O.E. Dogorova, M.K. Vinokurova

Characteristics of Newly Identified Patients with Infiltrative Pulmonary Multidrug-Resistant Tuberculosis in the Sakha Republic (Yakutia)

ABSTRACT

This paper presents social and clinical data on newly identified patients with pulmonary infiltrative multidrug-resistant tuberculosis in the Sakha Republic (Yakutia) treated at the Therapy Department for Pulmonary Tuberculosis no.3, the Research & Practice Center for Tuberculosis. The majority of the patients were unemployed individuals of active working age, with the history of close family exposure to sputum-positive case. Most often, tuberculosis was detected on presentation to a doctor, and the detected cases were mostly cases with extensive destructive disease and high bacterial loads of multidrug-resistant *M.tuberculosis (MDR)*.

Keywords: *Mycobacterium tuberculosis*, infiltrative pulmonary tuberculosis, multidrug-resistance, chemotherapy regimen, primary drug resistance, antitubercular agents.

INTRODUCTION

Multidrug resistance (MDR) of *M.tuberculosis* (MTB) is currently one of the most urgent problems in the science of tuberculosis treatment and prevention. In the Sakha Republic (Yakutia), the incidence of MDR MTB is tending to grow: in 2013 MDR cases made 32.4% among the newly detected pulmonary tuberculosis (TB) cases, which is 4.4% percent higher than in 2011.

MATERIAL AND METHODS

We observed 91 patients with newly detected infiltrative pulmonary MDR TB, who were undergoing intensive phase treatment with chemotherapy regimen IV in the settings of tertiary therapy department for patients with MDR MTB, in the Research & Practice Center for Tuberculosis. All patients were HIV-negative; all had primary type of drug resistance.

RESULTS AND DISCUSSION

Observation group included more males (50; 54.9%) than females (41; 45.1%). Patient age ranged from 18 to 65; the majority (80.2%) was individuals of active working age (21 to 50 years). More than half of the patients were urban residents (59.3%; 54), while the rest (40.7%; 37) resided in rural settlements. Social and living conditions for the patients diagnosed with infiltrative pulmonary MDR TB are presented in Table 1.

Table 1

Social and living conditions of patients with infiltrative pulmonary tuberculosis caused by multidrug-resistant mycobacteria

Parameter	Total (n=91)	Urban residents (n=54)	Rural residents (n=37)
Gender			
Males	50 (54.9%)	29 (58%)	21 (42%)
Females	41 (45.1%)	25 (61%)	16 (39%)
Social status			
Unemployed, active working age	43 (47.3%)	23 (53.5%)	20 (46.5%)
Employed	31 (34.1%)	18 (58.1%)	13 (41.9%)
College/Higher education undergraduates	13 (14.3%)	10 (76.9%)	3 (23.1%)
Retirees	4 (4.3%)	3 (75%)	1 (25%)
Living conditions			
Housing with modern conveniences	27 (29.6%)	20(74.1%)	7 (25.9%)
Partly lacking conveniences	24(26.4%)	14(58.3%)	10(41.7%)
Private housing	23(25.3%)	3(13%)	20(87.0%)
Hostel	10 (11%)	10(100%)	-
Homeless	7 (7.7)	7(100%)	-

There were 43 (47.3%) unemployed patients of active working age, 31 (34.1%) patients with permanent employment, 13 (14.3%) undergraduate students of colleges/higher education institutions; and 4 (4.3%) retirees. Among the patients with permanent job, the majority had blue-collar occupation (27; 87.1%), and 4 (12.9%) were white collar workers. Educational background was as follows: completed or unfinished higher education (13; 14.3%); vocational secondary college or secondary general school (71; 78%); unfinished secondary school or elementary education (7; 7.7%). As for living conditions, 27 (29.6%) patients resided in houses

with modern conveniences, 24 (26.4 %) were living in houses partly lacking conveniences, 23 (25.3%) were living in private houses, 10 (11.0%) patients resided in hostels, and 7 (7.7 %) patients were Of No Fixed Abode.

There were 22 (24.2%) patients with alcohol addiction, 40 (43.9%) patients with nicotine addiction, and 1 patient with substance addiction. Number of patients with a history of previous detention was 6 (6.6%).

Analysis of the frequency and timeliness of preventive chest x-ray examinations underwent by the patients before the detection of TB showed that only 20 (21.9%) underwent their exams in time; 18 (19.8%), 39 (42.9%), and 14 (15.4%) patients had been x-rayed for more than 2, 3, or 5 years, respectively. Among the employed and undergraduate patients, 16 (36.4%) had been examined for 2 or more years.

