Surgical Treatment of Cavernous and Fibrous-Cavernous TB in Children

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Abstract

Introduction Treatment of cavernous and fibrous cavernous tuberculosis in children, especially in the presence of multiple drug resistance-tuberculosis or extremely drug resistance-tuberculosis, presents a major challenge.

Materials and Methods We analyzed results of treatment of 65 patients (mean age 14.8 + 2.9 years) with cavernous TB (group I) and 116 patients (mean age 15.6 + 1.9 years) with fibrous-cavernous TB (group II). Evaluation of treatment efficiency was performed directly at discharge and 1 year after treatment according to Lazerson's criteria.

Results In group I, after 80 operations, two (2.5%) cases showed delayed expansion of the lung after combined resections, in group II, postoperative complications after 160 operations occurred in eight (5.0%) cases (the difference is reliable $p \leq 0{,}05$). There was no hospital fatality. The effectiveness at the time of discharge from surgery (cessation of bacterization and elimination of decay cavities in the lung) was 100% in groups I and II, respectively. A year later, according to Lazerson's criteria, the efficiency in group I was 100%, in group II was 97.4%.

Conclusion Operations in patients with cavernous tuberculosis performed after 10 to 12 months of conservative treatment present a lower risk of postoperative complications and relapses of cavernous tuberculosis than operations in patients with fibrous cavernous tuberculosis performed after 22 months or more of treatment.

Keywords
- surgery
- complications
- tuberculosis
- outcomes
- VATS
- computed tomography

Introduction

Treatment of destructive pulmonary tuberculosis in children and teenagers is a major problem worldwide, especially in the presence of multiple drug resistance-tuberculosis (MDR-TB) or extensively drug resistance-tuberculosis (XDR-TB), the frequency of which is constantly increasing in the world,[1–5] and even cases of the presence of multidrug resistance in the newborn have already been described.[4]

In the Russian classification, in the presence of caverns in pulmonary tissue, two clinical forms are distinguished: cavernous and fibrous-cavernous pulmonary tuberculosis.[6]

The duration of the disease with cavernous tuberculosis (TB) is less than 1 year and is most often the result of an unfavorable course of infiltrative pulmonary tuberculosis with the formation of thin-walled decay cavities in the pulmonary parenchyma (►**Fig. 1A**).

The fibrosis in cavernous TB is not pronounced, macroscopically (►**Fig. 1B**) the lung tissue is not reduced in size, microscopically the cavern is thin-walled and elastic, and the outer fibrous layer is not developed (►**Fig. 1C**).

The fibrous-cavernous TB is characterized by a chronic wave-like course with the formation of a thick-walled cavern or caverns with pronounced perifocal scarring, a volumetric

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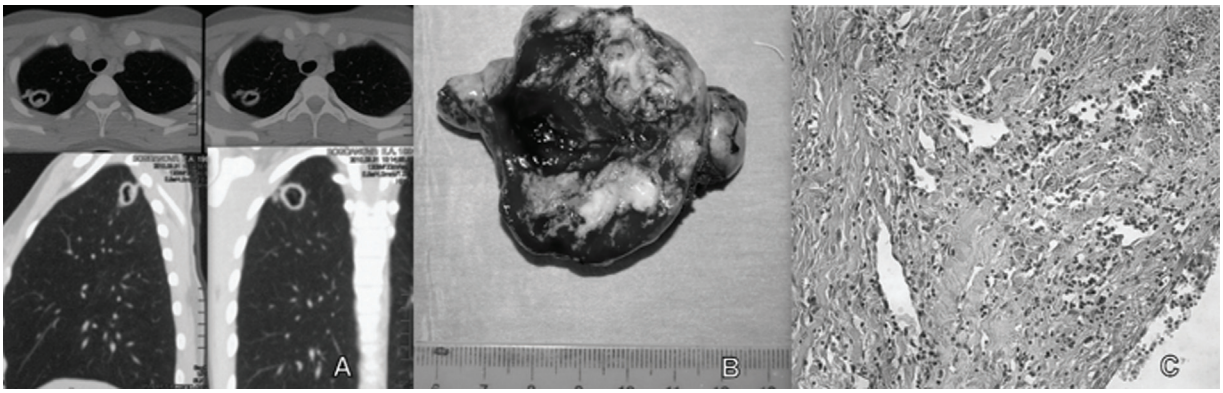

Fig. 1 (A) Computer tomogram of a patient with cavernous tuberculosis. (B) Macro preparation of the removed pulmonary lobe, on the section - cavernous tuberculosis. (C) Wall of cavity with diapiric hemorrhages. Coloring with hematoxylin and eosin. Zoom x200.

