BMJ case reports (2015.2) :.

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Unique MRI findings for differentiation of an early stage of hepatic alveolar echinococcosis

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Summary

Computed Tomography (CT) scan and Ultrasonography (US) images revealed a 74-year old man having two small uniformly low density and hypo echoic lesions in the liver, respectively, 7 years after curative resection of rectal cancer. The liver including those two lesions were segmentally resected. Two lesions were histopathologically confirmed as early but active stage alveolar echinococcosis (AE) caused by accidental ingestion of eggs of the fox tapeworm, *Echinococcus multilocularis*. This case is very unique and rare, since early stage AE cases have only accidentally been confirmed from cases in which malignant hepatic tumours were suspected, and two independent AE lesions were detected. Abdominal magnetic resonance imaging (MRI) showed two isointense tumour lesions with small areas of high-signal intensity in their centres on T2-weighted images. MRI findings appear to well be reflecting the macroscopic view and microscopic findings of early stage AE with active cyst in the centre of each hepatic lesion.

BACKGROUND

AE causes occupational and invasive lesions mainly in the liver like a malignant tumour. As early stage AE is asymptomatic, it is difficult or

impossible for clinicians to detect early stage AE until AE becomes late and advanced stages other than accidental differentiation of malignant tumour cases misdiagnosed as shown in this case.[1-4] However, recent great advances in diagnostic imaging techniques have greatly improved the opportunity of asymptomatic hepatic tumour detection.[3-5] Diagnosis of AE is based on partial calcification of cysts in several diagnostic imaging findings and serological diagnosis using such as Em18 in advanced AE.[6-12] As image diagnosis of early stage AE has not become clear until now, there are few reports of early stage AE.[5] We experienced one AE case with two small independent early stage lesions in the liver. MRI images are expected to be highly useful for differential diagnosis of early but active stage AE with hydatid cyst fluid in the centre of hepatic lesion.

CASE PRESENTATION

Two small low density lesions at Couinaud's segments 6 and 7 of the liver were detected by a CT scan and suspected to be metastasis of a rectal cancer when a 74-year-old man living in Hokkaido, Japan who got a rectal cancer surgery seven years before when he was 67 years old. Abdominal MRI showed two isointense tumour lesions with small areas of high-signal intensity in

their centres on T2-weighted images. These cystic lesions were histopathologically confirmed to be AE cysts caused by accidental ingestion of eggs of *E. multilocularis*.

The patient was a crane operator but worked temporarily in a mink breeding industry in Hokkaido, but had no particular complaint. Low anterior resection with lymph node dissection (pT3, pN0, M0, Stage IIA of the UICC classification) was performed for rectal cancer in January 2004. US showed two hypoechoic lesions (figure 1) and CT scan showed two uniformly circular low-density lesions with 16.2 × 12.7 mm and 13.5 × 8.9 mm in the segments 6 and 7, respectively (figure 2). MRI revealed two small lesions of high-signal intensity in their centres on T2-weighted images (figure 3). Cyst sizes inside the solid host tissues were 3.7 x 4.1 mm and 2.5 x 2.1 mm, respectively. As there was no calcified lesion which is one of the typical indices of advanced AE, metastatic liver tumours and other hepatic diseases were suspected. Two lesions (figure 4) completely resected in July 2011 were histopathologically confirmed as early but active stage AE: Two cysts with laminated and germinal layers inside were surrounded by fibrous tissue and leukocyte layers (figure 5). Mitochondrial DNA analysis revealed histological specimens as the

Asian genotype of *E. multilocularis*.[13-15] As we did not expect AE, we failed in keeping serum samples until 16 days after surgery. Serology by confirmative Western blottings using both crude *E. multilocularis* antigens[16] carried out at Hokkaido Institute of Public Health, Sapporo, and both an affinity purified Em18 and a recombinant Em18 carried out at Asahikawa Medical University[7 17] were negative when serum sample prepared 16 days after the surgery was examined (figures 6-A and 6-B). However, Western blotting using a crude *E. multilocularis* antigens showed several bands (figure 6-C) but it remains unclear if any of these bands are specific to AE or not. Furthermore, it is unclear if this case was sero-positive to Em18 if pre-operative serum sample was examined, since most recent work showed antibody responses to Em18 drastically dropped down within a few days after curative surgery.[9 12 17 18]

OUTCOME AND FOLLOW-UP

The patient's postoperative course is favorable. He is living healthy without actual signs of illness after three years of liver surgery.

