

## Diagnosis of a case of thymus area lymphoma

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### Abstract

This was a rare case, in which clinical manifestation was a thymus area tumor accompanied by proteinuria, kidney dysfunction and kidney enlargement. Tumor biopsy and bone marrow examination failed to clarify its diagnosis. Renal biopsy revealed diffuse infiltration by atypical lymphoid cells in renal interstitium. Immunoperoxidase studies demonstrated this case was non-Hodgkin's lymphoma (NHL) of the B cell type through the renal biopsy.

**Key words:** renal biopsy; malignant lymphoma; lymphomatous kidney infiltration

### INTRODUCTION

Diagnosis of malignant lymphoma is usually made by lymph node or bone marrow biopsy in most patients with widespread lymphoma and renal involvement. Renal lymphoma often occurs as a part of a multi-systemic disseminated lymphoma or as a recurrence of the tumor. Renal involvement usually occurs late in the course of the disease and is clinically silent<sup>[1]</sup>, although renal involvement has been reported in 6% to 60% of cases at autopsy<sup>[2]</sup>. Acute renal failure (ARF) from lymphomatous infiltration has been described but is quite rare<sup>[3–6]</sup>. In 1990, Miyake JS<sup>[7]</sup> reported a case of acute renal failure due to renal parenchymal lymphomatous infiltration, in which the phenotype of a non-Hodgkin's lymphoma was primarily established using renal biopsy tissue. Here we report a case of malignant lymphoma diagnosed by renal biopsy, presented with nonoliguric acute renal insufficiency.

### CASE REPORT

A 27-year-old female presented with swelling face

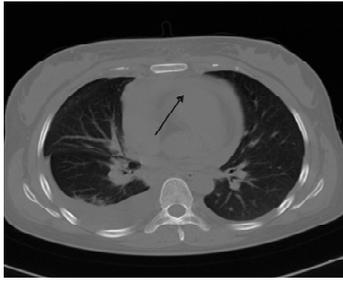
for 20 days and chest distress for a week. Laboratory tests revealed proteinuria(+~++) and serum creatinine concentration of 2.5–3 mg/dl. Her urinary production was always normal during the course of disease. The patient was referred to our institution for further evaluation.

Physical examination on admission revealed semireclining and respiratory rate of 28 breaths/min. Her blood pressure of 130/90 mmHg, pulse rate of 105 beats/min and temperature of 37.2°C were recorded. Her face was swollen, cervical part was thickened, and jugular was filled. Several mung bean size axillary nodes could be touched, but the liver and spleen were not palpable. Her breast bone had no tenderness, and lower limbs had no edema. An ultrasonograph revealed a great quantity of pericardial effusion, and a small quantity of right pleural effusion. The thorax CT scan presented a tumour in the thymus area (**Fig. 1**). Renal ultrasound showed a massively enlarged hypoechoic kidneys that measured 15.4 and 15.2 cm (right and left) in the longitudinal axis.

The white blood cell count was 5 700 cells/mm<sup>3</sup> with a normal differential count. The hematocrit value was 33%, and thrombocyte count was 115 000 cells/mm<sup>3</sup>. Urinalysis revealed a gravity of 1.005, pH of 5.0 and 1+ protein. No cells and casts were revealed in micro-

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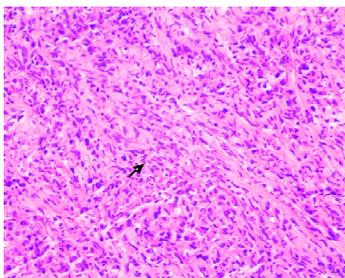
**Fig. 1** The thorax CT scan showing a tumour in thymus area

scopic examination of the spun urine. The following laboratory values were obtained: blood urea nitrogen (BUN), 25 mg/dl; creatinine, 3.5 mg/dl; sodium, 138 mmol/L; potassium, 4.1 mmol/L; chloride, 105 mmol/L; bicarbonate, 21 mmol/L; calcium, 2.11 mmol/L; phosphorus, 1.87 mmol/L; albumin, 3.55 mg/dl; total protein, 6.1 mg/dl; uric acid, 371 mmol/L; lactate dehydrogenase, 409 u/L; and total bilirubin, 10.4  $\mu$ mol/L; CRP, 91.6 mg/L. The detection of antinuclear antibody was negative. The serum level of immunoglobulin and complement was within the normal range.

