Nontuberculous mycobacteria infections in Russian HIV patients: clinical features and outcomes.

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BACKGROUND

People living with HIV are at risk of developing either pulmonary or disseminated form of mycobacterial infections, especially those who are diagnosed at late stages, who fail to stay on treatment, or fail to maintain viral suppression. Meanwhile treatment of the disease is complex and still lacks efficacy, since the question of macrolide resistance has never been solved.

METHODS

This study was conducted to investigate nontuberculosis mycobacterial rates in HIV patients in Russian infectious diseases hospital for a last decade, describe clinical features and analyze outcomes on different treatment regimens. Data was collected at the Saint-Petersburg Botkin Clinical infectious diseases hospital from January 2005 to January 2020. Cases were divided by etiology, forms of process. Student's t-test was used, survival time on different treatment regimens was evaluated with Kaplan-Meier estimator. **The inclusion criteria** were the presence of HIV, culturally confirmed diagnosis of mycobacteriosis. Patients who didn't receive specific antibiotic treatment were excluded.
We enrolled 114 HIV patients with different forms of NTM infections.
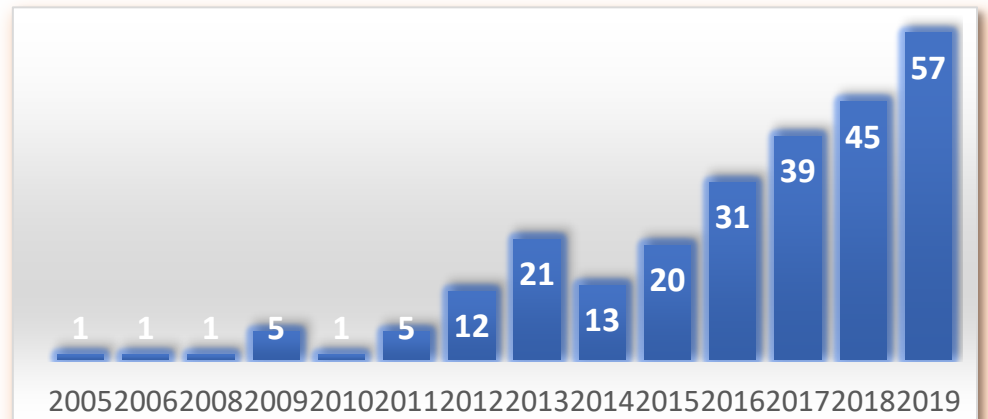
INCIDENCE

Figure 1. Incidence of nontuberculous mycobacteria in HIV patients at Botkin Clinical infectious diseases hospital (from January 2005 to January 2020)

RESULTS

M.avium as an etiological agent **83,0%**

Sexual route of HIV transmission **66,7%**

Lethal outcomes **29,8%**

Women 44,7%   *Men 55,3%*

- A prominent increase of NTM incidence was observed.
- The majority of patients were aged between 20 and 40 (76,3%), median age was 36 ± 0.7 years with a distribution from 20 to 61 years.
- A group of 37 patients (32,4%) were first time tested positive for HIV at the time of diagnosis of mycobacteriosis.
- In 28 cases manifestation of the disease developed after antiretroviral therapy initiation as a result of unmasking IRIS on average after period of $2,0 \pm 0,2$ months.
- In the latter cases symptoms usually persisted for a long period of time, more than 2 months in 64,0%.
- Median CD4 cell count at the time of diagnosis in the group was: $29,7 \pm 4,3$ cells/mm^3.
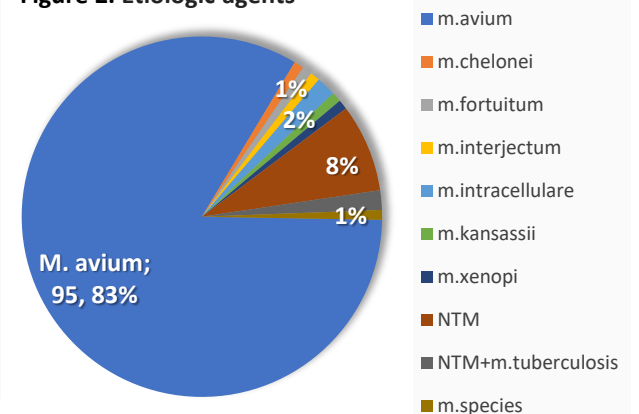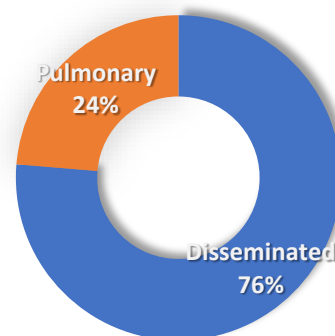
Figure 2. Etiologic agents

