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ORIGINAL PAPER

Lobar (croupous) pneumonia: old and new data

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Abstract

Background and aim Pneumonia remains one of the most frequent death causes worldwide. Among the etiological factors *S. pneumoniae*-causing lobar pneumonia plays a leading role. According to current textbook knowledge at least three sequential stages of lobar pneumonia are distinguished: congestion, red hepatization and gray hepatization. However, there are no detailed data supporting this stage concept. There are also controversial views on its etiology. In this study, the lung changes in lobar pneumonia were related to the cause and duration of the disease. In addition, the complications of the disease were evaluated. PCR studies verified the etiology of pneumonia.

Material and methods Lobar pneumonia was analyzed in 252 post mortem cases examined in a large hospital in Irkutsk. The pathology, etiology of pneumonia, course of disease and cause of death were recorded and correlated to its clinical course and duration. In the second part of the study, the results in 95 patients were analyzed in detail and related to PCR findings.

Results Most patients were adult men of low social status who showed signs of severe alcoholism. Lobar pneumonia was observed in 85% of the patients, while the remaining patients showed sublobar ("lobular", focal) lung involvement. Histologically, three patterns of inflammation were observed, which in most patients occurred concurrently in different parts of the involved lobe: "congestion", characterized by serous exudation with multiple cocci (41% of cases), "red hepatization" (41% of cases) and "gray hepatization" (100% of cases). The latter pattern was subdivided into three subgroups according to the ratio of fibrin—neutrophils and the presence of macrophages. The mean number of different histological patterns observed per patient was 3.8. There was no correlation between the inflammatory patterns and the duration of the disease. In 23% of the patients, the cause of death was of pulmonary origin, while the remaining patients died of extrapulmonary complications (i.e. acute heart failure 26%, acute vascular insufficiency 15% purulent meningitis 11–24.3%. In 29/95 patients (20 with lobar and 9 with focal pneumonia) pneumococcal etiology of pneumonia was established by PCR.

Conclusion Lobar pneumonia is a distinct clinico-pathological entity caused by *S. pneumoniae*, demonstrated by PCR testing and/or cytological examinations. Bacteriologic studies frequently give falsenegative results. Lobar pneumonia is characterized by three main histopathological patterns (congestion or microbeous edema, and red and gray hepatization) which usually occur side by side and not in chronological order. Early death is often related to heart failure and septic shock, while meningitis is a frequent complication later in the course.

Keywords Lobar pneumonia · *S. pneumoniae* · Inflammatory patterns · Clinico-pathological correlation · PCR

Introduction

Pneumonia still remains a very important cause of morbidity and mortality in the world. Covid-19 pandemia and related questions of mortality due to community-acquired pneumonia of undetermined etiology sharpens the problem.

Pneumonias are currently divided into "community" and "hospital acquired". While the "hospital acquired" pneumonias are mainly caused by such agents as Pseudomonas, Klebsiella, Staphylococcus and Candida, community

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acquired pneumonias are, commonly, due to infections with *Streptococcus pneumoniae* or pneumococcus. In the United States the number of pneumococcal pneumonia cases is estimated to be approximately 500,000 per year [1], and worldwide more than a million deaths are annually ascribed to this disease. This makes it to one of the leading infectious causes of mortality. Sir William Osler, therefore, called *Streptococcus pneumoniae* "the captain of the men of death" [1].

Morphologically pneumonias traditionally have been classified as lobar ("croupous") or lobular ("focal") pneumonia. The latter type is also known as bronchopneumonia. Lobar pneumonia is characterized by acute development and rapid involvement of an entire lobe by the inflammatory process. The main morphological change of the lung is called "hepatization", an alteration of the pulmonary tissue that is histologically characterized by a dense fibrinous-neutrophilic infiltration of the alveoli. In contrast to lobar pneumonia that may be fatal without antibiotic therapy, focal pneumonia shows a much slower development and usually a non-fatal course in adults. It is also usually noted that the fatal outcomes mainly occur in infants and elderly persons. These are the features of lobar and focal pneumonia that are still presented in the available pathology textbooks [2]. In the modern literature and pulmonology classifications the term "croupous" pneumonia disappeared.

