Point-by-point responses to the editorial's and reviewers' comments

Reviewer 1:

#1.

"It has been reported that myelolipoma is to be sufficiently diagnosable by ultrasound, CT, or MRI. Therefore, the argument that biopsy should be accompanied because diagnosis is difficult with conventional imaging is considered incorrect."

Response

Thank you for your valuable comments and insightful review. As you pointed out, it has been reported that adrenal myelolipoma can be diagnosed based on the appearance of fat, myeloid tissue, and pseudocapsules. However, hepatic myelolipoma is rarely seen, and previous reports have suggested that its diagnosis before performing pathological examination is difficult. Therefore, we explored the possibility of imaging-based diagnosis using bone marrow scintigraphy, which has not been previously reported.

#2.

"Although the diagnosis of hepatic myelolipoma by the accumulation of $^{111}InCl_3$ is rare, it is impossible to interpret its clinical implication (advantage, etc.) compared with the existing diagnostic imaging methods."

Response

Thank you for your comment. A previous study on adrenal myelolipoma reported the accumulation of $^{111}InCl_3$ and concluded that it was useful in its dagnosis. It was difficult to compare the diagnostic ability of $^{111}InCl_3$ with the existing diagnostic imaging methods, as you mentioned; however, we believe it is clinically important to assess whether bone marrow scintigraphy can also diagnose hepatic myelolipoma. Bone marrow scintigraphy revealed the accumulation of radiopharmaceuticals in the soft tissue component, except for the fat-dominant part, indicating that the lesion contained hematopoietic cells. However, these radiopharmaceuticals also accumulate in reticuloendothelial cells, thereby accumulating in the surrounding liver tissue.

Therefore, we have suggested the limited utility of bone marrow scintigraphy in diagnosing hepatic myelolipoma. We have rewritten the abstract, core tip, and conclusion extensively as follows.

P3, L1–P4, L9

Abstract

Background

As hepatic myelolipoma is rarely encountered, its radiological diagnosis using ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) is challenging. Hepatic myelolipoma is similar to fat-contained hepatic lesions seen in hepatocellular carcinoma and angiomyolipoma. Therefore, further development of techniques to diagnose hepatic myelolipoma is warranted.

Case Summary

A 44-year-old obese man was found to have a hepatic lesion during his medical checkup. The lesion was 50 × 57 mm in size and was detected in S8 of the liver with US. The patient was diagnosed with a hepatic lesion 20 years ago, but it was left unresolved. The patient had no symptoms, liver dysfunction, hepatitis virus antibody, or tumor marker elevation. Plain CT showed a well-defined lesion in S8 of the liver. The central and peripheral areas of the lesion primarily exhibited fat density and hypodensity, respectively. MRI revealed a capsule-like structure. Biopsy was performed to address the probability of hepatocellular carcinoma. The lesion was pathologically confirmed as a myelolipoma. Bone marrow scintigraphy performed using $^{111}InCl_3$ revealed accumulation of the radiopharmaceutical in the soft tissue component, except in the fat-dominant part of the tumor, as well as in the surrounding liver parenchyma due to the presence of reticuloendothelial cells in the liver.

Conclusion

This is the first report on the diagnosis of hepatic myelolipoma using $^{111}InCl_3$ scintigraphy. The effectiveness of bone marrow scintigraphy for diagnosing hepatic myelolipoma might be limited. As radiopharmaceuticals accumulate in

both hematopoietic and reticuloendothelial cells, the accumulation of radiopharmaceuticals in the lesion is obscured.

P4, L12–P4, L21

Core Tip:

We attempted to perform bone marrow scintigraphy for hepatic myelolipoma to determine whether $^{111}InCl_3$ accumulates in the lesion. We found that the radiopharmaceutical accumulated in the soft tissue component, except for the fat-dominant part. However, the radiopharmaceutical also accumulates in the surrounding liver parenchyma, which comprises reticuloendothelial cells. Therefore, the effectiveness of bone marrow scintigraphy in diagnosing hepatic myelolipoma may be limited.

P9, L10–P9, L16

Bone marrow scintigraphy showed the accumulation of the radiopharmaceuticals into the lesion's soft tissue components, except for the fat-dominant part. Therefore, the efficacy of the radiopharmaceutical was confirmed. However, the conspicuity of the accumulation of radiopharmaceutical was weak, because it accumulated in the surrounding liver parenchyma owing to the presence of reticuloendothelial cells [6].

P10, L6–P10, L10

CONCLUSION

Bone marrow scintigraphy has limited utility in diagnosing hepatic myelolipoma. As radiopharmaceuticals accumulate in both hematopoietic and reticuloendothelial cells, the accumulation of radiopharmaceuticals in the lesion is obscured.

Reviewer 2:

#1.

“There are many repetitive sentences in the article, such as “ Myelolipoma is a nonfunctioning benign tumor composed of mature fat tissue and hematopoietic cells”. It is hoped that it can be modified and polished to make the article more smooth”

Response

As suggested, we have heavily revised the core tip and discussion.

