INTRODUCTION
Reactive lymphoid hyperplasia (RLH), known as pseudolymphoma, is a rare condition that has also been termed nodular lymphoid lesion or pseudolymphoma of the liver. We report a case of hepatic RLH exhibiting unusual histiocyte-rich histologic features in a 47-year-old woman in conjunction with a renal cell carcinoma. A follow-up computed tomography scan was done 14 months after a right radical nephrectomy for renal cell carcinoma revealed a nodular lesion in segment 5 of the liver. The lesion was interpreted as metastatic renal cell carcinoma or hepatocellular carcinoma based on the history of the patient and radiologic findings. Wedge resection of segment 5 was done with sufficient distance from the mass. Microscopically, the lesion was composed predominantly of peculiar histiocytic proliferation and was characterized by lymphoid aggregates forming a lymphoid follicle with germinal centers. The present case and prior cases reported in the literature suggest that RLH of the liver appear to be a heterogenous group of reactive inflammatory lesions that are often associated with autoimmune disease or malignant tumors.

CASE REPORT
A 46-year-old woman underwent a radical right nephrectomy for stage I renal cell carcinoma of the clear cell type. A follow-up computed tomography (CT) scan was done 14 months later and revealed a new mass in segment 5 of the liver. It was 1.0 cm in diameter and well-defined round-shaped mass showing high attenuation at arterial phase imaging and slight low attenuation at portal and equilibrium phase imaging. For further evaluation of this mass, a magnetic resonance (MR) examination was performed. On T2-weighted MR imaging, this mass showed an intermediate hyperintensity-like liver malignancy (Fig. 1A). On gadolinium-enhanced MR imaging, this mass showed bright nodular enhancement at arterial phase imaging (Fig. 1B) and peripheral rim-like enhancement at delayed phase imaging, which was interpreted as a metastatic renal cell carcinoma or hypervascular hepatocellular carcinoma. A physical examination and chest roentgenogram were unremarkable. Laboratory data were all within the normal range and the results of liver function tests were normal (aspartate aminotransferase [AST] 21 U/L, alanine aminotransferase [ALT] 33 U/L, total bilirubin 0.66 mg/dL, alkaline phosphatase 94 U/L, and lactate dehydrogenase [LDH] 154 U/L). A test for the hepatitis B antibody was positive. The level of carcinoembryonic antigen was 3.7 ng/mL (normal -5), and CA19-9 was slightly elevated (41.98 U/mL, normal -36). Alpha-fetoprotein levels and anti-mitochondrial antibodies were not available. A diagno-
sis of metastatic renal cell carcinoma from the previous renal cell carcinoma was presumed, based on the prior history of the patient and radiological findings, and wedge resection of segment 5 including the mass was performed ensuring adequate distance from the mass. Grossly, the resected liver segment contained a well-circumscribed, yellowish-white, soli-
tary nodule of firm consistency, measuring 1 cm in diameter (Fig. 2A). Microscopically, the lesion was composed predominantly of a peculiar histiocytic proliferation without significant atypia and was characterized by lymphoid aggregates forming a lymphoid follicle with germinal centers (Fig. 2B, C). Most of the follicles were observed on the edge of the nodule. There was also marked hyalination in part of the mass, and several bile ductules were observed on the edge of the nodule. In the surrounding liver tissue, a marked periductular fibrosis with prominent lymphocytic infiltration was also observed (Fig. 2B). However, the hepatic parenchyma distant from this nodule was normal and lymphoid infiltration was not detected in the portal tracts. The bile duct system contained no stones. Lymphoid cells positive for L-26 (B cell marker, DAKO, Glostrup, Denmark) were distributed mainly in the germinal centers, while those positive for UCHL-1 (T cell marker, DAKO) were present around the germinal centers. There were no cytokeratin-positive malignant epithelial cells in the nodule. CD68 (histiocyte marker, DAKO) immunostaining highlighted the large number of histiocytes with epithelioid cell features (Fig. 2D). HMB45 (marker for angiomyolipoma, DAKO)-positive cells were not detected. Use of special stains, such as periodic acid-Schiff, Grocott, and Ziehl-Neelsen stains failed to demonstrate any microorganisms in the lesion. Furthermore, the histologic findings of lymphoid follicles with active germinal centers in our case are not seen in other granulomatous lesions, such as sarcoidosis. Among the RLH of the liver cases we reviewed, only one case exhibited aggregates of epithelioid histiocytes in the nodule as seen in the case presented here. These findings suggest that RLH of the liver appear to represent a heterogeneous group of reactive inflammatory lesions that share a varying degree of inflammation, rather than a specific entity.