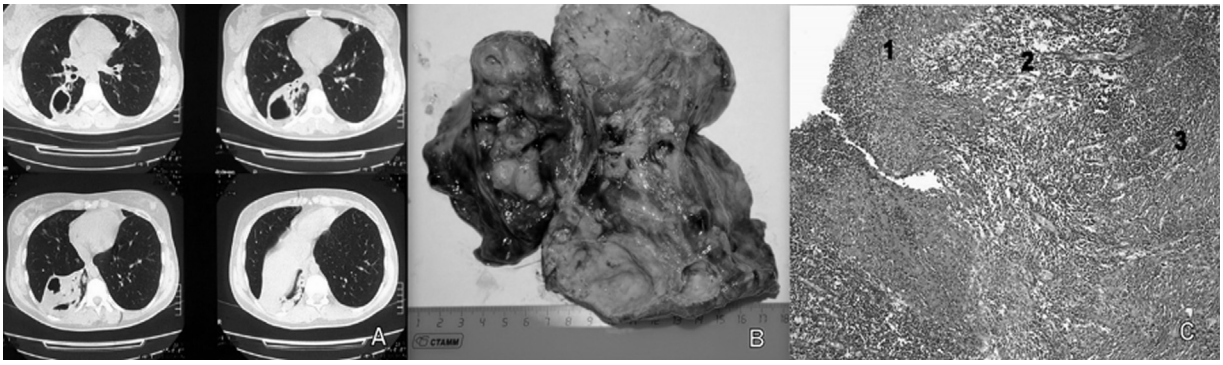

Fig. 2 (A) Computer tomogram of a patient with fibrous-cavernous tuberculosis. (B) Macro preparation of the removed lobe of the lung, on the section - fibrous-cavernous tuberculosis. (C) The wall of a chronic tuberculous cavity, whis has a 3-layer structure (1-an internal coarse fibrous capsule, 2 - a layer of specific granulation tissue, 3 - an external coarse fibrous capsule). Coloring with hematoxylin and eosin. Zoom x100.

decrease in the affected lobe, or the entire lung, and the presence of focal contamination around.

Radiologically, in fibrous-cavernous TB, a fibrous transformation of the lung with its decrease is noted; thick-walled cavities are formed in the lung, sometimes with the formation of a system of cavities and massive focal contamination of the surrounding lung tissue (►**Fig. 2A**). Macroscopically, there is a massive fibrosis in the lung, thick-walled cavities, and multiple foci in the pulmonary parenchyma (►**Fig. 2B**). Microscopically, the wall of a chronic tuberculous cavern has a three-layer structure (►**Fig. 2C**): the inner layer is caseous—necrotic, the middle layer is a specific granulation tissue with epithelioid-giant cell granulomas, less often with scattered epithelioid cells and giant cells of the Pirogov-Langhans type and foreign bodies, the outside is a coarse-fibrous capsule (in cavernous TB the outer layer is represented by loose, thin, intermittent connective tissue fibers).

Almost all patients with cavernous and fibrous-cavernous TB are bacterial extractors and, in the vast majority, MDR or XDR resistance of MBT (*Mycobacterium tuberculosis*) is determined.[1–5]

For indications for surgical treatment, we used the WHO guidelines "The role of surgery in the treatment of pulmonary TB and multidrug- and extensively drug-resistant TB."[7]

Materials and Methods

This study approved by the Local Ethics Committee of I.M. Sechenov First Moscow State Medical University (Sechenov University) (Extract from the protocol N° 18 to 21 of Local Ethic Committee, October 26th, 2021) was conducted on the basis of the Clinic for Thoracic Surgery and Tuberculosis. To determine the differences in the frequency of postoperative complications as well as the results of treatment after a year according to the Laserson criteria,[8] and in the long-term period from 2 to 15 years according to the criteria of clinical recovery (closure of the decay cavities, a cessation of bacterial excretion, absence of clinical and radiological signs of exacerbation of tuberculosis over the entire follow-up period), an observational retrospective cohort single-center study was conducted in patients aged 4 to 17 years who underwent surgery for cavernous and fibrous-cavernous pulmonary tuberculosis in the period from 2004 to 2017.

