Successful Induction Treatment With Rituximab of Isolated Pauci-Immune Pulmonary Capillaritis Presenting as Diffuse Alveolar Hemorrhage in a Pediatric Patient

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Diffuse alveolar hemorrhage often presents as dyspnea, cough, or hemoptysis, and it is mediated by both immune and nonimmune processes. Isolated pauci-immune capillaritis (IPPC) is a rare diagnosis in which capillaritis, small-vessel vasculitis of the lung, is found on biopsy in the absence of an underlying systemic disorder. Traditionally, IPPC has been treated similarly to anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis with cyclophosphamide and glucocorticoids. However, few cases describing management options are available in the literature, especially among pediatric patients. Our report of successful induction of remission in an adolescent girl suggests that the combination of IV rituximab and pulse methylprednisolone may be a viable option for disease control in pediatric patients with IPPC.

KEY WORDS: diffuse alveolar hemorrhage; interstitial lung disease; pediatric pulmonology

Pulmonary capillaritis, small-vessel vasculitis of the lung, is often associated with an underlying autoimmune disorder. Isolated pauci-immune capillaritis (IPPC) is a rare diagnosis in which capillaritis is found on lung biopsy with no identifiable systemic process. Given the rarity of IPPC, few case reports are available to guide management. We describe the case of a young girl with IPPC who underwent successful induction with rituximab.

Case Report

A 12-year-old Hispanic girl with a 2-year history of recurrent hemoptysis responsive to enteral steroids presented with 1 day of dyspnea and hemoptysis. She developed ARDS requiring mechanical ventilation. Her only medication before admission was albuterol as needed.

CT of the chest showed diffuse ground-glass opacities suggestive of diffuse alveolar hemorrhage (DAH) (Fig 1A). BAL showed many hemosiderin-laden macrophages. An infectious cause was not found.

Testing for autoantibodies was negative: Sjögren-syndrome-related antigen A, Sjögren-syndrome-related antigen B, ribonucleoprotein, double-stranded DNA, rheumatoid factor, anti-Sjögren's-syndrome-related antigen A (SS/A), Sjögren's-syndrome-related antigen B.
(SS/B), ribonucleoprotein (RNP), double-stranded DNA (dsDNA), anti-neutrophil cytoplasmic autoantibody (ANCA) immunofluorescence staining, and enzyme-linked immunosorbent assay anti-myeloperoxidase and anti-proteinase 3 antibodies. Antinuclear antibody was 1:40. A tissue transglutaminase-IgA was negative. Complement component 3/complement component 4 were normal. Cryoglobulins were not measured.

Urinalysis was negative for proteinuria or hematuria. The patient was extubated after receiving several days of low-dose methylprednisolone. A video-assisted thoracoscopic surgical lung biopsy (Fig 2A, 2B) from the left upper/lower lobes showed the following: DAH secondary to alveolar capillaritis, a pauci-immune pattern via immunofluorescence, and no evidence of necrotizing or granulomatous vasculitis or neutrophilic infiltrates typically associated with ANCA-associated vasculitis. Given a normal immune profile coupled with a physical examination lacking stigmata associated with rheumatologic disease, the diagnosis of IPPC was made.

Induction was initiated with rituximab (800 mg at 0 and 2 weeks) and methylprednisolone (1 g at 0, 2, 4, and 10 weeks). The patient was started on concomitant enteral prednisone dosed at 60 mg divided twice daily, which was slowly tapered. The dose of rituximab was chosen based on the patient’s request for fewer infusions. Remission was defined as requiring less than 10 mg enteral prednisone daily and was achieved within 3 months. Approximately 8 months after remission, the patient was readmitted because of concern regarding scant hemoptysis. At that time, she was on prednisone 5 mg daily. There were no changes in her chest radiograph, hemoglobin/hematocrit, or reticulocyte count. Her dosing of enteral steroids was briefly increased, and she was started on hydroxychloroquine.

Approximately 13 months after remission, a third dose of rituximab was administered for maintenance therapy. However, this was not tolerated because of the development of anaphylaxis. Thus, the patient is currently managed with intermittent pulse methylprednisolone, in addition to daily hydroxychloroquine and azathioprine. She remains on Pneumocystis jiroveci prophylaxis.

Figure 1 – A, CT scan showing diffuse ground-glass opacities. B, Repeat CT scan 16 months after achievement of remission demonstrating resolution of ground-glass opacities.

Figure 2 – A, Capillaritis with inflammatory infiltrates, extravasated RBCs, and hemosiderin. B, Iron stain accentuating hemosiderin-laden macrophages in the alveolar spaces.
A CT of the chest was repeated 16 months after induction and demonstrated resolution of the diffuse ground-glass opacities (Fig 1B). Serial pulmonary function tests have demonstrated a stable borderline restrictive pattern, which has improved slightly. Diffusing capacity has remained within normal limits. Symptomatically, the patient reports marked improvement in her exercise capacity. She has had no further episodes of hemoptysis. It has been 30 months since her initial presentation.

Discussion

Patients with DAH typically present with dyspnea, cough, or hemoptysis. There are numerous causes, including both nonimmune and immune-mediated processes. IPPC is a rare diagnosis in which pulmonary capillaritis is found on lung biopsy with no associated systemic process.

Historically, IPPC has been managed similarly to ANCA-associated vasculitis, with cyclophosphamide and glucocorticoids. Few cases are reported in the literature detailing management in pediatric patients. One report described the use of monthly IV cyclophosphamide infusions for disease control in a young boy, with clinical deterioration on discontinuation. His condition improved with the initiation of a combination of treatments, including plasmapheresis, rituximab, steroids, and mycophenolate.¹ A retrospective institutional review identified eight pediatric cases of pulmonary capillaritis, one of which was ultimately determined to have IPPC.² This patient was treated with pulse IV steroids, chronic oral steroids, and hydroxychloroquine, but experienced recurrence of pulmonary hemorrhage on weaning of steroids.²

The RAVE trial demonstrated that rituximab was not inferior to cyclophosphamide for induction of remission in patients with ANCA-associated vasculitis, and that it might be superior in relapsing disease.³ Regarding IPPC, there are reports of adults who underwent successful treatment with rituximab after experiencing inadequate control with cyclophosphamide.⁴ To our knowledge, there is one published report of a child with IPPC who underwent induction with rituximab.⁵ Given successful induction in the patient, this may be a viable option for disease control in those with IPPC. Furthermore, a maintenance schedule for rituximab has not yet been described and would be helpful for long-term management.

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References