Delay in the diagnosis of pulmonary tuberculosis, London, 1998-2000: analysis of surveillance data

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Noted cases of tuberculosis each year have doubled in London since 1987. In 2000, 12.9 cases per 100 000 population in England and Wales were recorded compared with 40.3 cases in London.[1] A delay in the diagnosis of tuberculosis increases the risk of poor clinical outcome—including death and transmission of tuberculosis.[2 3] Understanding which factors influence this delay is crucial for controlling tuberculosis.

Only one small study has previously investigated delays in the diagnosis of pulmonary tuberculosis in the United Kingdom.[4] Using surveillance data from London, we estimated the delays in diagnosis of tuberculosis and investigated the factors independently associated with delays.

Methods and results

We analysed surveillance data collected by doctors (1999-2000) and an anonymised national survey (1998) for cases of tuberculosis in London from 1998 to 2000. We calculated the delay in diagnosis as the number of days between the onset of symptoms and diagnosis or the start of treatment (which were on the same day in cases with both recorded). Delay was characterised as greater than the median or at or less than the median. We used unconditional logistic regression to investigate factors that were independently associated with delay.

A total of 1355 patients had a positive result in smear tests of pulmonary sputum; we give results for 853 (63%) about whom data on the time between onset of symptoms and diagnosis had been recorded. Patients with data and those without were similar for age, sex, and ethnic group.

The median age was 34 (interquartile range 26-51) years; 505/849 (60%) of patients were men. A total of 263/842 (31%) patients were white and 267/842 (32%) were black; 542/782 (69%) of patients were born outside the United Kingdom. Median delay was 49 (14-103) days. Univariate analysis showed that factors significantly associated with delay of longer than 49 days until diagnosis or treatment were age, birthplace (United Kingdom or overseas), sex, and ethnic group (table). The geometric mean delay in days were 72 (95% confidence interval 63 to 80) among white patients and 43 (39 to 45) among all other ethnic groups, 72 (66 to 77) among women and 61 (56 to 65) among men, and 64 (55 to 74) among those aged ≥40 years and 45 (40 to 51) among patients aged <40 years. Among patients not born in the United Kingdom, time since entry was significantly positively associated with delay being greater than the median (P=0.01). In multivariate analysis, delays were more likely for white patients (adjusted odds ratio 1.67 (1.2 to 2.5); P=0.01) and women (1.42 (1.1 to 1.9); P=0.01). Age and birth place were not independently associated with delay.

Comment

Delay between the onset of symptoms of pulmonary tuberculosis and diagnosis or treatment (median 49 days) was more common for white people and for women. This median delay is similar to findings in other

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Odds ratios for delay in the diagnosis of tuberculosis in patients testing positive for tuberculosis in smear tests, London, 1998 to 2000*

Characteristic	No (n=853)†	No (%) with longer than median delay	Unadjusted odds ratio			Adjusted odds ratio‡		
			Value	95% CI	P value	Value	95% CI	P value
Sex:								
Male	509	244 (48)	1	—	0.027	1	—	0.01
Female	344	196 (57)	1.37	1.05 to 1.82		1.46	1.1 to 1.9	
Age (years):								
<40	511	245 (48)	1	—	0.009	1	—	0.11
≥40	337	192 (57)	1.46	1.09 to 1.95		1.18	0.87 to 1.62	
Ethnic group:								
White	263	163 (62)	1	—	0.021	1	—	0.03
Black	267	112 (42)	0.44	0.30 to 0.63		0.52	0.33 to 0.80	
Indian subcontinent	224	114 (51)	0.61	0.42 to 0.89		0.64	0.42 to 0.99	
Other	88	43 (49)	0.62	0.37 to 1.02		0.73	0.41 to 1.29	
Birthplace:								
United Kingdom	240	146 (61)	1	—	0.0005	1	—	0.32
Other	542	255 (47)	0.58	0.43 to 0.79		0.82	0.56 to 1.21	
Time since entry to United Kingdom§:								
<2 years	49	16 (33)	1	—	0.010	—	—	—
2-5 years	180	79 (44)	1.73	0.87 to 3.43		—	—	
>5 years	204	112 (55)	2.65	1.34 to 5.25		—	—	

*Associations between categorical data were assessed using χ^2 or Fisher's exact tests, as appropriate. Continuous data were compared using *t* tests if approximately normally distributed or otherwise using the Wilcoxon test.
†Data are missing for sex in 0, for age in 5, for ethnic group in 11, for birth place in 71, and year of entry to the United Kingdom in 109 cases.
‡Adjusted for sex, age, ethnic group, and whether the patient was born in the United Kingdom.
§Not investigated in the multivariate model.

large cities in industrialised nations.[5] This might be because tuberculosis may be suspected and investigated more readily among men or black or Asian people.