The inclusion criteria were:

- Age of patients from 4 to 17 years.
- Presence of cavernous or fibrous cavernous TB.
- Different indications for surgical treatment according to the WHO guidelines "The role of surgery in the treatment of pulmonary TB and multidrug- and extensive drug-

resistant TB,"[7] exactly—a poli-resistance or MDR/XDR-TB; absence of a tendency to eliminate the cavity of destruction and elimination of bacterial excretion after 4 months of conservative treatment; presence of pulmonary bleeding; progression of tuberculosis during the treatment of adequate chemotherapy; and ongoing bacterial excretion.

The exclusion criteria were:

- Other forms of tuberculosis, other than those listed above.
- Age over 18 years.
- Only conservative treatment without surgery.

A total of 65 patients (mean age 14.8 + 2.9 years) with cavernous TB (group I) and 116 patients (mean age 15.6 + 1.9 years) with fibrous-cavernous TB (group II) were included in the study. All patients and their parents have given informed consent to the treatment, operation, and processing of their personal information. The collection of long-term results was completed in May 2019. Given the retrospective nature of the study, no target sample size was established.

The duration of preoperative antitubercular chemotherapy in patients with cavernous TB averaged 10.8 + 1.9 months, and in patients with fibrous cavernous TB significantly longer—22.3 + 5.8 months (the difference is significant $p \leq 0.05$), and in 26 (22.4%) patients of group II it was more than 2 years.

Results

In the first group of patients, bacterial excretion at the time of surgery was observed in 38 (58.5%) children, and in the second group in 95 children (81.9%) (the difference is significant, $p \leq 0.05$).

Sputum was examined in patients for MBT by luminescent microscopy and sowed on the dense nutrient medium of Löwenstein-Jensen to determine bacterial excretion; in case of culture growth, sensitivity to anti-tuberculosis drugs was determined by the method of absolute concentrations.[9] The surgical material (contents of cavities, removed lymph nodes) was also subjected to bacterioscopy with a culture study and determination of drug resistance of MBT. Since 2011, a comparative analysis of the material obtained from sputum and surgical material has been additionally performed, including using the MGIT-960 VASTES system, molecular genetic methods: real-time polymerase chain reaction—Xpert MTB/RIF (*Mycobacterium tuberculosis*/resistance to rifampin), and PCR-TB biochips.

►**Table 1** shows the data on drug resistance of MBT in both groups of children. In general, the frequency of MDR and XDR MBT in the group of patients with fibrous-cavernous TB was higher.

All patients had preserved cavities at the time of surgery, including multiple cavities in seven (10.8%) patients of group I and in 26 (22.4%) of group II (the difference is significant, $p \leq 0.05$). Bilateral processes were observed in three (4.6%) and 17 (14.6%) patients, respectively. Given the significant prevalence of the process, some patients required bilateral and multi-stage surgical treatment with VATS (video-assistant thoracoscopic surgery) of delayed thoracoplasty after extensive lung resections.

A total of 80 operations were performed in 65 patients of group I and 160 operations in 116 patients of group II (►**Table 2**).

All operations in children were performed under the control of a video thoracoscope made of mini-accesses ranging in size from 3 to 8 cm.

Bilateral operations were significantly more often performed in patients of group II – in 17 (14.6%) children versus three (4.6%) patients of group I (the difference is significant $p \leq 0.05$). Two or more operations were performed in 15 (23.1%) patients with cavernous TB and 44 (37.9%) with fibrous-cavernous TB (the difference is significant $p < 0.05$). Also, in group II patients, large-volume lung resections (lobectomies and more) were performed more often: among patients with fibrous-cavernous TB in 62 (53.5%) patients versus 26 (40%) patients with cavernous TB, as well as pneumonectomies: in 16 (13.8%) children of group II and four (6.2%) in group I (the difference is significant $p \leq 0.05$).