Legend:
- m.avium
- m.chelonei
- m.fortuitum
- m.interjectum
- m.intracellulare
- m.kansassii
- m.xenopi
- NTM
- NTM+m.tuberculosis
- m.species

M. avium; 95, 83%

1%, 2%, 8%, 1%

Table 1. Localizations of pathological process

Localization	N of cases	Percent.
mesenteric lymph nodes	80	70,20%
mediastinal lymph nodes	79	69,20%
peripheral lymph nodes	25	21,90%
bronchi (fistules)	6	5,20%
kidneys	15	13,20%
spleen	27	23,70%
liver	9	7,90%
intestine	26	22,80%
meninges	3	2,60%
pericardium	5	4,40%
spondylitis	3	2,60%

Figure 3. Distribution by types

Pulmonary 24%
Disseminated 76%

Figure 4. CD4 increase in pulmonary and disseminated types

CD4 (start): 52,9 / 23,3
CD4 (1 m): 137,4 / 62,1
CD4 (3 m): 182,3 / 67,7
CD4 (6 m): 180,2 / 71,3
CD4 (12 m): 257,2 / 165,1

MONTHS OF TREATMENT

CD4 was significantly higher in patients with pulmonary than disseminated forms: $52,9 \pm 12,2$ and $23,3 \pm 4,1$ cells/mm3 (p<0,05). Significant difference as well was obtained in CD4 account increase on treatment including antibiotics and antiretrovirals. Patients with pulmonary type were also characterized by a significantly higher hemoglobin level: $108,1 \pm 4,5$ and $88,7 \pm 2,3$ g/l (p<0,05).

TREATMENT OUTCOMES
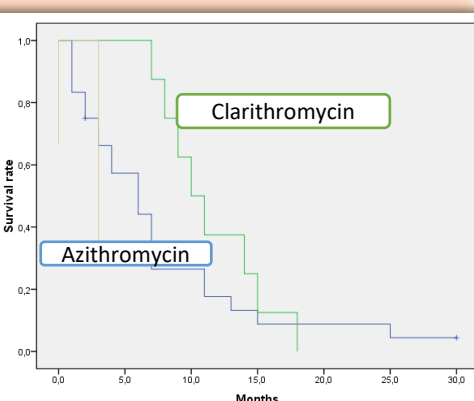

Clarithromycin

Azithromycin

Figure 5. Survival rates (macrolide base)

- There were 73 patients (64,0%) who have successfully completed the course of mycobacteriosis treatment;
- There were 41 lethal outcomes, among them in 34 cases (29,8%) – due to MAC progression;
- The median duration of treatment was $15,4 \pm 1,0$ months;
- Clarithromycin showed advantage over azithromycin when analyzing survival by the method of Kaplan-Meier (p <0,05 Breslow);
- There was no statistical difference observed in survival rates when adding aminoglycoside to the treatment regimen.

CONCLUSIONS

1. Despite the widespread introduction of antiretroviral therapy, unlike other countries in Russia there is a significant increase in the number of cases of infections caused by NTM in HIV patients.
2. Pulmonary forms are characterized by higher levels of CD4 and good immunological response.
3. Clarithromycin is preferable when choosing a macrolide base in the treatment regimen.

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