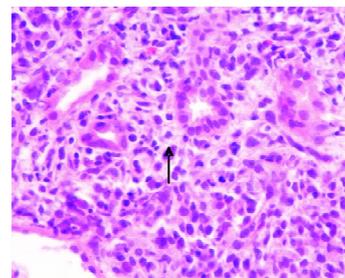
The pericardial effusion showed haematodes. Wright's staining revealed dysmorphic cells, mesothelial cells and mature erythrocytes. Flow cytometric examination of pericardial effusion presented that abnormal cells accounting for 12.8% of all cells and positive ratios of the following markers were CD<sub>4</sub> 97.3%, CD<sub>2</sub> 27.8%, CD<sub>7</sub> 30.2%, CD<sub>8</sub> 13.7%, CD<sub>3</sub> 16.4%, CD<sub>16+56+</sub> 7.2%, CD<sub>5</sub> 18.3%, CD<sub>20</sub> 13.9%, CD<sub>19</sub> 8.2%, CD<sub>3</sub><sup>-</sup>CD<sub>4</sub><sup>+</sup> 83.5% respectively, and CD<sub>10</sub>, FMC-7, CD<sub>103</sub> were negative. CT-guided

needle biopsy of the tumour in thymus area was difficult and the drawing from the tumour material was not satisfactory. Histology showed a kind of malignant disease but could not identify the origin of the neoplasm (**Fig. 2**), because immunohistology results showed that the staining of the neoplastic cells were CD<sub>20</sub>( $\pm$ ), CD<sub>79 $\alpha$</sub> (-) for B cell marker; CD<sub>3</sub>(-), CD<sub>45RO</sub>(-) for T cell marker; CD<sub>5</sub>(-) for thymocyte marker; CK(-) for epithelium marker; TdT(-), CD<sub>99</sub>(-) for lymphoblast marker. There was no abnormal cell infiltration in the bone marrow biopsy.

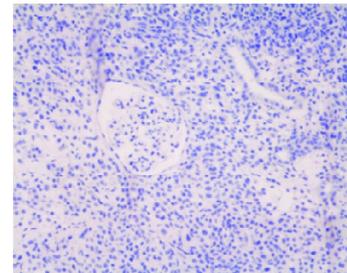
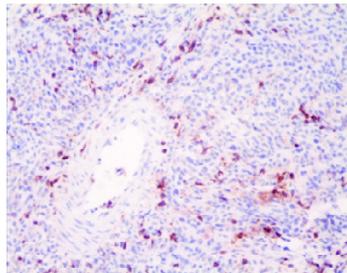
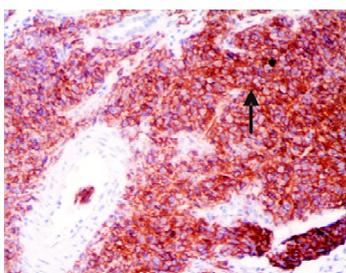
Definite diagnosis was obtained by renal biopsy, which revealed diffuse infiltration by atypical lymphoid cells in renal interstitium (**Fig. 3**). Immunoperoxidase studies demonstrated powerful positive staining of the neoplastic cells for the B cell antigen CD<sub>20</sub>, negative staining for the T cell antigen CD<sub>45RO</sub> and lymphoblast antigen TdT (**Fig. 4**). These results were consistent with non-Hodgkin's lymphoma (NHL) of the B cell type. The patient discharged before any specific treatment could be started for economic reasons.



**Fig. 2** Histology of tumour in thymus show a kind of malignant disease, but the origin of the neoplasm could not be identified (HE,  $\times$  200)



**Fig. 3** The observation of kidney biopsy. Light microscopy showing diffuse infiltration of the renal parenchyma by atypical lymphoid cells. (HE,  $\times$  400)



**Fig. 4** Immunocytochemistry result of neoplastic cells (biotin-streptavidine method,  $\times$  400). A: Lymphoma cells strongly express CD20 (B-cells); B: Negative staining for the T cell antigen CD<sub>45RO</sub>; C: Negative staining for the lymphoblast antigen TdT.