DISCUSSION

AE causes occupational and invasive lesions mainly in the liver like a

malignant tumour.[1-4] Recent advances in studies of imaging figures including US, CT, MRI and FDG-PET,[1-5] and serology to detect antibody responses to such a specific antigen as Em18, predominant in active but late or advanced stage AE,[6-12 17] can differentiate almost all AE cases with > 3-5 cm in size with or without partial calcification.[1-4] However, there is no tool suitable for detection of early stage AE with < 1 or even < 3 cm in size except a needle biopsy.[19 20] However, almost all patients do not accept an invasive needle biopsy. Therefore, early stage AE cases have never been identified as AE before surgery but exclusively and exceptionally been confirmed by histopathological examination of the resected lesions after surgery of cases in which malignant tumours were suspected.[5]

MRI figures revealed two cysts of early AE (liquid phase) as highly contrasted phase surrounded with solid phase of host tissues. These findings clearly reflect the macroscopic view of excised specimens (figure 4). MRI is superior in density resolution and can detect a difference of the density distribution much clearer than CT.

MRI of AE cases have been classified into five types.[5] So far we know, the earliest type is Type 1 showing multiple small round cysts without a solid

component confirmed from < 3cm in diameter.[5] However, the present case corresponds to none of the 5 types.[5]

This is the first report demonstrating two independent early stage AE lesions with < 5 mm in size in the liver by MRI. As one AE cyst is expected to be caused by one egg, this patient accidentally got infection with two eggs which developed into two cysts in different segments. In general, multiple lesions either in the liver or multiple organs have been conceived to be due to metastasis of the primary hepatic AE.[1-3] However, multiple primary infections may often occur in endemic areas.[21] Nonetheless, as there is no tool to identify or suspect early stage AE cases, there is no report demonstrating such multiple primary infections. This may be the first report demonstrating two independent early AE lesions.

We would like to launch a hypothesis that such MRI findings are unique to early stage AE. We expect MRI diagnosis of cyst(s) ≤ 1 cm or even < 3 cm in size without calcification may be highly useful for detection of early stage AE case. The imaging findings in early stage and advanced stage AE cases crucially differ each other, since small active hydatid cyst (liquid phase) in the centre of early stage AE lesion with outer solid cysts without calcification

differs from big necrotic cyst (abscess phase) in advanced stage AE with outer solid but big cysts with partial calcification.

Learning points

►Diagnosis of early stage AE is very difficult for diagnostic imaging especially without calcification.

►MRI imaging findings reflect early stage AE clearer than CT or US imaging.

►T2-WI MRI imaging introduces immediate diagnosis for early stage AE.

Acknowledgements

We sincerely thank K Ishibashi, H Takahashi, M Hashimoto and S Inaba who have seen this case at Department of Surgery, Hokkaido Kouseiren Engaru-Kousei General Hospital, and T Yanagida, K Nakaya, Y Sako, who have done laboratory diagnostics at Department of Parasitology, Asahikawa Medical University. This study was supported in part by a Grant-in-Aid for Scientific Research (no. 24256002) from Japan Society for the Promotion of Science, and the Hokkaido Translational Research Fund (2007-2011) and the Special Coordination Fund for Promoting Science and Technology (2010-2012) from the Ministry of Education, Culture, Sports, Science &

Technology in Japan (MEXT) to AI.

Competing interests None

Patient consent Obtained

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Figures legends

Figure 1 Ultrasonography showing two hypoechoic lesions in the liver.

Figure 2 CT scan showing two low density lesions in S6 and S7.

Figure 3 MRI showing two isointense tumours with high intensity in their centres on T2WI in S6 and S7.

Figure 4 Resected specimen.

Figure 5 Histopathology showing an AE cyst of 3.7 x 4.1 mm in size. ①: leucocyte layer, ②: fibrous layer, ③: normal liver tissue, ④: multilocular cysts, ⑤: laminated layer, ⑥: germinal layer.