The description and characterization of the morphological features of lobar pneumonia, in particular its macroscopy, go back to the work of Carl von Rokitansky [3]. On the basis of numerous postmortem examinations, he distinguished three stages of lobar pneumonia: "inflammatory congestion", "hepatization" and "suppurative infiltration". He also noted that the color of the lung cut surface in the stage of "hepatization" may be either gray or red. Rokitansky also noted that various stages may often be present simultaneously and that death can occur after different time periods. He did not discuss any theories concerning the development of the disease and a consecutive appearance of the stages he had described. However, in later Pathology textbooks written by German, American, Russian and other authors, the observations of Carl von Rokitansky were twisted and interpreted in a different way. It was stated that lobar ("croupous") pneumonia involves the whole lobe in one step and the red and gray hepatization followed each other in a chronological order. Despite all our efforts, we were unable to find any original articles, that provided evidence in support of these statements.

Textbooks that are currently in wide use also state that lobar pneumonia is infrequent and can be caused not only by *S. pneumoniae*, but also by Klebsiella, Staphylococci, Streptococci, Haemophilus, Pseudomonas and Proteus [2]. Some textbooks also contain speculative statements about the role of immediate hypersensitivity in the pathogenesis and development of lobar pneumonia.

In Russia lobar pneumonia has been intensively studied in Leningrad between 1930 and 1960 predominantly by Zinserling and his pupils [4–6]. Unfortunately, for historical reasons the results of their research remain unknown outside Russia. These studies, which were based on numerous postmortem examinations with detailed bacteriological and histological investigations postulated that lobar (croupous) pneumonia is caused only by pneumococci. Klebsiella strains may produce a variant of lobar pneumonia, which, however, displays specific findings allowing to classify it as a separate disease, so-called Fridlander pneumonia.

Although there are numerous studies on the molecular biology of the microbiological agents causing pneumonia, defense mechanisms of the host [1, 7–15] and the treatment of the disease, studies on the pathology, cause, course and epidemiology of lobar pneumonia are lacking since the middle of the 1970s. The objectives of this work were therefore to re-study the lung changes in lobar pneumonia in relation to the cause and duration of the disease in a large number of autopsies.

Material and methods

152 autopsies were performed in the department of pathology of the city hospital of Irkutsk, Russia in 1999–2006. The study included all cases with gross lobar pneumonia. Clinically pneumonia was recognized in 118 cases (77.6%). In all autopsies, multiple tissue samples for microscopic examination were obtained from all organs, including 3–7 samples from different lobes of the lungs. The tissue blocks were formalin fixed and embedded in paraffin. The sections were stained with hematoxylin–eosin and also with van-Gieson, Gram and azure-eosin. Lung tissue and, if necessary, also tissues from other organs were investigated bacteriologically with the use of standard solid and liquid media. Microscopical investigations for detecting and identifying bacteria were also performed in smears from the lung cut surfaces and in paraffin sections, stained with methylene blue. The smears from the lung cut surfaces were evaluated independently by a bacteriologist and a pathologist, the paraffin sections were only assessed by a pathologist. All accessible data from the medical records of the patients were carefully reviewed and analyzed.

In the second part of the investigation provided in 2017–2020 we analyzed 95 autopsy cases (age range 29–89 years) that showed different probably inflammatory lung lesions, with the above described morphological and bacteriological methods and additional molecular-biological study.

Multiplex PCR for pneumococcus. For extraction of nucleic acids from clinical material have been using a set of reagents "AmpliPrep DNA-Sorb-b". Detection of

capsule forms and molecular typing of pneumococcus was performed using primers for detection of cpsA locus. The primers were selected from the GenBank library and synthesized at NPF Sintol LLC. At the first stage, CPSA-f (gca-gta-cag-cag-ttt-gtt-gga-ctg-acc) and cpsA-r (gaa-tat-ttt-cat-tat-cag-tcc-cag-tc) primers were used for amplification, reacting with the cpsA locus of all serotypes. With a positive result, the resulting amplicons were subjected to molecular genetic typing with primers to 39 pneumococcal serotypes in a series of multiplex PCR of ten consecutive reactions with the following sets of primers: (1) 23F, 6A/B/C, 19A; (2) 14, 19F, 15A/F, 23 A; (3) 3,9V/A, 18A/B/C/F, 35A/C/42; (4) 1,4,9 L/N, 10A; (5) 5, 7F/a/, 11 a/d, 13; (6) 2, 12F/a/44/46, 17F, 20; (7) 8, 15B/C, 22A/f, 33 f/a/37; (8) 16F, 21, 35B, 38/25F/A; (9) 7C/b/40, 24A/B/F, 31, 34; (10) 10F/C/33C, 23B, 35F/47f, 39f. Amplification of fragments of the genome *S. pneumoniae* was performed in a reaction mixture containing a ready-made mixture for amplification of 5 * ScreenMix-HS and 10 pmol of each primer in a volume of 25 µl. The reaction was performed in a Tertsik amplifier ("DNA Technology") according to the universal amplification profile adapted for the maximum output of the PCR product of all the studied genome loci: 94 °C–3 min, 35 cycles: 94 °C–15 s, 56 °C–10 s, 72 °C–15 s, 72 °C–10 min, 22 °C–storage. Identification of PCR products was performed in 2% agarose gel with the addition of GelRed.

