Jpn. J. Infect. Dis., 66, 345-347, 2013

Short Communication

Renal Abscess Involving Mucormycosis by Immunohistochemical Detection in a Patient with Acute Lymphocytic Leukemia: a Case Report and Literature Review

Keishin Sunagawa[1]*, Toshiyuki Ishige[1], Yosiaki Kusumi[1], Masatake Asano[2], Eri Nisihikawa[3], Maiko Kato[3], Hiroshi Yagasaki[3], and Norimichi Nemoto[1]

[1]*Department of Pathology and* [3]*Department of Pediatrics and Child Health, Nihon University School of Medicine, Tokyo 173-8610; and* [2]*Department of Pathology, Nihon University School of Dentistry, Tokyo 101-8310, Japan*

(Received June 29, 2012. Accepted May 1, 2013)

SUMMARY: A 14-year-old girl with acute lymphocytic leukemia complained of right flank pain and fever. As her fever was prolonged, she underwent renal biopsy and was diagnosed with mucormycosis. We performed right nephrectomy, and subsequent pathological examination of her tissue specimen also detected mucormycosis. Here, we report a rare case of renal mucormycotic abscess.

Mucormycosis is an invasive fungal infection targeting compromised hosts and leading to hematological malignancy. Mucormycosis is the common name given to diseases caused by fungi belonging to the order Mucorales (1). Mucormycosis displays a high mortality rate without treatment. The genitourinary infections caused by *Mucor* spp. are rare (2–5).

Here, we describe in detail the histological, immunohistochemical, and microbiological detection of mucormycosis in a patient with acute lymphocytic leukemia (ALL).

A 14-year-old girl with a history of ALL was admitted to our pediatric department because of right flank pain combined with fever and chills. She underwent intensive chemotherapy for ALL and was scheduled to undergo an additional chemotherapy regimen. She experienced agranulocytosis for four times, for a total of 77 days, induced by nine courses of chemotherapy; however, it was treated by granulocyte colony-stimulating factor (G-CSF), and her condition promptly improved. Although her ALL was in remission and she displayed a reduced peripheral blast count, she suffered right flank pain on day 177 of her illness. The patient was a junior high school student and was otherwise healthy before admission for ALL. She had not suffered any trauma or bruising.

On admission, her temperature was 39.7°C, blood pressure was 96/58 mmHg, pulse rate was 118 beats/min, and respiration rate was 24 breaths/min. She had no apparent skin eruptions or urinary symptoms but displayed right costophrenic angle knock tenderness. Laboratory tests revealed a leukocyte count of 3,600 cells/l, hemoglobin level of 6.8 g/dl, and platelet count of 51,000 cells/l. In addition, her blood urea nitrogen level was 4.0 mg/dl and creatinine concentration was 0.57 mg/dl. Urinary analysis showed an occult blood score of 3+ without bacteria, and serological analysis detected a C-reactive protein level of 28.81 mg/dl and beta-D glucan concentration of <3.5 pg/ml. Two sets of blood cultures were negative for infection. Contrast enhanced abdominal computed tomography (CT) detected a suspected right renal abscess; however, there was no apparent abnormality in chest X-ray, thoracic CT, and brain magnetic resonance imaging (MRI). Initially, she underwent bactericidal antimicrobial therapy; however, her condition did not improve and fever continued. Because we had to rule out differential diagnoses, e.g., a non-bacterial infection such as candidiasis or a non-infectious condition such as a tumor or infarction, we consulted the urology department of our hospital to obtain renal biopsy. Thus, the patient underwent biopsy of her right kidney on day 199 of her illness. The renal tissue specimen was obtained by needle biopsy, and histopathological examination detected severe inflammatory cell infiltration and abscess formation. In addition, irregularly branched, thick, and aseptate hyphae were detected. Periodic acid-Schiff (PAS) staining and Grocott's staining depicted these hyphae more clearly, which was consistent with mucormycosis. Renal tissue culture was also performed, and *Mucor* sp. was detected in the fungal agar tissue culture.

