MULTIDRUG RESISTANCE IN PATIENTS WITH OSTEARTICULAR TUBERCULOSIS

This paper describes prevalence of multidrug resistant tuberculosis (MDR TB) among 285 patients treated in clinic of National Center for TB Problems (Kazakhstan) during 2007-2009. Data were obtained through clinical examination of patients and bacteriological culture investigation of postoperative material. The drug resistance in patients with osteoarticular tuberculosis (OAT) in 54.0% was confirmed on the base of microbiological investigation (cultering on Lowenstein-Jensen medium), and in 12.6% clinical resistance took place. The relatively high multidrug resistance revealed in patients with OAT is connected to the thorough sampling of the pathological material intraoperatively.

**Keywords:** Multidrug resistance, extrapulmonary tuberculosis, osteoarticular tuberculosis.

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**Introduction**

Nowadays among patients with TB in Kazakhstan there has been increase of not only primary but also secondary drug resistance which amounted 13.1% in 2006, 20.4% in 2010, 39.1% in 2006, and 53% in 2010 relatively (Ismailov, 2006; Abuzarov et. al., 2007; Statistical Review on Tuberculosis, 2007, 2010). Few literature has been published on prevalence of multidrug resistance in osteoarticular tuberculosis, and they concern rather limited observations. At this time, Nazirova and Kholikulov (2007) indicate on the relatively low percentage of its incidence (14.8%) among patients with osteoarticular tuberculosis. Possibly, it is associated to the oligobacillary emission of M. tuberculosis among this group of patients (Vishnevskiy et al., 2006). Aim of this work was to study the prevalence of multidrug resistance in patients with osteoarticular tuberculosis.

**Material and methods**

To study the indicators of MDR TB incidence among patients with osteoarticular tuberculosis (OAT) we analyzed the results of bacteriological investigations of postoperative material from 285 patients with OAT operated under conditions of the National Center for TB Problems (Kazakhstan) over 2007-2009. The pathological tissues taken from destruction focus during operation served as a material to be investigated since the diagnostics of MDR TB at OAT presented some complications because of significant difficulties in obtaining bioplate samples for investigation.

From total number patients adults constituted 90.8% (259) while children made 9.2% (26) of cases. All the patients were conducted the bacteriological and histological investigations of postoperative material. Among examined persons patients from 18 to 40 years old were prevalent, i.e. 56.1% of cases out of all patients studied. M. tuberculosis (MT) culturing was performed on solid Lewenstein-Jensen media. The resistance of MT to the drugs of the first line was determined by standardized direct method. Operational material (pus, caseous masses, bone sequesters, granulation tissue) was examined morphologically with staining a histological preparation by Ziehl-Neelsen.

**Results and discussion**

The investigation demonstrated that among examined patients those with tuberculosis spondylitis were prevalent: 169 (59.3%), while among other locations tuberculosis coxitis was predominant 46 (16.1%) (Table 1).
**TABLE 1. DISTRIBUTION OF PATIENTS HOSPITALIZED DURING 2007-2009 BY CLINICAL FORMS OF OAT**

<table>
<thead>
<tr>
<th>Clinical forms</th>
<th>2007-2009</th>
</tr>
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<tbody>
<tr>
<td>Tuberculosis spondylitis</td>
<td>169 (59.3%)</td>
</tr>
<tr>
<td>Tuberculosis coxitis</td>
<td>46 (16.1%)</td>
</tr>
<tr>
<td>Tuberculosis gonitis</td>
<td>38 (13.4%)</td>
</tr>
<tr>
<td>Tuberculosis of other bones</td>
<td>32 (11.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>285 (100%)</td>
</tr>
</tbody>
</table>

The bone specific process, because of the diagnostics delayed, in some patients examined led to the number of different complications in term of abscesses, spinal brain disturbances, fistulae, vertebral column deformations and contractures of major joints. The frequency of those complications is presented in the Figure 1.

**FIGURE 1. THE FREQUENCY OF COMPLICATIONS AT OAT DURING 2007-2009 (%)**

All the patients hospitalized were treated by available categories of DOT recommended by WHO. The retrospective analysis showed that the patients with OAT in 76.1% of cases received the treatment under category 1 regimen while 23.4.9% of cases were treated by category 2.

As it is seen in the Figure 2, positive cultures from pathological material were obtained in 26.6% out of 285 patients with OAT. The determination of frequency and spectrum of the drug resistance showed that in 35.5% (27) of cases the MT sensitivity to the anti-TB drugs of the first line was preserved, in 6.5% (5) the MT was resistant to one drug, in 3.9% (3) - to two drugs (besides HR), and in 54% (41) - to the drugs of the first line isoniazid (H) and rifampicin (R). These data are in accordance with the results of Vishnevskiy (2006) and Nazirov (2007).

There are the interesting data which are of evidence that during histological investigation of postoperative material in 50% of cases patients had the active tuberculosis process. Those patients were treated surgically due to the non-effectiveness of antibacterial therapy and aggravation of the neurological disturbances.

The treatment under category 4 regimen was implemented to 41 (14.4%) patients with laboratory confirmed MDR TB and to 36 (12.6%) patients with clinically confirmed multidrug resistance out of total number of operated patients. The clinical manifestation of drug resistance in examined patients was characterized by constant hyperthermia, remained intoxication, bone tissue destruction development and abscess in the osteoarticular system against the background of treatment with anti-TB drugs of the first line.
After administration of the drugs of the second line in the standardized regimen (6Ofl, Cs, Pto(Eto), Cap, Z, PAS/18Ofl, Cs, Pto, PAS) it was observed the positive clinical and roentgenological dynamics in term of body temperature normalization, improvement of indices in blood account, disappearance of abscess and destruction focus in bone tissue during 1.5 to 3 months of treatment. Thus, drug resistance at OAT in 54% of cases was verified by postoperative material bacteriological culturing into Lowenstein-Jensen medium and conducting drug sensitivity test to determine the sensitivity to the drugs of the first line.

Our investigation indicated on the growth of MT with multidrug resistance not only at pulmonary tuberculosis, but at its extrapulmonary location. Also, this growth could be explained by the fact that everywhere in the country the monitoring of the drug resistant TB is being conducted with implementing of cultural investigation of the pathological material including postoperative material for testing drug resistance. It obviously explains higher figures in the study than those of other mentioned researchers.

**Conclusion**

The drug resistance in patients with OAT in 54.0% was confirmed on the base of microbiological investigation (culturing on Lowenstein-Jensen medium), and in 12.6% clinical resistance took place. The relatively high multidrug resistance revealed in patients with OAT is related to the thorough sampling of the pathological material intraoperatively. Timely diagnostics of MDR TB in patients with OAT, totally in more than 66.6% of cases, favored to the adequate anti-TB treatment under category 4 regimen.

**References**


