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Bronchiectasis:
The Case for Intravenous Prophylactic Antibiotic Treatment

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SUMMARY

This case study describes the challenges of treatment strategies for a 63-year-old lady with a 38-year-history of bronchiectasis. She has been managed previously with 6-8 weekly prophylactic intravenous (IV) antibiotics during elective admissions to hospital, yet under new consultant care it is felt that this management is inappropriate and her time spent in hospital excessive. This report reflects upon the challenges of delivering patient-centered care for chronic conditions in a 'cash-strapped' NHS.[1] The discussion analyses the patient's disease progression and turns to review the current evidence base for prophylactic antibiotic treatment of bronchiectasis.

BACKGROUND

This case is of particular interest as it is a good illustration of a clash in the desires of a 'professional' patient[2] and a physician's judgment. Shared decision-making between doctors and patients is vital; Andrew Lansley famously coined the slogan 'nothing about me, without me'[3] reflecting the 'triumph' of autonomy[4] and the fact that 'medical paternalism no longer rules'.[5] However, achieving this end-goal is not always simple, and further complicated by the current economic strain on the NHS.[6]

It is also an example where different doctors have had contradictory opinions on how the same patient should be managed, arguably highlighting the need for a strong evidence base upon which to base treatment strategies. Establishing guidelines for antibiotic therapy for non-cystic fibrosis (CF) bronchiectasis[7] has been a challenge.[8] The evidence supporting its diagnosis, investigation, but above all management, has been largely empirical, and the condition has been the focus of comparatively few controlled clinical trials.[9] This case thus highlights the gap in evidence and gives direction for future research.

CASE PRESENTATION

A 63-year-old woman with known bronchiectasis came into hospital on an elective basis for a course of IV antibiotics.

Year	Notable History
1959	- Tuberculosis
1976	- Bronchiectasis diagnosis
1998	- Pseudomonas aeruginosa infection - Regular admissions for exacerbations
2002	- Has to give up work as a cleaner due to poor health
2003	- On nebulised bronchodilators and colomycin
2005	- Portal catheter requested for regular IV medication (inserted in 2006)
2007	- Established a routine of 6-8 weekly IV antibiotic therapy (most frequently gentamicin and ceftazidime) - Pseudomonas colonisation documented
2008	- Still able to do "plenty of gardening" - Pseudomonas colonisation documented
2009	- Leucopenia associated with ceftazidime use - Commenced low dose azithromycin
2012	- Under new consultant care - Now has oxygen as required at home - Azithromyicn discontinued due to associated leucopenia
2013	- Requested a wheelchair from occupational health for outdoor activity - Felt as if this was her worst year health wise - Specialist immunologist opinion sought, no immunodeficiency found
2014	- Can take an hour to get dressed

Figure 1. A table documenting the progression of the patient's disease.

The patient contracted tuberculosis when seven years old and experienced recurrent chest infections, subsequently being diagnosed with bronchiectasis when twenty-five years old. This has considerably affected her life, worsening particularly over the past fifteen years. She monitors her sputum and uses physiotherapy techniques daily.

She was managed under the same consultant for thirty years, who eventually established a routine of elective 6-8 weekly hospital admissions for prophylactic IV antibiotic therapy. This management is now considered unnecessary and inappropriate by her new consultant, who is attempting to wean her from her dependence on elective admissions. Understandably this is a challenge; her social life has revolved around these admissions, she trusted her previous consultant who established this routine, and she associates lack of elective admissions with a decline in her health.

Figure 1 summarises her relevant history and documents notable changes in her management and exercise tolerance:

Since 2007 she has had a total of forty-two hospital admissions, which average at tendays duration each. Thirteen of these have been emergency admissions for exacerbations, the remainder for elective antibiotic administration (see Figure 2).