Taking into account more voluminous resections in patients with fibrous-cavernous TB, VATS delayed thoracoplasty was performed naturally more often in these patients to correct the volume of the pleural cavity: in eight (12.3%) operated patients of group I and 35 (30.2%) of group II (the difference is significant $p < 0.05$).

Indications for performing delayed video-assisted thoracoplasty were not only the presence of a residual cavity after resection, but also volume of lung resection is more than four segments with the presence of focal contamination of the remaining lung sections and drug resistance of MBT. It significantly reduced the risk of relapse of tuberculosis in the long-term period. Since more severe operations were

Table 1 The degree of drug resistance of MBT in both groups

The degree of drug resistance	Cavernous tuberculosis (group I)	Fibrous-cavernous tuberculosis (group II)	The significance
The drug sensitivity	9 (23.7%)	17 (17.9%)	$p > 0.05$[a]
Monoresistance	2 (5.3%)	9 (9.5%)	$p > 0.05$[a]
Polyresistance	4 (10.5%)	5 (5.3%)	$p > 0.05$[a]
The multidrug resistance	15 (39.5%)	40 (42.1%)	$p > 0.05$[a]
The extensively drug resistance	8 (21.1%)	24 (25.3%)	$p > 0.05$[a]
Total	38 (100%)	95 (100%)	

[a]The difference is not significant.

Table 2 The volumes of performed surgical operations for fibrous-cavernous and cavernous tuberculosis

Type of operation	Cavernous tuberculosis $N = 65$	Fibrous-cavernous tuberculosis $N = 116$	The significance
The VATS pleural adhesiolysis	5 (6.25%)	3 (1.9%)	The difference is not significant $p > 0.05$
VATS segmental resections, including combined resections	35 (43.8%)	42 (26.3%)	The difference is significant $p \leq 0.05$
VATS lobectomy	15 (18.6%)	36 (22.5%)	The difference is not significant $p > 0.05$
VATS resections with a volume of more than a lobe	11 (13.8%)	26 (16.6%)	The difference is not significant $p > 0.05$
VATS pneumonectomy	4 (5.0%)	12 (7.5%)	The difference is significant $p \leq 0.05$
VATS pleuropneumonectomy	–	4 (2.5%)	The difference is not significant $p > 0.05$
VATS thoracoplasty	8 (10.0%)	35 (21.9%)	The difference is significant $p \leq 0.05$
Thoracocentesis	2 (2.5%)	2 (1.3%)	The difference is not significant $p > 0.05$
Total surgical operations	**80 (100%)**	**160 (100%)**	

Abbreviation: VATS, video-assisted thoracoscopic surgery.

Table 3 The effectiveness of surgical treatment

	The immediate effectiveness at discharge from a hospital (No cavities and bacterial excretion)	The effectiveness after 1 y according to the Laserson criteria	The long-term effectiveness
The group I ($N = 65$)	65 (100%)	65 (100%)	In 47 (100%) of the 47 tracked cases.
The group II ($N = 116$)	116 (100%)	113 (97.4%)	In 86 (97.7%) of the 88 tracked cases.

performed in patients with fibrous-cavernous TB, the frequency of postoperative complications in both groups was different. In group I, after 80 operations, in two (2.5%) cases delayed expansion of the lung after combined resections was noticed, in group II, postoperative complications after 160 operations occurred in eight (5.0%) cases (four patients had a residual pleural cavity, two patients had pleural empyema without bronchial fistula, and two more patients had rib osteomyelitis) (the difference was significant $p \leq 0.05$).

All postoperative complications in both groups of patients were successfully eliminated in the hospital. There was no hospital fatality. The effectiveness at the time of discharge from the surgical department (cessation of bacterial excretion and elimination of decay cavities in the lung) was 100% in group 1, and 100% in group 2. A year later, according to the Laserson criteria, the effectiveness in group 1 was 100%, in group 2 was 97.4% (►**Table 3**).

We studied the long-term results of treatment in terms of 2 to 15 years in 47 (72.3%) patients with cavernous TB and 88 (75.9%) patients with fibrous-cavernous TB (►**Table 3**).

In the second group, tuberculosis relapses were noted in two (2.3%) patients, who were treated conservatively. All patients with recurrent tuberculosis had XDR. In group I, there was no recurrence of tuberculosis (the difference is significant, $p \leq 0.05$).