Tuberculosis disease was detected more often on presentation to a physician (52 cases; 57.1%). On presentation, most patients complained of the symptoms typical for tuberculosis-induced intoxication: coughing for a long time (for more than 2 months), fever, fatigue, loss of weight, hemoptysis. 30 (33%) patients were found to be x-ray-positive during the scheduled preventive chest x-ray examination or else during job seeking; (9.9%) patients were detected after they were referred to TB Clinic for further examination due to exposure to contagious TB case.

Study of the epidemiological background showed that 39 (42.9%) patients had a recent contact with MDR TB case; of them, 21 (53.8%) were close family contacts, 18 (46.2%) were social contacts (i.e. with sick friends, relatives, or former prisoners, who had MDR MTB). Obviously, exogenous superinfection played a leading role in the development of TB disease in the lungs, as close contacts with pulmonary MDR TB cases were highly common in the epidemiological backgrounds of the patients.

Analysis of medical histories showed that before presenting to physician, patients with MDR TB had been considering themselves sick for a period ranging from 2 weeks to 2 months (54; 59.3%), from 3 to 4 months (16; 17.6%), or from 5 to 6 months (3; 3.3%). 18 (19.8%) patients thought they were not sick.

Patients with infiltrative pulmonary MDR TB commonly presented with symptoms of fatigue, fever, night sweats, and loss of weight. These symptoms were pronounced in 17 (18.3%)

patients and moderate in 59 (64.8%). Respiratory syndrome was observed in 77 (84.5%) patients. Of them, 92.2% had complaints of moist cough; 58 (63.8%) had shortness of breath on exertion; 33 (36.3%) admitted chest pain on breathing. 14 (15.4%) patients had hemoptysis as the reason to seek medical care. Half of the patients (52%) noticed loss of weight; average body mass index was less than 18; body weight deficit ranged from 5 to 10 kg.

Study of the immune status showed that B-cell activation was more common, with an increase in IgG levels from 20 to 380 mg/mL (5.3 to 16.5 mg/mL in health) in 90.5% of the cases; increase in IgM levels from 3 to 6.5 mg/mL (0.5 to 2 mg/mL in health) in 78.6% of the cases; and increase in IgA levels from 4.5 to 27.5 mg/mL (0.8 to 4 mg/mL in health) in 35.7% of the cases. These results confirmed the activation of secondary immune response typical for TB disease, and usually manifesting as increased Ig levels, especially IgG, a highly specific and one of the most important antibodies in terms of protection against infectious agents.

Radiological examinations, including chest x-ray and computed tomography, revealed that tuberculosis involved one lung in most cases (36.6%); in the rest of the cases, the disease involved one lobe (29.6%), or two segments of the one lung (18.3%), or both lungs (15.5%). All patients developed destructive TB; cavitations were sized <4 sm. in 71.8% of the cases; <2 sm. in 28.2% of the cases; multiple cavitations were observed in 41.8% of the cases; seeding to neighboring areas of the lung or to the opposite lung was found in the majority of the patients (73.6%).

Study of the respiratory function showed meaningfully decreased pulmonary ventilation and vital capacity of the lungs (60 %); of them, 20 (27.8%) patients had restrictive impairments; 40 (55.6%) had moderate decrease; in 12 (16.6 %) patients no impairments were detected.

Based on the fiberoptic bronchoscopy findings, the following conditions were diagnosed: draining purulent endobronchitis (22; 24.2%); diffuse cataral endobronchitis with the inflammation stage I or II (49; 53.8%); atrophic endobronchitis (10; 11%); no pathologic conditions (10; 11%).

Culture testing was performed using BACTEC MGIT-960 liquid medium system and absolute concentration method on Lowenstein-Jensen medium for drug sensitivity determination. Sputum culture tests were performed in all patients before the prescription of chemotherapy.

Most newly identified cases were started on standard chemotherapy regimen I (57.1%). Regimen IIB was prescribed in 42.9% of the cases who had been exposed to MDR TB.

Use of BACTEC MGIT-960 system for culture tests shortened time to determination of M.tuberculosis drug sensitivity. Determination of MDR required 1 to 1.5 months in 73 (80.2%) patients, and <3 months in 18 (19.8%) patients. Patients with confirmed MDR TB were started on chemotherapy regimen IV and transferred to the specialized department for MDR cases in 3 to 7 days, after the decision of the Centralized Medical Supervisory Committee.