In order to allow the patient to continue and complete her chemotherapy for ALL, we performed right nephrectomy to remove the renal abscess. Grossly, the removed right kidney weighed 400 g, measured 8 cm along its longest axis, and displayed a large necrotic abscess with hemorrhage in the renal capsule (Fig. 1a). Histopathological examination revealed neutrophilic, lymphocytic, and giant cell infiltration with necrosis (Fig. 1b, ×400). The presence of fungi was also confirmed. Broad, pleomorphic hyphae that predominantly branch at right angles besides non-septae, which are characteristic features of mucormycosis, were observed (Fig. 2a, ×400; Grocott's staining). In addition, severe inflammation and multinucleated giant cell granuloma

*Corresponding author: Mailing address: Department of Pathology, Nihon University School of Medicine, 30-1, Kamicho, Oyaguchi, Itabashi-Ku, Tokyo 173-8610, Japan. Tel: +81-3-3972-8111 ext. 2256, Fax: +81-3-3972-8830, E-mail: garjyusaiga@gmail.com

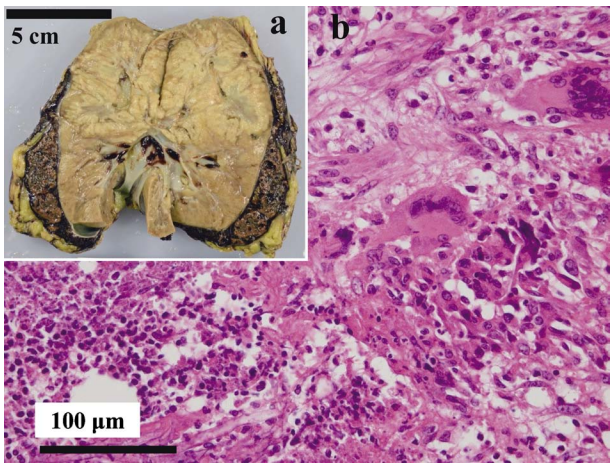

Fig. 1. (a) Gross findings of the excised right kidney. It displayed a necrotic and large abscess with hemorrhage in the renal capsule. (b) Microscopic view of the kidney showed the severe inflammation with giant cells (×400).

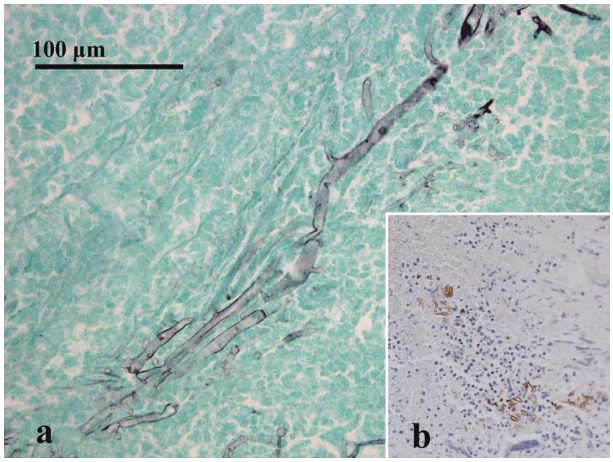

Fig. 2. (a) Microscopic view of *Mucor* hyphae (×400, Grocott's staining). (b) *Rhizomucor* was detected by immunohistochemistry (×400).

were observed. Although any organisms could not be detected in the kidney tissue culture, we diagnosed this patient with a renal abscess involving mucormycosis.

Finally, in the kidney tissues, we immunohistochemically detected *Rhizomucor* (Fig. 2b). In brief, the kidney tissue samples were stained, fixed in 10% formalin, and embedded in paraffin. In 4-μm thick tissue sections, immunohistochemical studies were performed using anti-*Rhizomucor* antibody (1:500 dilution, monoclonal mouse, clone: WSSA-RA-1; DAKO, Glostrup, Denmark). Next, the samples were rinsed with citrate buffer solution (10 mM, pH 6.0), heated for 10 min, and hybridized. Finally, using the amino acid polymer method (simple stain), visualization was performed using 3,3′-diaminobenzidine, and counterstaining was performed with hematoxylin. Based on our immunohistochemical results, we diagnosed the causative agent as belonging to the order Mucorales.

The entry sites of the organism were unclear, and there was no apparent abnormality of thoracic organs. Following nephrectomy, her postoperative course was good and ALL went into complete remission; therefore, she was discharged on postoperative day 383.

