosing cholangitis: patterns of cirrhosis in relationship to clinical severity of disease. Radiology 2003; 226: 675-685.
25. Blachar A, Federle MP, Brancatelli G. Primary biliary cirrhosis: clinical, pathological, and helical CT findings in 53 patients. Radiology 2001; 220:329–336.
26. Valeasn S, Acalovschi M, Dumitrascu DL, et al. Hepatocellular carcinoma in patients with autoimmune hepatitis-a systematic review of the literature published between 1989-2016. Med Pharm Rep 2019; 92(2):99-105.
27. Hunter M, Loughrey MB, Gray M, et al. Evaluating distinctive features for early diagnosis of primary sclerosing cholangitis overlap syndrome in adults with autoimmune hepatitis. Ulster Med J 2011; 80(1):15-18.

READY - MADE CITATION

Maskalidis C, Tsitouridis A, Sousanova M, Iordanidou N, Manika C, Kariki EP. MRI findings of autoimmune hepatitis and brief review of the literature. *Hell J Radiol* 2022; 7(2): 15-23.