Fluorescence microscopy of the sputums from patients with infiltrative pulmonary MDR TB performed on admission to hospital showed that mycobacterial counts were predominantly excessive (34; 47.9%), or moderate (19; 26.7%), or scarce (18; 25.4%).

Drug resistance profiles are presented in Table 2. As is seen from the table, there was a high incidence of DR to first and second line drugs (42.8%).

Table 2

Primary multidrug-resistance profiles (n=91)

Combination of anti-TB drugs	Number of cases
HR	3 (3.3%)
HR /S /E	49 (53.9%)
HRSKm / Cm /E /PAS /Et /Cs	31 (34%)
HRSOf /E /Et	8 (8.8%)

Notes: *H – Isoniazid; R – Rifampicin; S – Streptomycin; Km – Kanamycin; E – Ethambutol; Cm – Capreomycin; Et – Ethionamide; PAS – Para-aminosalicylic acid; Fq – Fluoroquinolone.

Fig. 1 shows that DR to isoniazid and rifampicin is most often associated with DR to streptomycin (88%), kanamycin (37.4%), or ethambutol (29.7%).

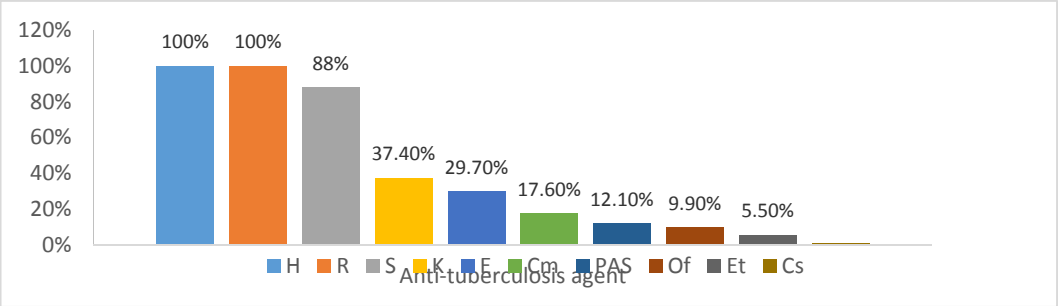

Fig.1. Incidence of drug resistance to individual anti-tuberculosis agents

CONCLUSIONS

In the Sakha Republic (Yakutia), patients who develop infiltrative pulmonary MDR TB were mostly urban residents, male, of active working age but unemployed, with nicotine and alcohol addiction. Commonly observed delays in regular preventive chest x-ray examinations coupled with late presentation to a physician stems from poor health education among the population.

Infiltrative pulmonary MDR TB was characterized by subacute onset, with moderate tubercular intoxication and a respiratory syndrome typical for TB (prolonged moist cough; shortness of breath on exertion; chest pains; coexistence of nonspecific endobronchitis; impaired respiratory function). As a rule, patients with pulmonary TB developed an extensive and destructive disease with seeding lesions and excessive mycobacterial sputum counts. This emphasizes once more the high epidemiological danger that drug-resistant cases present. It is important to stress out that the majority of patients with primary DR had high incidence of DR to the first- and second-line drugs, which suggests prolonged close contact with a sick person already harboring MDR M.tuberculosis.

In view of the stressed epidemiological situation for TB in the Sakha Republic, health education activities among the population and preventive medical examinations must be expanded, especially among the unemployed population, primary network health personnel must be educated to prevent and detect TB, and learn the correct patient referral during population examination for the presence of TB, to identify epidemiologically dangerous cases. The detection of DR forms of TB must be based on the use of up-to-date diagnostic culture

methods enabling fast determination of drug sensitivity, and initiation of adequate chemotherapy in the specialized TB facility.

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Dogorova Oksana Egorovna, research staff member, TB Physician, Therapy Department for Pulmonary Tuberculosis no.2, Research & Practice Center for Tuberculosis of the Sakha Republic (Yakutia), Sakha Republic (Yakutia), Yakutsk, 677000, ul. Petra Alekseeva 93, Phone: +7 (914)263-06-38, e-mail:dogorova2904@mail.ru.

Vinokurova Maria Konstantinovna, Dr. Med. Sc.(MD), Deputy Director for Science, Research&Practice Center for Tuberculosis of the Sakha Republic (Yakutia), Sakha Republic (Yakutia), Yakutsk, 677000, ul. Petra Alekseeva 93, Phone: +7 (964)423-94-94, e-mail: mkvin61@mail.ru.