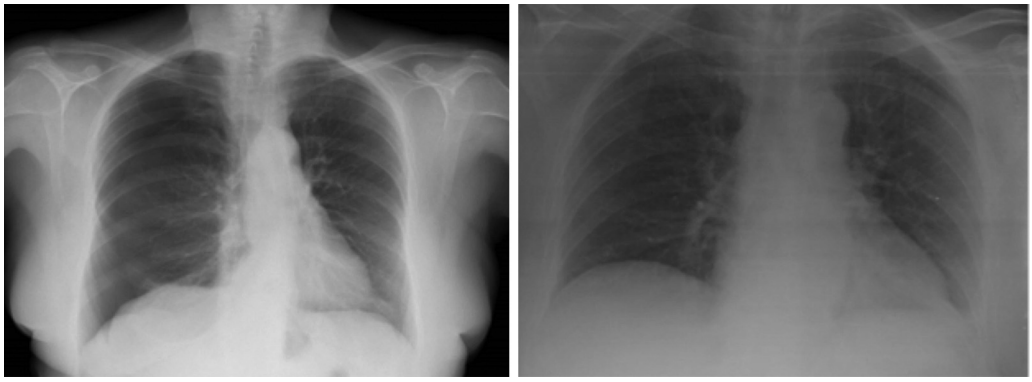

Fig. 1. Left: pneumothorax in right hemithorax. Right: pneumothorax resolved after chronic drainage.

The thoracic location of postherpetic neuralgia, in most cases, and the emergence of new techniques for pain control can lead to complications not initially considered, such as the case of our patient who presented pneumothorax in a healthy lung. The management of these cases begins with clinical suspicion, particularly in patients with risk factors. Treatment depends on the size of the pneumothorax. In the case of our patient, inter-procedural hemodynamic changes required urgent placement of a chest tube.

Despite their low incidence, facilities for the diagnosis and treatment of these complications must be available in these units, in the event that they do occur.

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Effect of Isoniazid Resistance on the Tuberculosis Treatment Outcome

Efecto de la resistencia a la isoniazida en el resultado del tratamiento de la tuberculosis

Dear Director,

Tuberculosis (TB) remains a serious public health problem, and about one-third of world's population has active or latent TB. In Europe, there are 49 new cases and 7 deaths from TB every hour.[1] In Portugal, the incidence has been decreasing in recent years, and in 2014 the annual incidence was 20/1,00,000.[2]

Drug-resistant *Mycobacterium tuberculosis* has become a major threat to the control of TB and, among all first-line drugs, resistance is greatest to isoniazid (INH).[3,4] In Portugal, INH resistance was 10.5% in 2014 among TB cases in whom susceptibility testing was performed.[2] In fact, there has been an increasing resistance to INH, despite the decreasing number of TB cases.[2]

INH is a first-line anti-TB drug because of its potent early bactericidal activity against rapidly dividing cells.[3,5] However, treatment of active TB requires multiple anti-TB drugs along with INH to prevent selection and emergence of a drug-resistant population of *M. tuberculosis*. According to current World Health Organization (WHO) recommendations, INH mono-resistant TB should be treated with 6–9 months of rifampicin, ethambutol, and pyrazinamide, plus or minus a fluoroquinolone.[6] These are also the current treatment guidelines in Portugal.

TB is a notifiable disease in Portugal, so clinicians report all cases to National-Tuberculosis-Surveillance-System (SVIG-TB) that has data on patient demographics, comorbidities, risk behaviors, and clinical, radiological, and microbiological information, as well as treatment outcomes.[7]

The objectives of this study were identify factors associated with INH mono-resistance, compare treatment outcomes of INH mono-resistant patients with drug-susceptible patients and understand the causes of unsuccessful treatment among INH mono-resistance TB cases.

Table 1
Demographic and clinical characteristics of enrolled TB patients.

