taken for other pathologies. It designates inflammation and fibrosis occurring predominantly in membranous and respiratory bronchioles walls and contiguous tissues, sparing distal respiratory bronchioles, with resultant lumen narrowing.[3] Histology is characterized by focal changes, which are difficult to read, making diagnosis sometimes problematical.

Clinically, patients usually report dyspnea and cough and, like both our patients, have functional airflow limitation. This reflects the effect of bronchiolar lumens concentric narrowing and eventually luminal obliteration.[1] It is a chronic, slowly progressive disease.

Chest X-ray is often normal or shows signs of hyperinflation or decreased vascular reticulum. Chest CT scan may help diagnosis, sometimes demonstrating the existence of a mosaic pattern, with areas of air-trapping caused by constricted and partially obstructed bronchioles.[4] There are also frequently parenchymal densifications and bilateral ground glass opacities.[2]

There are several causes attributed to this entity. Even though it may be idiopathic, most commonly it is secondary to sequelae from childhood infections or inhalation of toxic gases. It can also occur in patients with connective tissue diseases and is a well-known complication of bone and lung transplantation. More recently, it has been associated with ulcerative colitis, proliferation of neuroendocrine cells in the lung or with cystic fibrosis.[5]

Treatment is based on oral systemic corticosteroid therapy. However, it appears that most cases are steroid-resistant, with development of irreversible airway obstruction.[6] Association with other immunosuppressants is also controversial, due to the absence of directed studies. Recent trials have also shown that macrolide in the form of azithromycin (250 mg three times a week) may be important in reducing the inflammatory component.[7]

Prognosis is difficult to establish since most of the available studies only enrolled patients with constrictive bronchiolitis associated to organ transplantation. In such patients, the overall mortality rate is 25%.[7] However, for 87% of patients who were asymptomatic there was resolution or stabilization of the disease, compared with 38% of those with moderate symptoms and 40% of those with severe symptoms.[2]

The authors describe two patients with histological diagnosis of constrictive bronchiolitis in order to highlight an uncommon entity that in clinical practice is often misread. Further studies targeting treatment regimens are needed in the near future.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Tuberculosis retreatment in Northern Portugal

Dear Editor,

Tuberculosis (TB) continues to be a global public health problem.

In Portugal, the incidence is higher in several urban centers, some of which are in northern Portugal, like Porto and Viana do Castelo (20–50 cases per 100,000 people). The retreatment takes place annually in these centers and the rate is also higher (2.97/100,000 people and 2.45/100,000 people, respectively) than in others in Portugal.[1]

The persistence of tuberculous bacilli in patients who are cured or in those whose treatment was not correctly completed is an important issue.[2] Published risk factors for treatment failure or relapse include medical factors like HIV infection, diabetes mellitus, low body weight, cavitation on chest X-ray, high bacterial burden, short duration of treatment, drug resistance, positive culture after two months of treatment and socio-demographic factors like male gender, unemployment, drug abuse, alcoholism, smoking and poor treatment adherence.[2–5]

Retreatment cases are the leading risk factor for drug resistance if not appropriately and effectively managed, especially in HIV-seronegative patients.[4,6]

We carried out a study to assess risk factors and outcome for retreatment in TB patients in northern Portugal.

The World Health Organization (WHO) standard definition was used for treatment outcome (treatment success, death, failure, default and transferred out).[3,5,7]

The cases included were all retreatment TB cases (having received previous treatments) reported in 2012 in Northern Portugal and controls were the new cases (having received

Table 1 Risk factors for retreatment.

