Bronchiectasis in mycophenolate mofetil-treated children: not just a matter of renal transplantation

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Topic: Pediatric nephrology (29)

Introduction and objectives: Mycophenolate mofetil (MMF) is an immunosuppressive agent which acts as a potent inhibitor of T- and B-cell proliferation. Initially used as part of immunosuppression in renal transplantation, MMF has been shown to be effective in the treatment of various immunological disorders, including idiopathic nephrotic syndrome. In kidney transplant recipients receiving MMF, there have been reports of acquired hypogammaglobulinemia, chronic bronchitis and bronchiectasis.

Methods: We report the cases of 3 children who developed bronchiectasis while being treated with MMF for steroid-sensitive nephrotic syndrome (SSNS) or kidney transplantation (*see Table*).

Results: *see Table*

No other immunosuppressive drug for 2/3 patients (SSNS). None of the children had previous history of recurrent infections.

Diagnosis of bronchiectasis, based on clinical history and thoracic computed tomography scan. The symptoms of bronchiectasis began 16 to 28 months after the introduction of MMF.

Hypogammaglobulinemia was found in 1/3 patient, neutropenia in 2/3 patients.

MMF was discontinued in all patients, and replaced by another immunosuppressive agent. Parenteral immunoglobulin replacement was started in the SSNS patient with hypogammaglobulinemia.

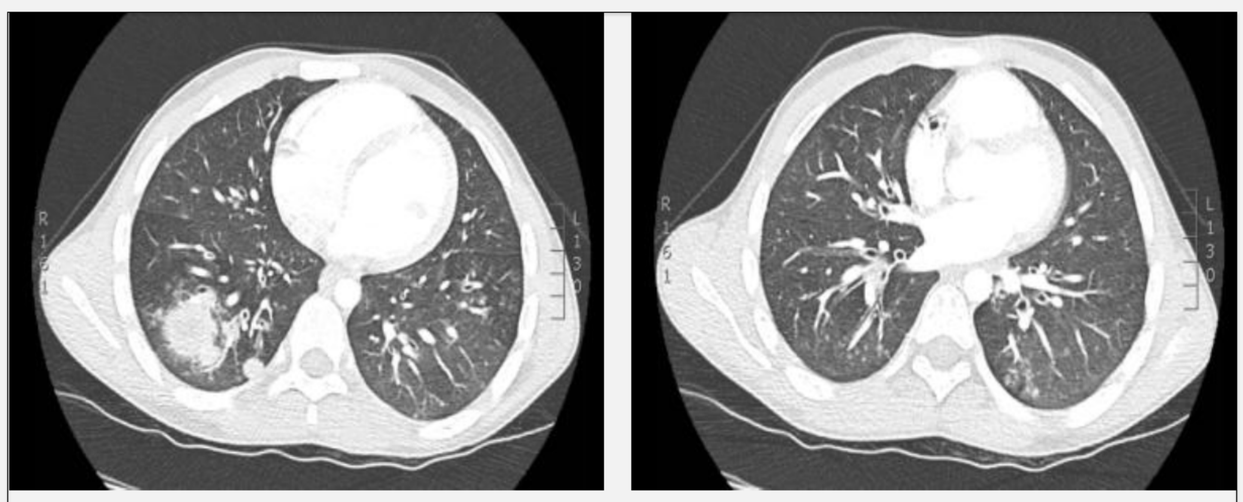
Pulmonary manifestations disappeared 9 and 18 months after MMF discontinuation in 2 patients, but still persisted at 18 months follow-up after MMF withdrawal in the last patient with SSNS.

Discussion: Cases of bronchiectasis under MMF are described in the literature (adults and children), but **only in transplant recipients** (kidney, heart, liver, bone marrow), **no report in SSNS**. Most of these patients had hypogammaglobulinemia, but not all. Unlike 2 of our patients, they received **multi-drugs immunosuppression**. In all cases, pulmonary symptoms improved after MMF withdrawal.

Conclusion: This report suggests that bronchiectasis may occur in patients receiving MMF, **independently of the underlying condition or the immunosuppressive regimen**. It underlines that **even normal immunoglobulin level does not prevent the development of bronchiectasis**. Thus, recurrent respiratory symptoms in MMF-treated children should imperatively prompt further investigations for bronchiectasis.

Patient age (years old)	Girl 6 y.o.	Boy 12 y.o.	Girl 17 y.o.
Kidney disease	SSNS (started 4 y.o.)	SSNS (started 6 y.o.)	Kidney transplantation for hypodysplasia and clear cell carcinoma
MMF dose mg/m²/12h	600	650	600
Other treatment	no	no	Prednisone, Tacrolimus
Time after MMF	16 months	28 months	16 months
IgG level Leucopenia	**4 g/L** (not nephrotic) **Neutropenia**	11 g/L no	10 g/L **Neutropenia**
CT scan	bronchiectasis left lower lobe	bronchiectasis 2 lower lobes	bronchiectasis left lower lobe
Respiratory functional test	restrictive syndrome	no data	restrictive syndrome
Sputum	Haemophilus influenzae	Haemophilus influenzae	no data
Action	MMF switched to **levamisole** Alternate antibiotics **Parenteral immunoglobulin**	Switch to **levamisole** after 7 months of evolution Alternate antibiotics	Switch to **azathioprine** Antibiotics for exacerbation
Outcome	Favourable (18 months) Normal IgG level	Many exacerbations (18 months)	3 exacerbations in 8 months, then favourable after 9 months

Table: Patient characteristics and outcome



Chest CT scan of Boy aged 12

Biblio ref.: Significant post-transplant hypogammaglobulinemia in six heart transplant recipients: an emerging clinical phenomenon? (Corales, Transpl Infect Dis. 2000); Hypogammaglobulinemia and bronchiectasis in mycophenolate mofetil-treated renal transplant recipients: an emerging clinical phenomenon? (Boddana P, Clin Transplant. 2011); Mycophenolate mofetil and bronchiectasis in kidney transplant patients: a possible relationship. (Rook M, Transplantation 2006); Bronchiectasis in children after renal or liver transplantation: a report of five cases. (Pijnenburg MW, Pediatr Transplant. 2004); Improved outcome of pediatric kidney transplantations in the Netherlands -- effect of the introduction of Mycophenolate mofetil? (Cransberg K, Pediatr Transplant. 2005)

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