Variable	Total (n = 7345)	INH mono-resistant (n = 242)	Drug-susceptible (n = 7103)	p-Value
Male	5013 (68%)	160 (66%)	4853 (68%)	0.512
Age (years), median (IQR)	44 (24)	44 (24)	44 (23)	0.713
Country of origin				
Portugal	6099 (83%)	191 (79%)	5908 (83%)	
Other country	1246 (17%)	51 (21%)	1195 (17%)	0.100
HIV positive	796 (11%)	18 (7%)	778 (11%)	0.104
Alcohol use	1077 (15%)	36 (15%)	1041 (15%)	1.000
IV-drug use	535 (8%)	11 (8%)	524 (8%)	0.116
Other drug use	655 (9%)	14 (6%)	641 (9%)	0.094
Correctional facility residence	130 (2%)	1 (0.4%)	129 (2%)	0.165
Homeless	134 (2%)	4 (2%)	130 (2%)	1.000
Clinical history				
Diabetes	479 (6%)	16 (7%)	463 (6%)	1.000
Silicosis	101 (1%)	2 (1%)	99 (1%)	0.642
Lung cancer	65 (1%)	0	65 (1%)	0.252
Other cancer	205 (3%)	7 (3%)	198 (3%)	1.000
Hepatic disease	334 (4%)	10 (4%)	324 (5%)	0.874
COPD	229 (3%)	3 (1%)	226 (3%)	0.128
X-ray				
Non-cavitary TB	2518 (40%)	84 (41%)	2434 (40%)	
Cavitary TB	3559 (57%)	114 (56%)	3485 (57%)	
Normal	159 (3%)	5 (3%)	154 (3%)	0.933
Pulmonary TB	6510 (89%)	210 (87%)	6300 (89%)	0.411
Other localization TB	835 (11%)	32 (13%)	803 (11%)	
Previous treatment	610 (8%)	17 (7%)	593 (8%)	0.538
Positive initial microscopy	4812 (69%)	154 (66%)	4658 (69%)	0.494
Positive initial culture	6819 (97%)	221 (97%)	6598 (97%)	1.000
Toxicity during treatment	158 (3%)	7 (3%)	151 (3%)	0.579
Outcome				
Successful (n = 7185)	6385 (89%)	210 (90%)	6175 (89%)	
Unsuccessful (n = 7185)	800 (11%)	24 (10%)	776 (11%)	0.743
Death (n = 7185)	461 (6%)	14 (6%)	447 (6%)	0.889
Treatment duration (days), median (IQR)	254 (104)	279 (94)	251 (104)	<0.001

TB: tuberculosis; INH: isoniazid; IQR: interquartile range; HIV: human immunodeficiency virus; IV: intravenous; COPD: chronic obstructive pulmonary disease.

To achieve the goals, data from Portuguese SVIG-TB were retrospectively analyzed from 1/January/2008 to 31/December/2014. INH mono-resistant cases were compared with drug-susceptible cases.

Culture-confirmed cases tested against first-line anti-TB drugs were included. INH mono-resistant TB cases were defined as having resistance to INH, but susceptibility to all other first-line anti-TB drugs. Drug-susceptible cases were those that had documented sensitivity to INH, rifampin, pyrazinamide, and ethambutol.

Susceptibility testing was carried out according to international standards; the method of proportions (liquid medium in the MGIT 960 system) was used to determine susceptibility to anti-tuberculosis drugs on: isoniazid (0.1 μg/ml), rifampicin (1 μg/ml), ethambutol (5 μg/ml), pyrazinamide (100 μg/ml) and streptomycin (1 μg/ml).

The WHO standard definitions were used for treatment outcomes.[6] Unsuccessful treatment includes failure, death during treatment and default. Cured patients and those with completed treatment were defined as treatment success. Cases with unknown outcomes ("in treatment" and "transferred") were excluded.

Data were summarized by descriptive statistics, consisting of absolute (relative) frequencies or median (minimum–maximum), according to nature of variables.

Comparisons of demographic and clinical variables between two groups used the Chi-squared test (or Fisher's test, as appropriate) for categorical variables and the Mann–Whitney U-test for continuous variables. A univariate analysis evaluated the effect of demographic characteristics and risk factors on treatment outcome for INH mono-resistance TB, through simple logistic regression.

Statistical analyses were performed with SPSS version 18.0 (PASW Statistic 18). Significance level was set at 0.05.

This study used surveillance data, with no possibility of linking patient records to patient personal data, so ethical approval was considered unnecessary.

Between 2008 and 2014, 18,429 TB cases were reported to SVIG-TB, from them 12,031 had culture confirmation and 10,588 of them were tested for sensitivity to first-line anti-TB drugs. According to drug susceptibility test, 7103 cases were susceptible to all first-line anti-TB drugs and 242 cases were INH mono-resistant. 3243 cases were excluded: 657 cases had resistance to rifampin and/or pyrazinamide and/or ethambutol and/or streptomycin, and 2061 had susceptibility to isoniazid and rifampin and no results for pyrazinamide, ethambutol and streptomycin.

Table 1 shows the characteristics of INH mono-resistant, drug-susceptible, and all eligible TB cases. In all groups, median patient age was 44 years, men were more likely to be cases than women, and most patients were born in Portugal. Most of studied clinical factors were not statistically different between INH mono-resistant and drug-susceptible groups. Although the two groups had no significant difference in treatment outcome and toxicity during treatment, the median treatment duration was longer in INH mono-resistant group (279 *vs.* 251 days, $p < 0.001$).