



Fig. 1. Periodic acid–Schiff stain demonstrates numerous fungal profiles (arrows) in the thyroid stroma with angio-invasion (original magnification, $\times 200$).

were identified. These findings were consistent with a fungal thyroiditis caused by *Aspergillus*. Blood vessels were invaded by the hyphae of the fungus (Figure 1). A culture of the aspirated fluid showed no growth. The results of repeated tests with an *Aspergillus* antigen (galactomannan) enzyme-linked immunosorbent assay (ELISA) were negative. There was no evidence of aspergillosis in the other organs. Blood and sputum cultures were negative. Intravenous liposomal amphotericin B (5 mg/kg daily) was initiated, and later switched to oral voriconazole (200 mg twice a day for 2 days, and then 100 mg twice a day) on the day of discharge, 2 weeks after the initiation of amphotericin B, and was continued for the following 12 weeks. Because tests showed a decreasing thyroid function, hormone replacement was begun 10 days after surgery.

Discussion

Isolated fungal infections of the thyroid are uncommon because of its rich vascular and lymphatic supply, well-developed capsule, and high iodine content [1]. Although involvement of the thyroid gland has been detected at autopsy in 9–15% of patients with disseminated fungal disease, there are few reports of isolated infections of the gland without signs of disseminated disease in a living patient [1]. Biopsy, direct microscopy and culture of fine-needle aspirate are still essential for obtaining a diagnosis because systemic antigenaemia (as measured by galactomannan screening) may not develop in patients with localized cases [2].

It is clear that the introduction of the serum *Aspergillus* galactomannan antigen detection test has made earlier diagnosis possible in high-risk patients. Nonetheless, a major problem with the galactomannan test is that its sensitivity varies greatly, reportedly ranging from 30% to 100%, and its specificity 38% to 98% [3]. Such wide variation in the levels of circulating galactomannan may be attributable to the administration of antifungal drugs, a low frequency of sampling, or a low fungal burden [3,4]. One clinical study suggests that the lesser sensitivity of galactomannan in some patients, especially patients with airway-invasive as-

pergillosis, might be a result of the minor intravascular fungal burden in these patients [4]. Hence, the cut-off value in the galactomannan assay may need to be set differently for different risk populations [5]. Another possibility is that *Aspergillus* could be secreting a galactomannan antigen with only one galactofuranose epitope not detected by some ELISA methods. Finally, already formed antibody to *Aspergillus* might influence the result of the galactomannan test [6].

In conclusion, we report a rare case describing the successful treatment of serum galactomannan-negative isolated *Aspergillus* thyroiditis in a haemodialysis patient with end-stage renal disease due to lupus nephritis.

Division of Nephrology,
Department of Internal
Medicine, College of
Medicine, The Catholic
University of Korea, Seoul,
Republic of Korea
E-mail: ysc543@unitel.co.kr

Sungjin Chung
Jae Ho Lee
Yejee Lim
Hae Kyung Yang
Yoon Sik Chang

Acknowledgements. This case report was approved by the Catholic University of Korea Yeouido St. Mary's Hospital Institutional Review Board (No. SC10ZZZ0042).

Conflict of interest statement. None declared.

1. Goldani LZ, Zavascki AP, Maia AL. Fungal thyroiditis: an overview. *Mycopathologia* 2006; 161: 129–139
2. Guetgemann A, Brandenburg VM, Ketteler M *et al.* Unclear fever 7 weeks after renal transplantation in a 56-year-old patient. *Nephrol Dial Transplant* 2006; 21: 2325–2327
3. Hachem RY, Kontoyiannis DP, Chemaly RF *et al.* Utility of galactomannan enzyme immunoassay and (1, 3) beta-D-glucan in diagnosis of invasive fungal infections: low sensitivity for *Aspergillus fumigatus* infection in hematologic malignancy patients. *J Clin Microbiol* 2009; 47: 129–133
4. Hidalgo A, Parody R, Martino R *et al.* Correlation between high-resolution computed tomography and galactomannan antigenemia in adult hematologic patients at risk for invasive aspergillosis. *Eur J Radiol* 2009; 71: 55–60
5. Guinea J, Jensen J, Peláez T *et al.* Value of a single galactomannan determination (Platelia) for the diagnosis of invasive aspergillosis in non-hematological patients with clinical isolation of *Aspergillus* spp. *Med Mycol* 2008; 46: 575–579
6. Saito T, Shime N, Itoh K *et al.* Disseminated aspergillosis following resolution of *Pneumocystis pneumonia* with sustained elevation of beta-glucan in an Intensive Care Unit: a case report. *Infection* 2009; 37: 547–550

doi: 10.1093/ndtplus/sfq163

Advance Access publication 23 September 2010

A rare presentation of pulmonary hemorrhage with hepatitis C-associated cryoglobulinemia and membranoproliferative glomerulonephritis

Cryoglobulinemia (CG)-associated pulmonary hemorrhage is an unusual entity. An even rarer occurrence is that of membranoproliferative glomerulonephritis (MPGN) in a patient with CG and alveolar hemorrhage. As far as we can tell, there has been no more than a total of four such

cases that have been formally published, and this would be the fifth case [1,2].