Figure 6 Western blotting figures using both affinity purified Em18 (A) and recombinant Em18 (B) which are negative, and crude antigens (C) which illustrates several bands which appear to differ from several other bands which have been expected to be specific or unique to echinococcosis.[16 17]

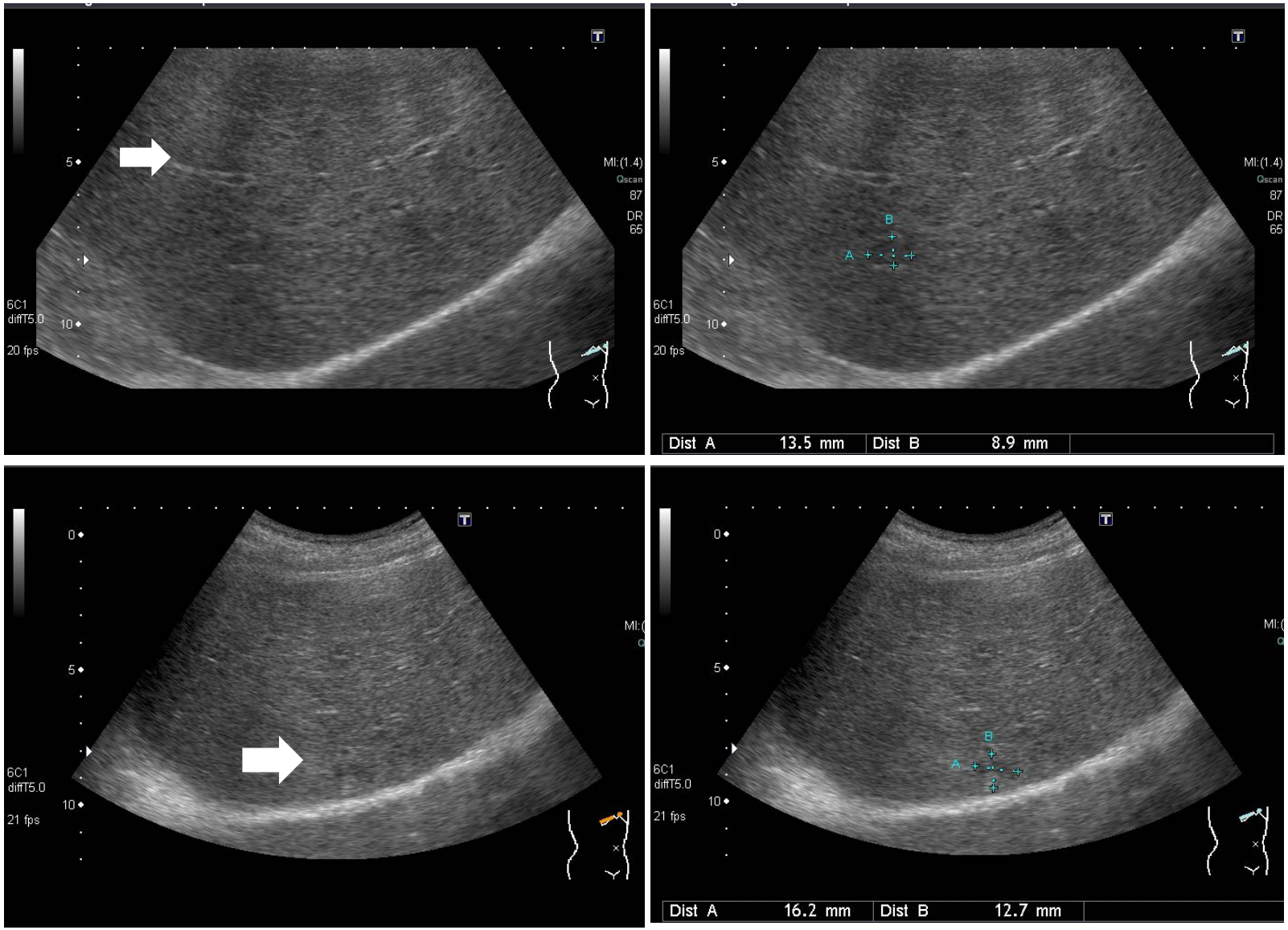

6C1
diffT5.0
20 fps
MI:(1.4)
Qscan
87
DR
65
B
A
Dist A 13.5 mm
Dist B 8.9 mm
6C1
diffT5.0
21 fps
Dist A 16.2 mm
Dist B 12.7 mm