Risk factors	New cases (n = 118)	Retreatment (n = 57)	Univariate analysis		Multivariate analysis	
			OR* (95% CI)	p-value	aOR* (95% CI)	p-value
Age						
≤40 years	47 (39.8)	12 (21.1)	1.0		1.0	
>40 years	71 (60.2)	45 (78.9)	2.48 (1.19–5.18)	0.015	3.12 (1.38–7.06)	0.006
Sex						
Female	51 (43.2)	10 (17.5)	1.0		1.0	
Male	67 (56.8)	47 (82.5)	3.58 (1.65–7.76)	0.001	2.87 (1.25–6.57)	0.013
Risk factors						
None	95 (80.6)	44 (77.2)	1.0			
Alcohol abuse only	22 (18.6)	9 (15.8)	0.88 (0.38–2.08)	0.776		
Injection drug use only	1 (0.8)	4 (7.0)	8.64 (0.94–79.54)	0.057		
HIV status						
Negative	110 (93.2)	45 (78.9)	1.0		1.0	
Positive	8 (6.8)	12(21.1)	3.67 (1.41–9.57)	0.008	5.31 (1.80–15.66)	0.002
Site of disease						
Extra-pulmonary	18 (15.3)	2 (3.5)	1.0		1.0	
Pulmonary	100 (84.7)	55 (95.6)	4.95 (1.11–22.13)	0.036	6.56 (1.26–34.22)	0.026
Chest radiography						
No cavitation	65 (55.1)	29 (50.9)	1.0			
Cavitation	53 (44.9)	28 (49.1)	1.18 (0.63–2.23)	0.601		
Diabetes Mellitus						
No	6 (5.1)	3 (5.3)	1.0			
Yes	112 (94.9)	54 (94.7)	1.04 (0.25–4.31)	0.96		
Unemployed						
No	98 (83.1)	41 (71.9)	1.0			
Yes	20 (16.9)	16 (28.1)	1.91 (0.90–4.06)	0.091		
MDR TB						
No	110 (93.2)	55 (96.5)	1.0			
Yes	8 (6.8)	2 (3.5)	0.50 (0.11–2.44)	0.391		

no previous treatment for TB) that were registered during the same period. Cases and controls were selected from the national database, which integrates the data from the mandatory registration of TB. For each case we randomly selected 2 controls. Risk factors (male sex, age over 40, HIV infection, diabetes mellitus, drug resistance, cavitation on chest X-ray, pulmonary vs. extra-pulmonary TB, unemployment, intravenous drug abuse and alcohol abuse) and outcomes for retreatment cases were compared against those for new cases.

We analyzed 57 cases and 118 controls (Table 1). In the cases, the median age was 48.0 years (range: 27.0–83.0) and 47 patients (82.5%) were male. In controls, the median age was 45.0 years (range: 14.0–85.0) and 67 patients (56.8%) were male.

The number of cases of pulmonary TB was higher in retreatment group (96.5% vs. 84.7%, p = 0.04). There were no differences when factors such as diabetes mellitus, immunosuppression, drug resistance, unemployment, intravenous drug abuse and alcohol abuse were compared.

Male sex (adjusted OR: 2.87, 95% CI: 1.25–6.57, p = 0.013), HIV-positive status (adjusted OR: 5.31, 95% CI: 1.80–15.66, p = 0.002) and age over 40 (adjusted OR: 3.12, 95% CI: 1.38–7.06, p = 0.006) were independent risk factors identified for retreatment (Table 1). Of the 57 retreatment cases identified, 46 (81%) had been successfully treated in the past.

The treatment success rate was lower among patients who had received prior TB treatment than in patients who had never been treated for TB (80.7% vs. 92.5%, p = 0.04). In retreatment group 6 patients (10.5%) died while 7 patients (5.9%) died among the new cases, although this was not a statistically significant difference (p = 0.36) (Table 2).

Male sex appears as a risk factor for retreatment, in ours and in other studies.[2–4,8] Although it is not fully understood why this is a risk factor for retreatment of tuberculosis, it is thought that this may be due to habits associated more to men than women as smoking, intravenous drug abuse and alcohol abuse.

Table 2 Patients outcome.

Categories	Treatment success	Poor outcome			*p*-Value
	Treatment completed	Died	Failed	Defaulted	
Treatment history					
Never treated for TB	109 (92.5)	7 (5.9)	1 (0.8)	1 (0.8)	0.04
Previously treated for TB	46 (80.7)	6 (10.5)	3 (5.2)	2 (3.6)	
Total	155 (88.5)	13 (7.4)	4 (2.3)	3 (1.8)	

Dooley et al.[3] commented that although retreatment guidelines are often the same for patients with failure of, default from, or relapse after initial treatment, these groups may benefit from different management strategies.

The number of cases of pulmonary TB was also higher in the retreatment group, although there are no studies in the literature that can explain this result.

In our population there were no differences when comparing factors such as diabetes mellitus, drug resistance, unemployment, intravenous drug abuse and alcoholism.

The low rate of multi drug resistance (MDR) TB in the retreatment group and the fact that there were no statistically significant differences when compared with the control group suggests that these patients may not have been exposed to many drugs in the past or that they had had a complete treatment, which was also noted by Kritski et al. in their population.[6]

Despite this result, the treatment success rate was lower among patients who had received prior TB treatment than in patients who had never been treated for TB.

Identifying local patient characteristics that confer higher risk of relapse, failure or default from primary TB treatment may help inform country-specific prevention strategies aiming to reduce the need for retreatment, resulting in cost savings and diminished morbidity and transmission.

Conflict of interest

The authors have no conflicts of interest to declare.

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