Our study was limited by the amount of missing surveillance data. It was also impossible to determine the relative contribution of patient and healthcare provider to the total delay. Potential confounders—for example, coinfection with HIV or the accuracy of the data among patients whose first language was not English—were not taken account of.

Recent campaigns have tried to raise awareness of tuberculosis, particularly among ethnic minority groups. Our data suggest that campaigns also need to be targeted at white people, who comprise a third of cases.

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Drug points

Erythromelalgia induced by possible calcium channel blockade by ciclosporin

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Erythromelalgia, a symptom complex of painful inflammatory vasodilatation of extremities, is usually idiopathic or due to thrombocythaemia. It has often been regarded as inverse Raynaud's phenomenon, rarely induced by calcium channel blockers.[1] We report a case of erythromelalgia induced by ciclosporin.

A 37 year old man had been taking ciclosporin 75 mg twice daily for psoriasis vulgaris for four weeks when he developed marked erythema, oedema, and tenderness over fingers and toes. Symptoms increased with warmth and were relieved partially with cold compresses. His full blood count, serum biochemistry, urine analysis, and collagen profile were normal. Erythromelalgia induced by ciclosporin was considered, and the drug was withdrawn. Lesions regressed within a week but recurred when ciclosporin was restarted. No recurrence was observed at one year follow up.

Erythromelalgia is a multifactorial peripheral vascular phenomenon akin to sympathectomy, with attenuation of vasomotor tone probably mediated through vasoactive substances and drugs such as nifedipine, nicardipine, verapamil, and bromocriptine.[1]

Ciclosporin, a calcineurin antagonist, acts by inhibiting calcium-calmodulin signalling systems of target cells in a way similar to calcium channel blockers.[2] It binds to calmodulin, with a consequent inhibition of dephosphorylation of calmodulin induced kinases and other calmodulin dependent intracellular activities.[3] Ciclosporin also affects the calmodulin regulated activity of the actomyosin complex of smooth muscle of peripheral vessels, which leads to vasodilatation. In this way, ciclosporin has also been observed to potentiate the peripheral vasodialatory effects of calcium channel blockers.[4]

The erythromelalgia in this patient may have been the result of ciclosporin acting in a similar way to calcium channel blockers. Though burning sensation of the hands and feet has been mentioned as an adverse effect in the product leaflet of ciclosporin (Panimun Bioral, Panacea Biotec) and a leg pain syndrome has been described, an erythromelalgia-like effect has not been reported.[5] This possible vasoactive effect of ciclosporin needs further evaluation given that vasoactive peptides may be present in psoriasis.

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Corrections and clarifications

Mark Twain on evidence based practice
This Endpiece attributed the quotation "It ain't what people don't know that hurts them it's what they know that ain't so" to Mark Twain (25 January, p 211). However, a reader has corrected us, confirming that this quotation is attributable not to Mark Twain but to Josh Billings (and in support has cited various sources, including the *Penguin Dictionary of Modern Humorous Quotations*, Penguin, 1987). A trawl of the web, however, has revealed that people often get it wrong, attributing the quotation in question not to Josh Billings but to Mark Twain—or to Will Rogers or Herbert Stein (or possibly others). The quotation always appears in slightly different forms; indeed, the one cited in the Penguin dictionary is not exactly the same as the one we published.

Filler: He died "peacefully" at home
Although editors are aware of the dangers of confusing words that differ in spelling by only one letter, there is always a danger that the wrong word will slip through. Unfortunately, this is what happened in this account by David Veale of the death of his father—we used the word prostrate, rather than prostate (12 April, p 792).