Fig. 1

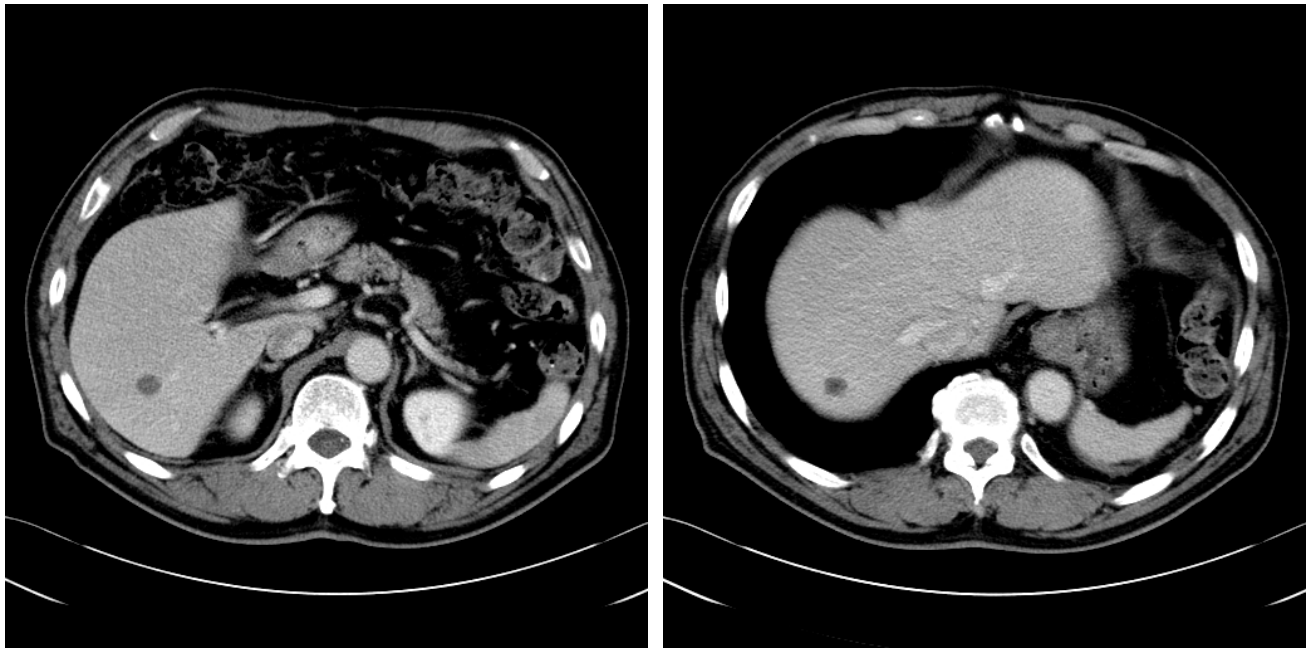


Fig. 2

