A new approach to the treatment of *Xanthomonas maltophilia* respiratory infection in a patient with cystic fibrosis

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Introduction

Xanthomonas maltophilia is a recognized although unusual pathogen in patients with cystic fibrosis (CF). The present report describes the case of an adult with CF from whose sputum *X. maltophilia* was isolated repeatedly, and despite intensive intravenous (i.v.) antibiotic therapy, his condition deteriorated until high-dose oral co-trimoxazole was introduced. For the next 12 months, he remained well on intermittent high-dose co-trimoxazole and daily nebulized colistin. As his condition had stabilized, a trial period off co-trimoxazole was embarked upon, and 1 month later, he deteriorated and was re-admitted for i.v. antibiotic therapy. He is now back on regular thrice-weekly high-dose co-trimoxazole and nebulized colistin, and has remained well for a further 6 months.

Case Report

A 25-year-old garage mechanic was diagnosed as having CF at the age of 10 years when he presented with a persistent cough, failure to gain weight and steatorrhea. Over the next 3 years, he was admitted three times with meconium ileus equivalent and remained well otherwise, performing daily physiotherapy. At 15 years of age, *Staphylcoccus aureus* was cultured from the sputum, and the following year, he was admitted for the first time for treatment of an infective pulmonary exacerbation. Five years later, having been admitted on three further occasions for intravenous (i.v.) antibiotics, *Pseudomonas aeruginosa* was isolated from the sputum. At this stage, pulmonary function was fairly well maintained with a forced expiratory volume in 1 s (FEV_1) of 2·7 l (65% predicted normal range (1)) and a forced vital capacity (FVC) of 3·8 l (76% predicted). Eighteen months later, he developed asthma and started inhaled cortico-steroids.

Table 1 illustrates his subsequent progress. At the age of 24 years, *X. maltophilia* was isolated from the sputum for the first time. Over the next 18 months, the number of exacerbations requiring hospital admission increased to eight. Despite intensive therapy with i.v. and nebulized antibiotics, and continuous oral and inhaled corticosteroids for associated bronchospasm, his lung function deteriorated markedly (FEV_1 20% predicted) and he was no longer able to continue working. During this time, *X. maltophilia*, which was isolated consistently from the sputum, remained resistant to all conventional agents, save colistin. Susceptibility testing was extended to co-trimoxazole to which the pathogen was found to be susceptible. Following high-dose co-trimoxazole (1·44 g b.i.d.) and an increase in the dose of nebulized colistin (from 1 to 2 mega units b.i.d.), his clinical condition improved markedly (Table 1). Fourteen days later, he was discharged home taking high-dose co-trimoxazole for a further week. In order to try and maintain his lung function, a regimen of daily nebulized colistin (one mega unit b.i.d.) and co-trimoxazole (1·44 g b.i.d.) thrice weekly was instituted. This therapy was continued for the following 12 months and as his condition had stabilized (Table 1), a trial period off co-trimoxazole was embarked upon, although colistin was continued. *X. maltophilia* continued to be isolated consistently from the sputum.

One month later, his clinical condition deteriorated. He was re-admitted for i.v. antibiotics and was treated for 10 days with i.v. gentamicin (100 mg t.i.d.) and i.v. aztreonam (2 g t.i.d.). He is now back on regular thrice-weekly high-dose co-trimoxazole with daily nebulized colistin and has remained well for 6 months; indeed, for the last four months, *X. maltophilia* has not been isolated from the sputum which has been cultured every 4–8 weeks. Chest radiographic appearances have not changed greatly over the past 2 years.

Discussion

X. maltophilia is a recognized sputum pathogen in cystic fibrosis (2); it is not clear if its presence contributes to deterioration in lung function. A recent review of 23 CF children showed that acquisition of this organism was not associated with unexpected deterioration (3). Should, however, *X. maltophilia* contribute significantly to deteriorating lung function, the choice of effective therapy is limited in view of its inherent resistance to the majority of antimicrobial agents available (4,5). *In vitro* susceptibility of

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TABLE 1.

Year	Age (years)	FEV_1 (% predicted)	FVC (% predicted)	No. admissions per year for i.v. antibiotics	Sputum pathogens	Additional data
1983	16	3·2 (91%)	4·2 (111%)	1	*S. aureus*	
1987	20	3·0 (72%)	4·17 (83%)	1	*H. influenzae* *S. aureus*	Flucloxacillin started
1988	21	2·7 (65%)	3·8 (76%)	2	*P. aeruginosa*	
1989	22	2·3 (55%)	3·1 (62%)	2	*P. aeruginosa* *S. aureus* *H. influenzae*	
1990	23	1·2 (29%)	1·9 (38%)	1	All above	Oral and inhaled steroids started
1991	24	1·5 (36%)	2·5 (50%)	3	*X. maltophilia*	Developed diabetes, nebulized antibiotics started
1992		0·85 (20%)	1·25 (25%)		*X. maltophilia*	Marked deterioration
	25			5	*S. aureus*	FEV_1 reduced to 20%
1992		1·8 (42%)	3·4 (66%)		*H. influenzae*	High-dose co-trimoxazole started
1993	26	1·5 (34%)	3·1 (61%)	0	*X. maltophilia* *S. aureus* *H. influenzae*	Regained stability

X. maltophilia to co-trimoxazole has been demonstrated previously (6) and it is of interest that synergism of aztreonam and clavulanic acid has also been described (5).

To the authors' knowledge, this is the first report of successful clinical application of co-trimoxazole in CF pulmonary infection associated with *X. maltophilia*. This agent has been effective both in the treatment of acute exacerbations associated with *X. maltophilia* and also in the maintenance of lung function for 18 months. Long-term therapy has been well tolerated and, indeed, its protracted use may have contributed to the eradication of this pathogen. The intermittent time course using high-dose therapy was introduced in an attempt to achieve bactericidal effects whilst minimizing the development of resistance to co-trimoxazole. Sequential sputum cultures of *X. maltophilia* from this patient have been of varying sensitivity to both trimethoprim and sulphamethoxazole, although it appears that *in vivo* activity has been maintained. It is of note that prolonged use of high-dose nebulized colistin was also well tolerated and *in vitro* sensitivity to this agent was retained. The possibility of nebulized co-trimoxazole may be considered in the future for the treatment of *X. maltophilia* infection in CF. However, it should be recognized that as *X. maltophilia* was retained during periods of clinical stability despite concurrent co-trimoxazole therapy, this antibiotic may have been effective by reducing exo-enzyme expression by *X. maltophilia* and/or by controlling the effects of other infective agents, e.g. *Pneumocystis carinii*, which were not identified by routine microbiological screening tests.

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