A 46-year-old Caucasian woman presented to the emergency department with acute respiratory failure, petechiae, pulmonary hemorrhage, azotemia, proteinuria, and hematuria for 10 days. A ventilation/perfusion lung scan was read as low probability for a pulmonary embolism. Additional serologic examinations included negative ANA, anti-GBM, pANCA, cANCA, hepatitis B and HIV antibody. SPEP (serum protein electrophoresis) was also unremarkable. Hepatitis C antibody was positive, and quantitative testing for CG revealed type II (mixed CG, 0.2 g/dL). C3 and C4 complement levels were low. Renal biopsy revealed MPGN. Bronchoscopy did not demonstrate any endobronchial abnormality. The patient was treated with intravenous methylprednisolone, and both hemoptysis and renal function improved. She did not return for follow-up care.

CG associated with HCV has been recognized to cause pulmonary complications which are usually mild and without any significant signs or symptoms. Alveolar hemorrhage in CG is rare; there have been only 10 case reports in English medical literature [1]. Patients with the cryoglobulinemic pulmonary hemorrhage have an extremely poor prognosis and high mortality at presentation and even a poorer prognosis in survivors having further hemorrhagic episodes [1]. Diagnosis of pulmonary hemorrhage associated with HCV-associated CG requires a high index of suspicion; in this case, the patient presented to the emergency services with severe respiratory insufficiency and bilateral alveolar infiltrates on chest radiograph. Her acute respiratory decompensation with diffuse alveolar infiltrates and hemoptysis is indicative of alveolar hemorrhage syndrome [3]. The diagnosis can also be confirmed with the demonstration of hemosiderophages in alveolar lavage obtained by bronchoscopy. It has been established that patients with CG with chronic infection by HCV are sometimes linked to membranoproliferative glomerulonephritis with a survival rate of 33–49% after a mean follow-up of 10 years.

Managing an autoimmune manifestation of an infectious disease is complex. Although immunosuppressive agents may be needed to control potentially life-threatening autoimmune complications, there is a risk that the infection might get worse. A reasonable approach is first to control the acute autoimmune manifestations of disease with immunosuppressive therapy and then to deal with the underlying infection to prevent relapse [3].

We conclude that both alveolar hemorrhage and renal involvement associated with HCV-related type CG are exceptional entities. This poses problems regarding treatment as each patient may need a tailored treatment [1].

Conflict of interest statement. None declared.

Dayton Veteran's Affairs
Medical Center, Wright State
University, Boonshoft
School of Medicine, Dayton,
OH, USA
E-mail: drkhumabbass@gmail.com

Khurram Abbass
Jack M. Bernstein
Ali Ajam

1. Amital H, Rubinow A, Naparstek Y. Alveolar hemorrhage in cryoglobulinemia—an indicator of poor prognosis. *Clin Exp Rheumatol* 2005; 23: 616–620
2. Prasad M, Buller GK, Mena CI. Clinical problem-solving. Sum of the parts. *N Engl J Med* 2006; 355: 2468–2473
3. Iannuzzella F, Vaglio A, Garini G. Management of hepatitis C virus-related mixed cryoglobulinemia. *Am J Med* 2010; 123: 400–408

doi: 10.1093/ndtplus/sfq169

Advance Access publication 4 October 2010

Proteinuria-associated nutcracker syndrome: an amyloid-negative familial Mediterranean fever patient

Sir,

Familial Mediterranean fever (FMF) is an autosomal recessive disease, and the most important complication is amyloidosis which leads to end-stage renal disease [1]. Nutcracker syndrome (NCS) is a rare clinical condition manifested by haematuria, proteinuria, gonadal varicose veins and side pain, all due to compression of the left renal vein and renal congestion [2]. Not all the cases of proteinuria in familial Mediterranean fever are due to amyloidosis, and the 'nutcracker syndrome' can be one of the confounding causes.

Case

A 22-year-old female with an 11-year history of FMF was referred to our clinic for sustained proteinuria. The patient had undergone multiple kidney biopsies with no specific pathology and negative amyloid tests. Physical examination was unremarkable. Laboratory results revealed the following: white blood cells 6000/mm³, haemoglobin 10 g/dL, erythrocyte sedimentation rate 78 mm/h, creatinine 0.46 mg/dL, urea 12 mg/dL and albumin 3.2 g/dL. Urine sediment was normal, and 24-h urinary protein was 1.1 g/day. The immunological markers were negative. Renal Doppler ultrasound revealed a narrowing in diameter of the left renal vein at the aortomesenteric level and also mild dilation 2 cm distal to that level. The findings of the CT angiography study confirmed anterior NCS and compression of the anteroposterior and craniocaudal diameter of the left renal vein at the anterior aspect of the aorta as well as dilation of the left renal vein in the mid-section (Figure 1). Due to the lack of pathology in all three renal biopsies, it was found that the patient's proteinuria was due to NCS. Because of the mild symptoms, no invasive treatment was given, and treatment with an ACE inhibitor was initiated.

Discussion

The association between FMF and non-amyloid glomerulopathy is unusual. Previously, IgA and IgM nephropathies and polyarteritis nodosa (PAN) have been reported [3,4]. NCS, characterized by the compression of the left renal vein between the superior mesenteric artery and the ab-