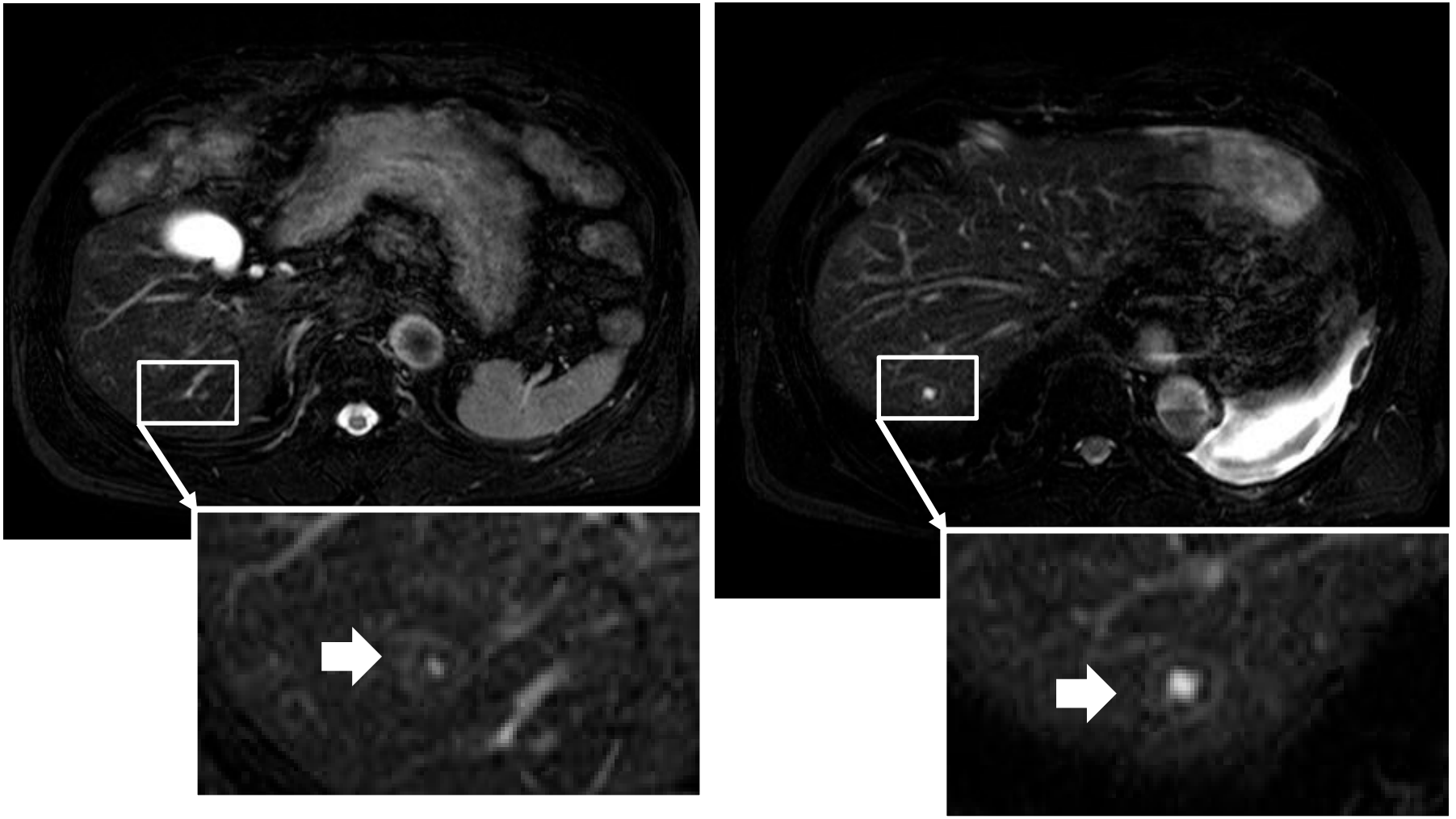


Fig. 3