This is a rare case of renal infection involving mucormycosis. Most patients with invasive mucormycosis are compromised hosts that display an acute and progressive course. Accordingly, this infection displays a high mortality rate. *Mucor* spp. often invade blood vessels. Rhinocerebral mucormycosis is the most common form of mucormycosis; however, other sites such as the lungs, intestinal tract, and skin can also be affected, although kidney involvement is rare (3–6). The risk factors for mucormycosis are hematological malignancies such as leukemia or malignant lymphoma, multiple trauma, diabetes mellitus, malnutrition, severe burns, immunosuppressive therapy, cancer chemotherapy, steroid therapy, receiving an iron chelate preparation, or undergoing bone marrow or organ transplantation. Because it is difficult to detect species belonging to the *Zygomycota* phylum using antigenic and molecular detection methods, the diagnosis of mucormycosis depends on the identification of morphological and pathological features of the causing fungus (1). Levy and Bia reported that the differential diagnoses of renal mucormycosis include renal tumors, infarction, and abscesses (5).

Genitourinary infections of mucormycosis are rare, and previous cases were traced to a renal cortical abscess or positive urine culture derived from the infection of an occult site, and others (2–5). Our case involved a renal abscess that was confirmed as mucormycosis by immunohistochemical and microbiological examinations.

On pathological examination, fungal infection was confused with tuberculosis or other infections because they share similar characteristics such as tissue necrosis, neutrophil and macrophage infiltration, Langerhans giant cell accumulation, and granuloma formation, which are induced by the host immune response. *Mucor* spp. often invade vessel walls and cause vascular necrosis or thrombosis as well as necrosis or bleeding within the surrounding tissues. Their hyphae have also been found within glomeruli, tubules, and the interstitium (5).

The entry sites of these organisms remain unclear; however, they live in natural and environmental habitats, and susceptible hosts are always at a risk of exposure. The major mode of disease transmission for *Zygomycetes* is presumed to be the respiratory tract by inhalation of spores from environmental sources, and while that for others is the percutaneous or gastrointestinal route. The traumatic implantation of spores has been observed in a number of patients. Exposure can also occur at medical injection sites, catheter insertion sites, injection sites for illicit drug use, and the sites of other traumas such as wounds or insect bites or stings (7).

Our patient was diagnosed with mucormycosis based on renal biopsy, and we confirmed the diagnosis using tissue cultures and by pathological examination in addition to immunohistochemistry. Thus, life-saving nephrectomy was promptly performed. Mucormycosis is an invasive fungal infection with a poor prognosis. Renal biopsy is contraindicated for detecting renal infection, including renal abscesses. However, in the present case, we had to differentiate between a renal abscess, renal infarction, and invasion of the right

kidney by ALL cells. Pathological examinations are useful to arrive at a definitive diagnosis; therefore, we recommend more aggressive surgical treatment (removal or resection) in complex cases.

Acknowledgments The authors thank Prof. Yutaka Tsutumi, 1st Department of Pathology, Fujita Health University School of Medicine, for the excellent technical assistance.

Conflict of interest None to declare.

REFERENCES

1. Eucker, J., Sezer, O., Graf, B., et al. (2001): Mucormycoses. Mycoses, 44, 253–260.
2. Florentine, B.D., Carriere, C. and AbdulKarim, F.W. (1997): Mucor pyelonephritis—report of a case diagnosed by urine cytology, with diagnostic considerations in the workup of funguria. Acta Cytol., 41, 1797–1800.
3. Goel, S., Carter, J.E., Culpepper, M., et al. (2009): Primary renal zygomycotic infarction mimicking renal neoplasia in an immunocompetent patient. Am. J. Med. Sci., 338, 330–333.
4. Guardia, J.A., Bourgoigni, J. and Diego, J. (2000): Renal mucormycosis in the HIV patient. Am. J. Kidney Dis., 35, E24.
5. Levy, E. and Bia, M.J. (1995): Isolated renal mucormycosis: case report and review. J. Am. Soc. Nephrol., 5, 2014–2019.
6. Orr, W.A., Mulholland, S.G. and Walzak, M.P., Jr. (1972): Genitourinary tract involvement with systemic mycosis. J. Urol., 7, 1047–1050.
7. Ribes, J.A., Vanover-Sams, C.L. and Baker, D.J. (2000): Zygomycetes in human disease. Clin. Microbiol. Rev., 13, 236–301.