Pediatr Nephrol (2013) 28:987–988
DOI 10.1007/s00467-013-2457-0

LETTER TO THE EDITORS

Difficulties in diagnosing severe *Pneumocystis jiroveci* pneumonia after rituximab therapy for steroid-dependent nephrotic syndrome

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Received: 22 February 2013 / Revised: 25 February 2013 / Accepted: 1 March 2013 / Published online: 4 April 2013

Dear Editors,

We read with great interest the article by Sato et al., recently published in *Pediatric Nephrology*, who presented a patient with atypical *Pneumocystis jiroveci* pneumonia (PCP) with multiple nodular granulomas after rituximab therapy for refractory nephrotic syndrome [1]. We would like to present a case of our patient who, interestingly, revealed a different clinical course compared with that described by Sato and colleagues.

An 11-year-old boy with steroid-dependent nephrotic syndrome was on immunosuppression therapy for 9 years. Renal biopsy revealed minimal-change nephrotic syndrome (MCNS). In the course of the disease, he was treated with steroids, cyclophosphamide, levamisole, mycophenolate mofetil, and cyclosporine A (CsA). Because of the high degree of steroid dependency and calcineurin–inhibitor toxicity confirmed on renal biopsy, we decided to start rituximab therapy (RTX). The first course of RTX treatment consisted of two intravenous infusions of 375 mg/m^2 given at a weekly interval, with no short- or long-term side effects. Simultaneously, prednisone and CsA at low doses was continued. Six weeks after the first course of RTX, the patient was admitted to our department because of fever 38° C, fatigue even after minimal physical exercise, dyspnea, and tachycardia. Physical examination revealed only stomatitis; laboratory tests showed white blood cell count (WBC) 16.0 g/dl, C-reactive protein (CRP) 10 mg/l, blood urea nitrogen (BUN) and creatinine (Cr) within normal range, depletion of CD19 and CD20 (i.e. <0.01 g/l), and decreased immunoglobulin G (IgG) level. Standard blood and urine cultures were negative, as were blood tests for *Chlamydia* and *Mycoplasma* infections as well. Polymerase chain reaction DNA (PCR-DNA) examination excluded cytomegalovirus (CMV) and Epstein Barr virus (EBV) infections. Diagnostic evaluation pointed toward *P. jiroveci* and consisted of microscopy with staining of an induced sputum specimen, which was negative. Both chest X-ray and high-resolution computed tomography (HRCT) were negative. Although antibiotic therapy with IV azithromycin was started and CsA was tapered, after 7 days, his general condition deteriorated. Because of severe dyspnea, oxygen therapy was initiated, and immunoglobulins were administered. His poor clinical condition, stomatitis, dyspnea, and positive *Candida* antigen mannan indicated a fungal infection. Caspofungin therapy was started, with no improvement. Due to progressing respiratory failure, the PCP test was repeated (positive microscopy with staining of a subepiglottal smear). Simultaneously, repeated chest HRCT showed massive interstitial changes with crazy-paving and extensive ground-glass patterns. Cotrimoxazole therapy with 120 mg/kg/24 h, i.e. 20 mg/kg/24 h of trimetoprim (TMP) was started [2]. Within a few days of cotrimoxazole introduction, a dramatic improvement in his general status was observed. The therapy was continued for 21 days, followed by a prophylactic dose of TMP: 5.0 mg/kg/day administered orally in equally divided doses twice a day on three consecutive days per week. After 4 weeks of cotrimoxazole therapy, complete resolution of chest HRCT changes was observed.

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The clinical course of PCP in immunocompromised patients may vary widely: from subtle, almost asymptomatic, as described by Sato and colleagues, to respiratory failure as seen in our patient. Moreover, radiographic findings could be very different: unusual multiple nodular changes in contrast to massive diffuse interstitial pneumonia.

Summarizing, we observed gradual deterioration in the general status of our patient, with escalating respiratory failure and no changes in chest HRCT on admission. A fungal infection was recognized, but its treatment did not improve the clinical condition of the patient. We found that negative microscopy with staining of a sputum specimen absolutely does not exclude a PCP infection, and a subepiglottal smear or bronchoscopy with bronchoalveolar lavage should be performed. As did Sato and colleagues, we propose initiating PCP prophylaxis at the beginning of RTX protocol.

References

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