An example of a good clinical effect of surgical treatment of common fibrous-cavernous TB can be the following observation.

Clinical Case

Patient V., 14 years old, on admission to the hospital, complained of shortness of breath during a minor physical exertion, an increase in body temperature to 37.9, weakness, sweating, poor appetite, weight loss (height 160 cm, weight 37 kg).

From the anamnesis: patient has been ill since 2009 when he was diagnosed with pulmonary tuberculosis. Against the background of treatment for category I DOTS, the progression of the process was noted in the form of increased infiltration and destruction, and constant bacterial excretion was noted. In July 2012, MDR (HRSPt) was detected in sputum. From December 20th, 2012 to May 17th, 2013, patient V. received treatment: levofloxacin, cycloserine, pyrazinamide, prothionamide, PASC, and amikacin with positive dynamics (she gained weight; it reduced symptoms of intoxication).

During preoperative fibrobronchoscopy, scar stenosis of the left major bronchus of grade II was detected. For the mixed type, the functional indicators of ventilation were also reduced (forced vital capacity [FVC] 62% of the proper, forced expiratory volume in 1 second [FEV1]-59% of the proper).

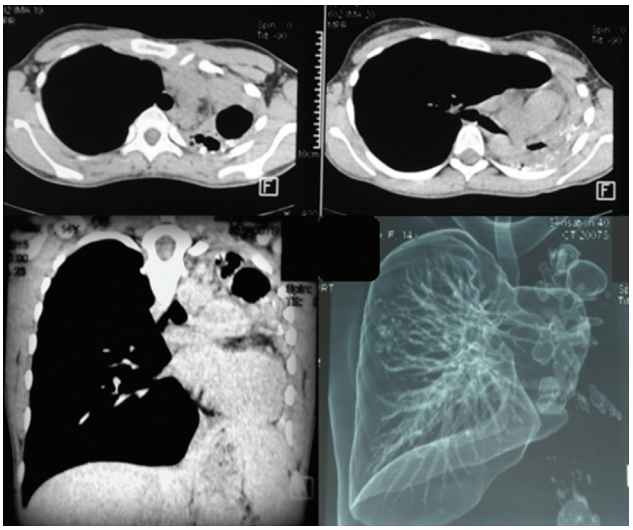

Fig. 3 Scan of computer tomography before surgery: the left lung was significantly reduced in volume and fibrotically altered. Against this background, multiple multi-chamber cavities and foci were determined.

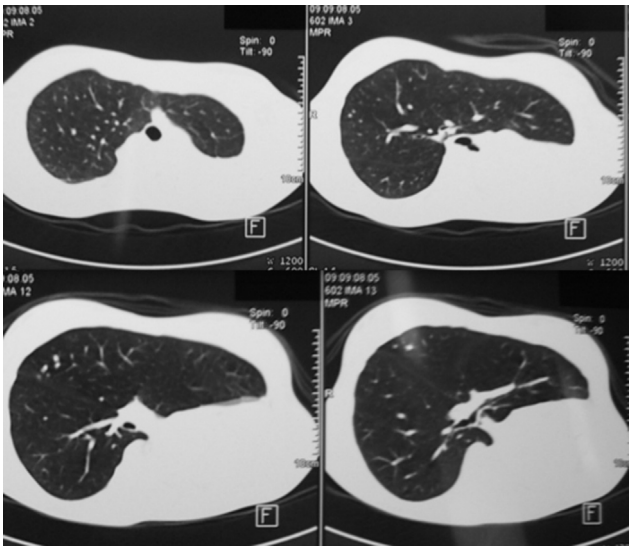

Fig. 5 Scan of computer tomography (5 years after a surgery): the left hemithorax is homogeneously darkened, the mediastinal organs are significantly shifted to the left; the upper lobe of a right lung have several small calcified foci.

During the computed tomography before the operation, the following changes were revealed (►**Fig. 3**): the left lung was significantly reduced in volume, fibrotically altered. Against this background, multiple multi-chamber cavities and foci were determined.