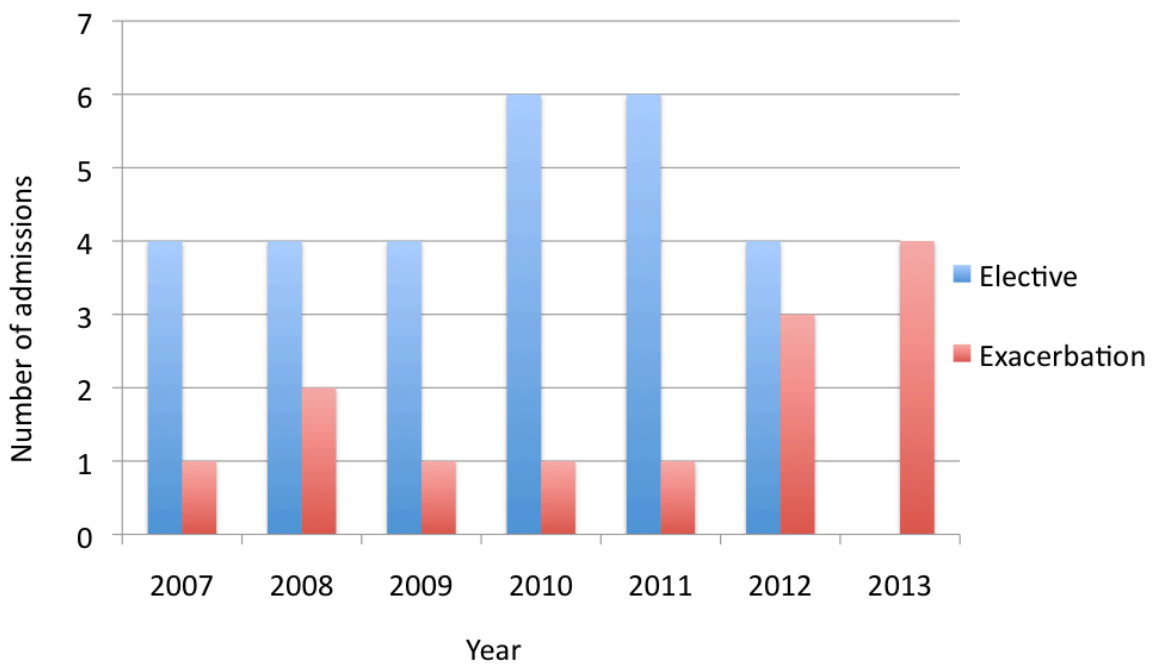

Figure 2.
Graph documenting number of hospital admissions (elective and exacerbations).

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DRUG	DOSE	FREQUENCY	ROUTE
Colomycin	1 vial (2 million U)	BD	NEB
Ipratropium	500mcg	QDS	NEB
Seretide 500	T	BD	INH
Salbutamol	5mg	QDS	NEB
Montelukast	10mg	ON	PO
Prednisolone	10mg	OD	PO
Carbocysteine	750mg	TDS	PO
Sodium chloride 0.9%	5ml	QDS	NEB
Temazepam	10mg	ON	PO
Alendronic acid	70mg	Weekly	PO
Omeprazole	20mg	OD	PO
Adcal D3	T	BD	PO
Tramadol	50-100mg	QDS	PO
Fluoxetine	20mg	OD	PO

Figure 3. A chart showing the patient's regular medications.
Key: T: one tablet/puff, OD: 1x daily, ON: 1x nightly, BD: 2x daily, TDS: 3x daily, QDS: 4x daily. IV: Intravenous, NEB: Nebulised, PO: Oral.

On this admission to hospital the patient felt generally well, yet appreciative of being able to rest. Her baseline symptoms include constant chest pain like an 'elastic band' whilst breathing. She becomes short of breath with very mild exertion- performing tasks such as washing herself. Review of systems revealed that she experiences recurrent oral thrush infections, dry mouth, palpitations, stomach pain and restless legs. She attributes most of these to medication side effects.

Other medical history includes asthma, depression, osteoporosis, and osteoarthritis. She suffered from a low impact right mid-foot fracture in 2011, associated with osteoporosis and long-term steroid use.

The patient takes the regular medications (see Figure 3).

Both of her children have asthma. She lives alone in a house and is a non-smoker and non-drinker. Whilst independent with activities of daily living, it can take her up to an hour to get dressed and she is sometimes too tired to make herself a cup of tea. She finds it tough to cope and is worried about what the future holds. She feels that her treatment options are becoming narrowed and that her exacerbations are more frequent and harder to predict, saying that she never knows if she will 'wake up with raging pneumonia'.

On examination the patient looked comfortable and was well perfused. A portal catheter was observed. She was apyrexial with a stable blood pressure (130/72 mmHg), pulse (72) and respiratory rate (20), saturating at 96% on air. She had slightly reduced chest expansion bilaterally. A wheeze and course crackles could be heard bilaterally, in a scattered distribution. The cardiovascular, neurological and abdominal examinations were unremarkable.