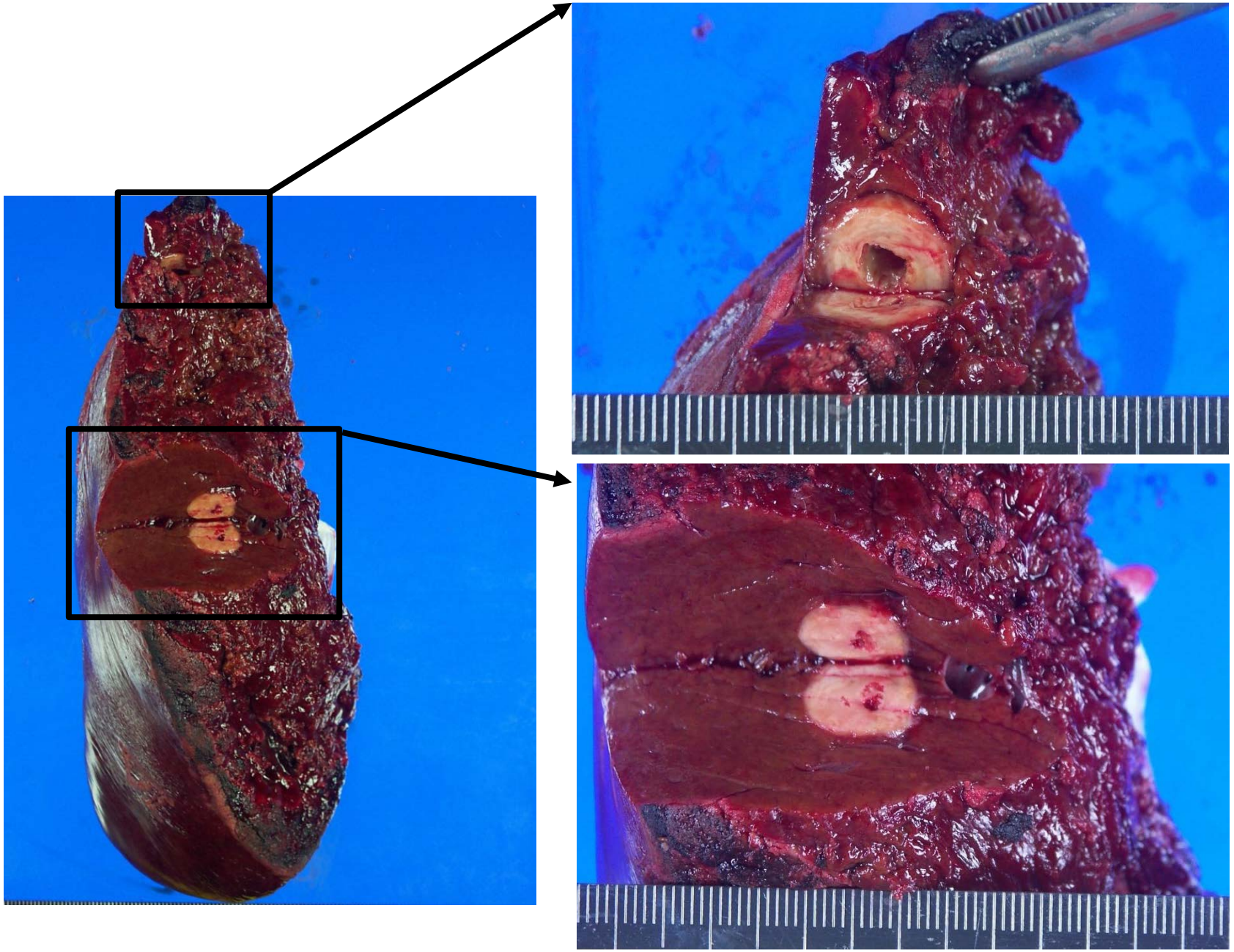
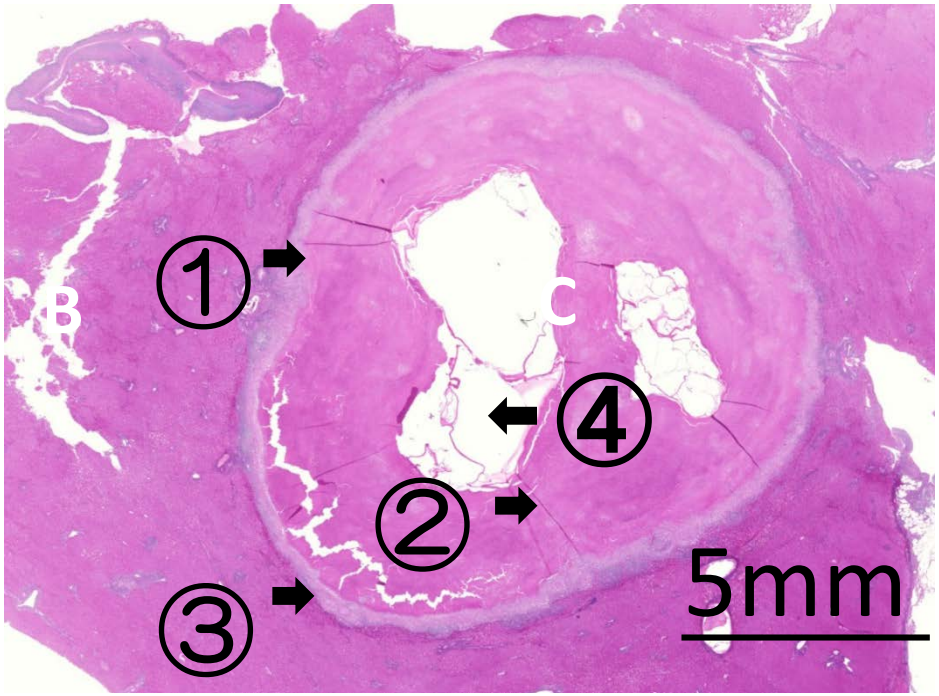