P4, L8–P4, 15

Previous version

> **Core Tip:**
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> Myelolipoma is a nonfunctioning benign tumor that is composed of mature fat tissue and hematopoietic cells. It is usually found in the adrenal cortex and, in rare cases, in the liver [1]. According to previous reports, myelolipomas of liver origin are lesions with fatty and soft tissue density components accompanied by capsular-like structures. Therefore, it is crucial to differentiate it from other tumors, including hepatocellular carcinoma. Since the radiological diagnosis of hepatic myelolipoma using US, CT, and MRI is challenging, its diagnostic process generally requires a biopsy [2-4].

Revised version

> **Core Tip:**
>
> We attempted to perform bone marrow scintigraphy for hepatic myelolipoma to determine whether $^{111}InCl_3$ accumulates in the lesion. We found that the radiopharmaceutical accumulated in the soft tissue component, except for the fat-dominant part. However, the radiopharmaceutical also accumulates in the surrounding liver parenchyma, which comprises reticuloendothelial cells. Therefore, the effectiveness of bone marrow scintigraphy in diagnosing hepatic myelolipoma may be limited.

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P8. The first paragraph of the discussion

The repeated sentences were deleted.

#2

“Whether the “20XX” in the history of the present illness can be replaced by “2020” , which is consistent with the abstract, so that the context echo and the logic will be more rigorous”

Response

Thank you for your suggestion. We have followed your advice and corrected this part. (P6, L1)

Previous version

“20XX”

Revised version

“2020”

#3.

“There are many contents in the abstract. If it can be modified, the article will be more concise.”

Response

Thank you for your advice. As suggested, we rewrote the abstract as follows.

Original version

Background

Myelolipoma is rare nonfunctioning benign tumor that is composed of mature fat tissue and hematopoietic cells. It is usually found in the adrenal cortex and, in rare cases, in the liver. The radiological diagnosis of hepatic myelolipoma using US, CT, and MRI is challenging. Therefore, further development of the diagnostic techniques for hepatic myelolipomas is necessary.

Case Summary

This study included a 44-year-old obese man that showed no symptoms. Twenty years ago, he presented with a liver lesion that was more than 50mm during a medical check but neglected it. In July 2020, during an abdominal ultrasound examination at a medical checkup, a 50 × 57 mm hyperechoic lesion was observed in S8 of the liver. He came to our hospital on the suspicion of

hepatocellular carcinoma. His blood tests showed no liver dysfunction, no hepatitis virus antibody, and no tumor marker elevation. The lesion showed a heterogeneous low density and fat content based on plain CT. The MRI results indicated that the lesion contained fat and had a cuspule-like structure. Since the lesion was suspected of hepatocellular carcinoma or angiomyolipoma, we performed a biopsy. Through pathological examination, it was diagnosed as a myelolipoma. After the diagnosis, the patient underwent bone marrow scintigraphy with $^{111}InCl_3$ to confirm the presence of bone-marrow elements radiologically.

Conclusion

$^{111}InCl_3$ may mildly accumulate in well-differentiated hepatocellular carcinoma as in myelolipoma since it accumulates in the reticuloendothelial system. Therefore, it is difficult to exclude hepatocellular carcinoma. We found that the diagnosis of hepatic myelolipoma was difficult despite using 111InCl3 scintigraphy and that biopsy is necessary when diagnosing hepatic lesions with predominant fatty tissue.

Revised version

Background

As hepatic myelolipoma is rarely encountered, its radiological diagnosis using ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) is challenging. Hepatic myelolipoma is similar to fat-contained hepatic lesions seen in hepatocellular carcinoma and angiomyolipoma. Therefore, further development of techniques to diagnose hepatic myelolipoma is warranted.

Case Summary

A 44-year-old obese man was found to have a hepatic lesion during his medical checkup. The lesion was 50 × 57 mm in size and was detected in S8 of the liver with US. The patient was diagnosed with hepatic lesion 20 years ago, but it was left unresolved. The patient had no symptoms, liver dysfunction, hepatitis virus antibody, or tumor marker elevation. Plain CT showed a well-defined lesion in

S8 of the liver. The central and peripheral areas of the lesion primarily exhibited fat density and hypodensity, respectively. MRI revealed a capsule-like structure. Biopsy was performed to address the probability of hepatocellular carcinoma. The lesion was pathologically confirmed as a myelolipoma. Bone marrow scintigraphy performed using $^{111}InCl_3$ revealed accumulation of the radiopharmaceutical in the soft tissue component, except in the fat-dominant part of the tumor, as well as in the surrounding liver parenchyma due to the presence of reticuloendothelial cells in the liver.

Conclusion

This is the first report on the diagnosis of hepatic myelolipoma using $^{111}InCl_3$ scintigraphy. The effectiveness of bone marrow scintigraphy for diagnosing hepatic myelolipoma might be limited. As radiopharmaceuticals accumulate in both hematopoietic and reticuloendothelial cells, the accumulation of radiopharmaceuticals in the lesion is obscured.