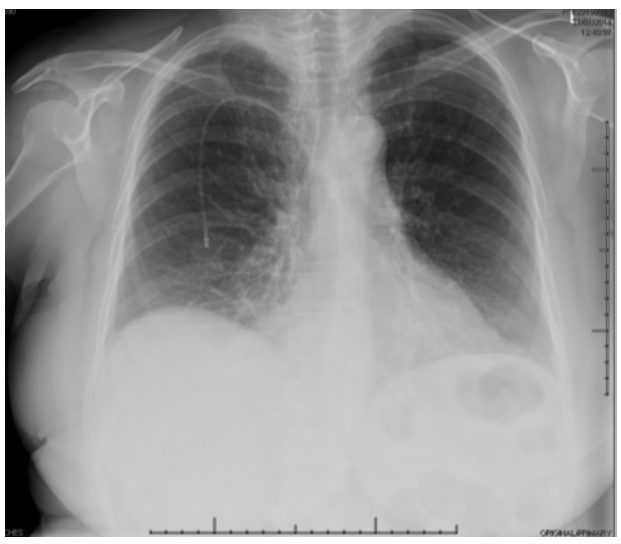
INVESTIGATIONS

The patient had bloods taken on admission, including FBC, U&Es, LFTs and CRP. She was found to have slight neutropenia: 1.63x109 (Normal 1.8-7.5 x109/L). This was not regarded as significant, considering her October 2013 review by the immunologist who found no immunodeficiency.

She had a chest X-Ray taken (Figure 4 – note the portal catheter), which demonstrated changes consistent with bronchiectasis. Compared to previous radiographs, even dating to 2006 (Figure 5), no change or new lesions were seen.

The patient also had a bronchoscopy and washings performed for microscopy & sensitivity. No cultures were grown.

Figure 4. CXR 31/01/14



TREATMENT

The patient completed a 7-day course of Tazocin (4.5g, TDS, IV) and was seen by the physiotherapy team for chest clearance.

OUTCOME AND FOLLOW-UP

The patient's stay in hospital was largely unremarkable. She was discharged as planned; a follow-up appointment was booked in clinic in 6 weeks.

DISCUSSION

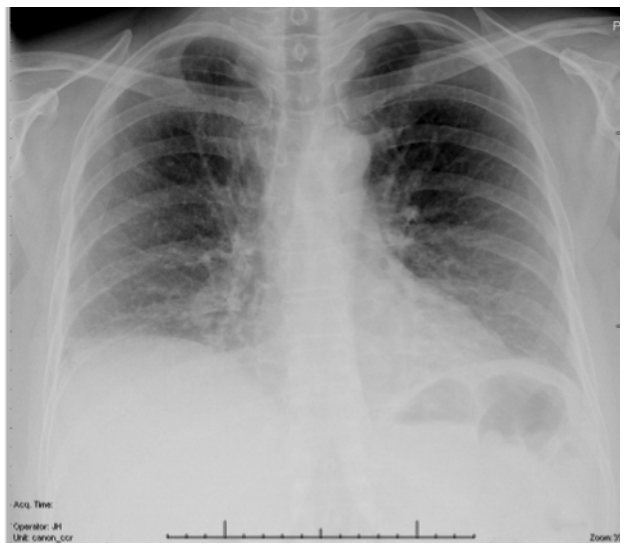
Cole first proposed the 'vicious cycle' hypothesis of bronchiectasis in the 1980s - that initial airway insult leads to inflammation and damage, disordered mucociliary clearance and predisposition to further infection and inflammation.[10] It is widely regarded that the key of bronchiectasis' management lies in preventing infections and exacerbations in order to break this cycle.[11]

The latest British Thoracic Society Guidelines lay out the essence of treatment as being annual influenza vaccination, pharmacotherapy, chest physiotherapy and clearance, and antibiotics.[7] Antibiotics are vital and have greatly improved prognosis; prior to antibiotics death could occur within 5 years.[7] Antibiotic therapy can be sub-divided into exacerbation treatment and prophylactic treatment[12] - the latter being the focus of this discussion. Based on consensual view, rather than on a specific evidence base, it is recommended that long-term antibiotics (oral or inhaled) be prescribed for patients with ≥3 exacerbations per year.[7]

The rationale behind prophylatic antibiotic treatment lies in an attempt to improve symptoms and reduce exacerbations. The likely mechanism behind this is hypothesized to be reduction of bacterial load and airway inflammation; it is also thought that long-term macrolide antibiotics have immunomodulatory benefits.[9] The sequelae of reducing exacerbations include an improved quality of life; notably, exacerbations have been associated with higher levels of depression and anxiety.[13]