Including the present patient, seven cases of hepatic RLH accompanying malignant tumors have been reported (3, 5, 8, 11, 13): in two each cases of colon cancer (3) and gastric cancer (5, 8). One patient with multiple carcinomas (gastric, cecal, and colon cancer) has presented with hepatic RHL (13). Pantanowitz and colleagues have described an RLH of the liver in a patient with a renal cell carcinoma (11). Surprisingly, the histopathologic findings including the presence of lymphoid follicles with germinal centers, hyalinized trabecular structures, and lymphocytic infiltration in the portal tracts around the nodular lesion, are very similar to those seen in the present case. These findings suggest a possible correlation between hepatic RLH and renal cell carcinoma. However, there have been very few cases, so it is not clear whether the renal cell carcinoma was involved in the onset of the hepatic RLH. We can speculate that the etiology of RLH of the liver may be related to an immunologic abnormality that is caused by the malignant tumor itself or previous surgery for the tumors. The prognosis of the RLH associated with malignancies is good, and most patients treated by resection of this lesion have shown no recurrence or progression to lymphoma (3, 11).

Although our case showed some features of an inflammatory pseudotumor, it has other histologic findings that are not seen in an inflammatory pseudotumor, including the absence of fibroblastic proliferation, a lack of prominent fibrosis, collection of foamy histiocytes, or occlusive endophlebitis. Furthermore, the histologic features of inflammatory pseudotumors do not necessarily contain lymphoid follicles that are always found in RLH (7). Thus, our lesion is histologically different from an inflammatory pseudotumor.

Radiologically, RLH should be differentiated from other
solid focal hepatic lesions as both conditions show intermediate hyper-intensity on T2-weighted MR imaging. In particular, the RLH in our case showed bright nodular enhancement on arterial phase MR imaging, which may be misinterpreted as hypervascular metastasis from a renal cell carcinoma or a hypervascular hepatocellular carcinoma. The imaging findings of our case might be similar to those of previous reports demonstrating variable enhancement of RLH using contrast-enhanced CT, CT during angiography, and direct hepatic angiography (3, 6, 8, 10, 12). However, since the imaging modalities used in published reports were variable, a further evaluation with a large number of cases will be required in order to define clearly the radiological findings of this entity.

| Cases (reference) | Age/Sex | Size (cm) | Special histologic features in addition to lymphoid follicles with germinal center | Associated disease |
|-------------------|---------|-----------|----------------------------------------------------------------------------------|-------------------|
| Grouls (5)        | 85/F    | 1.4 × 0.8 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Gastric cancer    |
| Isobe et al. (1)  | 59/F    | 0.9       | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Diabeite mellitus|
| Ohtsu et al. (6)  | 42/F    | 1.5 × 1.3 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Chronic hepatitis B|
| Katayanagi et al. (7) | 66/F | 1.5 × 1.0 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Diabeite mellitus|
| Tanizawa et al. (14) | 67/F  | 2.0       | Angiofollicular structures mimicking Castleman’s disease                         |                    |
| Kim et al. (8)    | 72/M    | 1.7 × 1.5 | Chronic active hepatitis of the non-tumorous liver                               | Chronic hepatitis C|
| Sharifi et al. (2) | 52/F  | 0.4       | Lymphoepithelial lesions                                                         | Primary biliary cirrhosis|
| Sharifi et al. (2) | 56/F  | 1.5       | Aggregates of epithelioid histiocytes Lymphocytic infiltration in the portal tracts around the nodular lesion | CREST syndrome |
| Sharifi et al. (2) | 56/M  | 0.7       | Lymphoepithelial lesions Scattered giant cells and epithelioid histiocytic aggregates | Chronic diverticular disease |
| Nagano et al. (10) | 47/F  | 1.0       | Numerous hyalinized trabeculated structures                                     | Drug-induced hepatitis |
| Pentonowitz et al. (11) | 69/F  | 1.7 × 1.0 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Chronic thyroiditis |
| Okubo et al. (9)  | 49/F    | 2.0       | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Renal cell carcinoma|
| Takahashi et al. (3) | 77/F  | 1.5       | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Colon cancer      |
| Maehara et al. (12) | 72/F  | 1.3 × 1.0 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Colon cancer      |
| Willenbrock et al. (4) | 38/F  | 1.8       | Epithelioid cells, and giant cells in the interfollicular area                    | Focal nodular hyperplasia |
| Sato et al. (13)  | 75/F    | 1.4       | Lymphoepithelial lesions                                                         | Hemangioma         |
| Present case      | 46/F    | 1.0 × 1.0 | Lymphocytic infiltration in the portal tracts around the nodular lesion          | Renal cell carcinoma|

Rt., right; Lt., left; Seg, segment.
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