Fig. 4



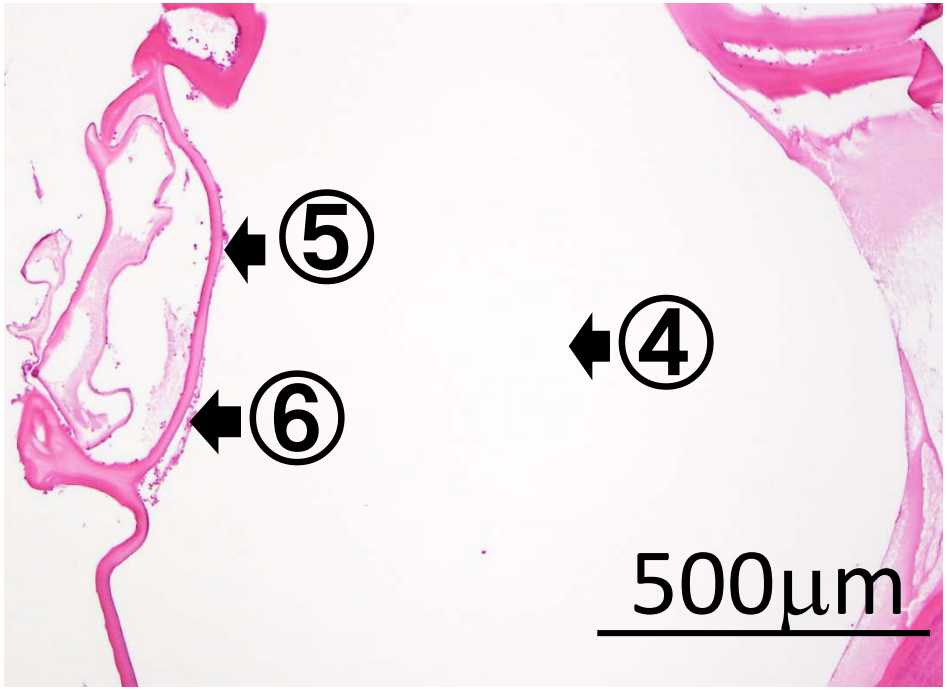
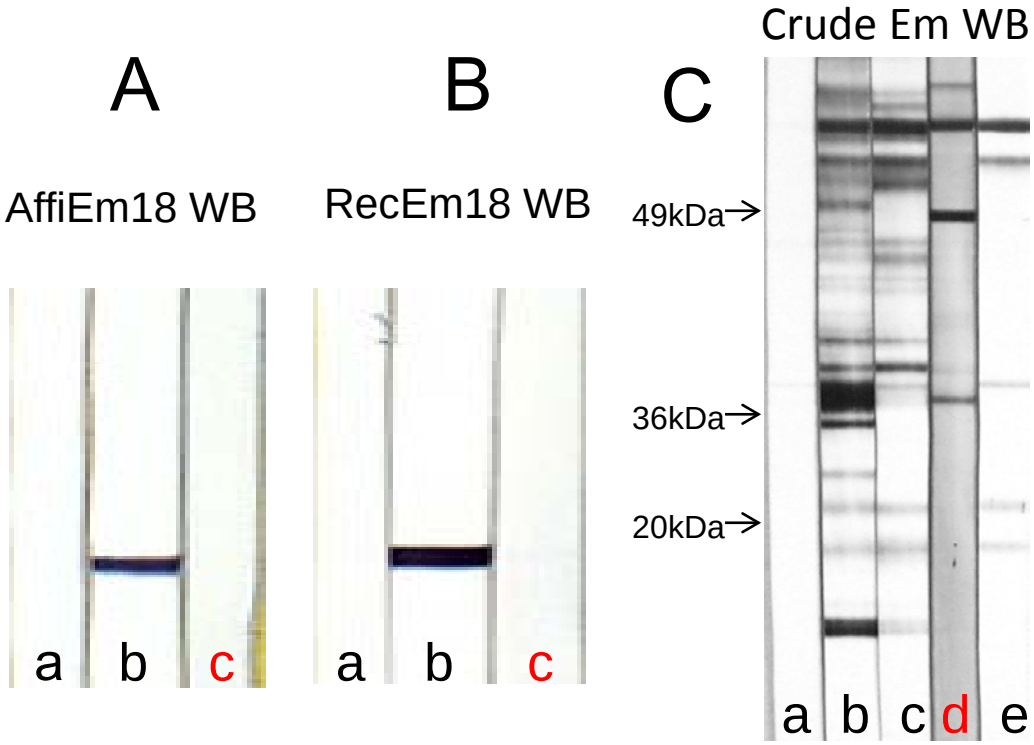


Fig. 5



a : negative control (1:50)
b : positive control (1:100)
c : the patient (1:20)

a: negative control (1:50)
b: positive control 1 (1:100)
c: positive control 2 (1:100)
d: the patient (1:20)
e: rabbit serum against Em18 (1:500)*

Fig. 6