Taking into account the presence of MDR in the patient, constant bacterial excretion, and a destroyed lung with fibrous cavities, on August 26, 2013, she underwent a VATS pneumonectomy on the left (the duration of the operation was 2 hours 35 minutes, blood loss—50 mL). The removed left lung contains a system of fibrous cavities and polymorphic caseous foci in the section (►**Fig. 4**). In bacteriological research, MBTs were identified. There were no complications in the postoperative period.

Within a year of the operation, the patient received antituberculosis chemotherapy (levofloxacin 0.5; PASK 8.0; ethambutol 0.8; cycloserine 0.5; capreomycin 0.75).

During the control examination, 5 years after the operation, there were no exacerbations of tuberculosis, good health was noted along with shortness of breath with significant physical activity. On the scan of computer tomography (►**Fig. 5**), the hemithorax on the left is darkened, the mediastinal organs are significantly shifted to the left. In the upper lobe on the right are several small calcined foci.

At the present time, the patient is in a state of stable cessation of bacterial excretion, her ability to work is restored, and she studies at a university and works.

Fig. 4 The removed left lung on the section, there are the system of fibrous caverns and polymorphic caseous foci almost all over the lung.

Discussion

The need for surgical treatment in cavernous and fibrous-cavernous TB, especially in the presence of drug-resistant MBT and persistent bacterial excretion with the ineffectiveness of controlled conservative treatment, was noted by many authors.[7,10–16]

In a few recent world publications devoted to the surgery of pulmonary tuberculosis or pulmonary surgery in children, single operations for child and adolescent destructive pulmonary tuberculosis were mentioned without giving their separate results.[12–17]

In a series of cases with children aged 6 months to 14 years, Blyth et al[16] reported eight pneumonectomies performed in the period 1991 to 1997 (15). The vast majority of operations in this series were performed for bronchiectasis (38) and only eight for tuberculosis. When performing pneumonectomy in 59 children with various pulmonary pathologies, the authors noted intraoperative complications in 10.1% of cases, postoperative complications in 11.8%, but did not provide a separate analysis of complications in tuberculosis.[16]

Eren et al[17] reported four pneumonectomies performed in children from 3 to 16 years of age for tuberculosis over 15 years. The authors described these operations in a series of 17 pneumonectomies performed for various pathologies with the development of postoperative complications in

23.5% of cases and mortality in 11.7%, but also did not analyze the results in children with tuberculosis separately.[17]

Drebov[13] and co-authors shared their experience of surgical treatment of 13 children with primary tuberculosis. According to the authors, the most common operation was a lobectomy. Postoperative mortality and complications were not observed in this series of operations.

Singh et al[15] cite the experience of five cases of successful surgical treatment of tuberculosis empyema in the third stage of the process. All patients underwent pleurectomy with lung decortication.

We have not found in the literature a comparative study of the results of surgical treatment of cavernous and fibrous-cavernous TB in children.

According to our study, patients with fibrous-cavernous pulmonary tuberculosis had to undergo large-volume operations more often, and postoperative complications and relapses of tuberculosis were significantly more frequent. In group I, after 80 operations, postoperative complications occurred in two (2.5%) cases, in group II, after 160 operations, they occurred in eight (5.0%) cases. Also, relapses and exacerbations of tuberculosis were significantly more frequent in group II patients in the long-term period (relapses were not observed in group I) and in group II in three cases (3.4%) of 88 patients (the difference is significant $p \leq 0.05$).

Conclusion

In the treatment of cavernous and fibrous-cavernous pulmonary tuberculosis in children, the surgical method occupies an important place, especially in the presence of drug resistance MBT.

The data obtained by us suggest that operations in patients with cavernous TB performed after 10 to 12 months of treatment present a lower risk of complications and relapses of tuberculosis than operations in patients with fibrous cavernous TB performed after 22 or more months of treatment.

In the long-term period, in group II, tuberculosis relapses occurred in two (2.3%) cases of patients after surgery. These patients had XDR-TB, which confirms a higher risk of tuberculosis relapses in this category of patients. Later operations are performed against the background of significantly greater morphological changes in the lungs and pleura, more pronounced drug resistance, and more often end with the removal of large volumes of lung tissue. All this suggests that it is necessary to establish timely indications for surgical treatment of cavernous and fibrous-cavernous TB during the first year of treatment.

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Conflict of Interest
None declared.

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