However, the question of what prophylactic

Figure 5. CXR 10/02/06



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strategy is ideal still remains. The most recently published guidelines emphasised that formulating recommended antibiotic regimens was a real challenge due to the deficient evidence base.[6] The 'surprising lack'[14] of research on bronchiectasis is dwarfed[15] by the output on the more 'fashionable' Cystic Fibrosis (CF).[16] The authors of the guidelines felt that it was important not to simply extrapolate from the CF data. This is for good reason - in some instances trails of proven CF therapies have had deleterious results when applied to subjects with bronchiectasis.[13] It was necessary therefore for the authors to draw from information gleaned in studies from the 1950s, open to the criticism that the studies have poor and outdated methodology.[6]

Whilst there is consequently a call for 'large multicentre trials to evaluate efficacy of different management options',[11] in Janurary 2014 the Lancet heralded 'the arrival of better evidence' and reported the findings of recent randomised-controlled-trials.[17] To highlight a few examples: Murray et al. studied the efficacy of twice daily nebulised gentamicin over a period of twelve months, randomising sixty-five patients to gentamicin or placebo. Whilst there was no improvement in lung function, the group receiving gentamicin doubled the time to next exacerbation (from 61.5 to 120 days) and experienced an increase in exercise tolerance and quality of life. Significantly, pseudomonas aeruginosa was eradicated in 30.8% of cases, and other pathogens in 92.8%.[18] Similarly studies have shown that nebulised drugs such colomycin and tobramycin can reduce symptoms, decrease hospital admission time and eradicate pathogens. However, as McDonnell notes, recurrence of colonisation of pseudomonas aeruginosa when treatment is withdrawn is 'almost universal'.[19]

Altenburg et al. conducted a multicentre Dutch trial of eighty-one patients to examine the efficacy of low-dose azithromycin over a twelve-months period. This drug has gained attention for its immunomodulatory benefits, and the study showed reduction in exacerbation frequency (1.28 per year, $P < 0.0001$).[20] There is still a need for future studies of the ideal duration, dosage and route of administration, and of the possibility of bacterial resistance.[17]

Specifically relevant to this case is the use of IV antibiotic prophylaxis. If we return to examine Figure 2, we can observe that an increase in exacerbations correspond to change in consultant care in 2012. One could hypothesise that this relationship is causal, and that regular IV antibiotic treatment prevented the patient's exacerbations. However, it has to be considered that bronchiectasis is a progressive disease[21] and that a decline with time is expected. An increasing proportion of exacerbations could be viral in nature. Furthermore, no data is available on her health between admissions – the patient could have had a higher proportion of outpatient exacerbations in the years prior to 2012. Many factors could confound the data.

It is thus required that we assess the evidence base from trials. The use of regular elective IV antibiotics has been shown to increase survival probability in CF,[22] arguably justifying this strategies' use in bronchiectasis. Only one prospective cohort study has looked into the benefits of regular IV antibiotics in severe bronchiectasis: Mandal et al. recruited nineteen patients who all experienced ≥5 exacerbations per year. They all received eight weekly IV antibiotics in a domiciliary setting (specific to their swabbed cultures).[9] The reduction in exacerbations from an average of 9.3 to 8 was significant ($P=0.02$) along with increase in exercise capacity (58.7 m, $P=0.004$) and health-related quality of life (assessed by validated questionnaire, $P=0.006$). However, there can be no denial of the study's limitations: the small study size and consequent lack of generalisability, and as it is not an RCT confounding factors will have influenced the findings. The participants were not blind to their exposure status, so a placebo effect could have resulted, and their report of their quality of life affected. The study nonetheless paves the way for future trials, especially considering the impressive statistic of saving 1020 bed days and £357,000.

Nevertheless, given the complexity of human nature, no number of clinical trials will tell us exactly what is appropriate for this individual patient. The answer, as with most conflict, most probably lies in compromise and communication. There can be no denial that even if prophylactic IV antibiotic therapy was giving her significant therapeutic benefit, despite the lack of concrete evidence base for such a strategy, it would be rational to save bed days and costs by delivering this treatment at home. Yet the issue of her psychological and social dependence on admission would still exist. Simple cessation of this routine risks jeopardising the crucial doctor-patient relationship. She needs to be given social support, true acknowledgement of her concerns, and thorough explanation of the rationale behind any changes in her trusted regimen.

TAKE HOME MESSAGES

The management of patients with chronic conditions poses a challenge for healthcare professionals, especially considering the economic strain on the NHS.

Formulating guidelines as how best to give prophylactic treatment for bronchiectasis has been difficult. Current strategy is based largely on consensus view; the gaps in the evidence base highlight areas for future research.

Guidelines cannot provide perfect solutions, irrespective of evidence base. Patients, being human, are complex, and management strategies have to evolve and be sensitive to this.

Shared-decision making between doctors and patients is key. When differences in opinion arise between patient and doctor, good communication and holistic management are vital.

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