**Fig. 4** Immunocytochemistry result of neoplastic cells (biotin-streptavidine method,  $\times$  400)

## DISCUSSION

Although renal lymphoma infiltration has been documented in about one-third of all diffuse lymphoma patients at autopsy<sup>[8]</sup>, kidney biopsy is not an imperative means for diagnosing lymphoma. Renal involvement in lymphoma is usually subclinical, and clinically overt renal disease is rare. Diffuse lymphomatous infiltration of the kidneys may cause tubular dysfunction<sup>[9]</sup>. We performed bone marrow biopsy and mediastinal tumour biopsy in this case, but we couldn't establish the definite diagnosis. This case presented with mild proteinuria, enlarged kidneys and renal insufficiency. These clinical manifestations suggested renal involvement, so we performed a percutaneous needle biopsy of the kidney. Light microscopy showed diffuse infiltration of the renal parenchyma by atypical lymphoid cells. Immunoperoxidase studies demonstrated the positive staining of the infiltration cells for the B cell antigen CD<sub>20</sub>. Renal involvement by lymphoma has been classified as two categories: intraglomerular intravascular lymphoma and tubulointerstitial diffuse invasion type. This case showed an interstitial type of lymphomatous infiltration. The kidney biopsy not only established the diagnosis but also provided immunophenotype of the lymphoma. Hunter S *et al.*<sup>[10]</sup> retrospectively reviewed a total of 407 image guided focal renal lesion biopsies, in which a diagnosis of lymphoma was made in 11 patients(3%). Törnroth T *et al.*<sup>[11]</sup> reviewed 55 cases of diffuse bilateral renal lymphoma presenting with acute renal failure(ARF) of unknown cause. They found that signs of extrarenal lymphomatous involvement were detected in 24 cases(44%) at the time of kidney biopsy or shortly thereafter. Percutaneous kidney biopsy is believed to provide the most expedient means of establishing the diagnosis in those patients whose lymph node or bone marrow biopsy fails to confirm diagnosis, as well as tissue sources are not easily accessible. This viewpoint is consistent with other authors<sup>[12-14]</sup>.

To identify the clinical and pathological characteristics of lymphomatous kidney infiltration, Törnroth T *et al.*<sup>[11]</sup> reviewed 55 cases. They found that 87% of cases with interstitial and 45% with intraglomerular lymphoma presented with ARF. In contrast, 5 of 10 cases with intraglomerular (but none with interstitial infiltration) presented with nephrotic range proteinuria. All but 2 cases(95%) with ARF and interstitial lymphoma (but none with ARF and intraglomerular lymphoma) showed bilaterally enlarged kidneys. Primary renal lymphoma has been reported, but is controversial. Reports on primary renal lymphoma are scarce in the urological literature, and the most part of them are secondary to a lymphomatous infiltration of the kidneys<sup>[15-16]</sup>. Renal infiltration in malignant lymphomas may involve the

interstitium, but rarely causes acute renal failure. Highly aggressive intravascular lymphoma may have hemophagocytosis and capillary hyperpermeability syndrome, then leads to anuric prerenal acute renal failure<sup>[17]</sup>. Our case presented with non-oliguric acute renal insufficiency, low-grade proteinuria, bilaterally enlarged kidneys, interstitial lymphomatous infiltration and mediastinal tumor. These features corresponded with the general characteristics outlined above.

Mediastinal large B-cell lymphomas are uncommon haematologic malignancies mostly seen in women<sup>[18]</sup>. Satouchi M<sup>[19]</sup> carried out clinical evaluation of mediastinal hematologic malignancies. His study identified 22 cases(24.2%) with mediastinal lymphoma. Histology revealed 6 cases of diffuse large B-cell lymphoma, 6 of lymphoblastic lymphoma, 6 of Hodgkin's disease, 2 of granulocytic sarcoma, and 1 of lymphoplasmacytic lymphoma. Definitive diagnoses were obtained only by flow cytometric examination of pleural or pericardial effusion in two cases. Pradhan SB<sup>[20]</sup> reported the cytology of body fluids from different sites. The results showed that 18.66% cases were found to have malignancy and Non Hodgkin's lymphoma comprised 6.5% of the malignancy. This case presented with mediastinal tumor, but histology and flow cytometric examination of pericardial effusion could not obtain definitive diagnosis. From the view of monism, we diagnosed this case of mediastinal lymphoma accompanied with lymphomatous kidney infiltration.

It was reported that impaired renal function was a poor prognostic factor for non-Hodgkin's lymphoma<sup>[21]</sup>. Renal function should therefore be monitored closely in such cases. Renal dysfunction caused by direct tumoral involvement may complicate the therapy and shorten the chances of survival.

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