Results

Among the 152 patients from Irkutsk there were 117 (77%) men and 35 (33%) women. One-hundred-eight (71%) patients were younger than 60 and in the age range between 40 to 59 years. The majority of patients (72.4%) had a low social status; in 11.8% the social status remained unknown. In 45% of the cases, alcoholism was mentioned in the medical records and these data corresponded well with the presence of liver steatosis, which was found in 78% of the patients. The majority of patients developed their disease in spring and summer (62%).

Eighty-four patients (55.3%) died during the first day after admission to the hospital, 36 (23.7%) during the next 2 days. A correct clinical diagnosis was made in 22.4% of patients. Among the incorrect premortem diagnoses the most frequent were myocardial infarction, septicemia, shock of unclear origin and lung tuberculosis.

The most important clinical symptoms were acute onset (in 63.8%), high fewer (documented in 62.5%) and the manifestations of septic shock (in 87.5% cases). Leukocytosis (more than 7×10^9) was recorded in 67.8%; 11.2% had leucopenia (less than 4×10^9).

In 110 patients information on the duration of the disease from the first clinical manifestation till death was available. In 93.6% of the cases, the duration of the disease was less than 2 weeks (mean 7.1 ± 0.39 days). In 21.8% of cases, the illness lasted less than 3 days.

In all patients, typical lancet-shaped diplococci were found in the smears from the cut surface of the lungs. In slides from paraffin-embedded and formalin fixed tissue blocks stained with azure-eosin the typical diplococci were seen in 86% of cases, in 26% the diplococci were found in conjunction with other bacteria and also with fungi. The diplococci were mainly observed in the intraalveolar edematous fluid but were also seen in alveoli containing granulocytes and fibrin. A positive post mortem culture of *S. pneumoniae* was obtained in 24% of all patients (Table 1).

Macroscopical investigation revealed pneumonia with lobar involvement in 85% of the cases (Fig. 1A). Pneumonia affected only one lung in 61% (77.4% of the right lung), and both lungs in 39%. It was restricted to one lobe in 16.4% of cases, to two in 30.3%, to three in 30.3%, and to four in 9.2%. All lobes were affected in 13.8%. In 15% (mostly in patients over 70 years) the pneumonic infiltrates involved only approximately two thirds of the lobe (Fig. 1B). The color of infiltration differed from gray to red and was identical to classical descriptions.

Microscopic investigation revealed inflammatory changes that could be assigned to 6 diagnostic qualifiers: "congestion (C)" ("engorgement") (Fig. 2A), "red hepatization" (RH) (Fig. 2B), "gray hepatization" with neutrophils and fibrin in equal quantity (GH) (Fig. 2C), "gray hepatization" with predominance of leucocytes (GHL) (Fig. 2D), "gray hepatization" with predominance of fibrin (GHF), "gray hepatization" with predominance of macrophages embedded in fibrin (GHM). In Table 2, the predominant inflammatory variant that was identified in the pneumonia of each of the 110 patients whose course of the disease was known, is correlated to the time period that had elapsed between the onset of clinical symptoms and death. In addition to the predominant inflammatory change, almost all patients showed other

Table 1 Results of bacteriological postmortem examination of the lungs (total number of the investigations 129)

Result	Number of cases	Percentage	CI 95%
Streptococcus pneumoniae	31[a]	24.0%	16.7–31.3
Staphylococcus aureus	18	14.0%	8.0–20.0
Escherichia coli	18	14.0%	8.0–20.0
Different gram negative rods	40	31.0%	23.0–39.0
No growth	22	17.0%	10.5–23.5
In total	129	100	

[a]Including 7 cases where *S. pneumoniae* combined with other microbiota

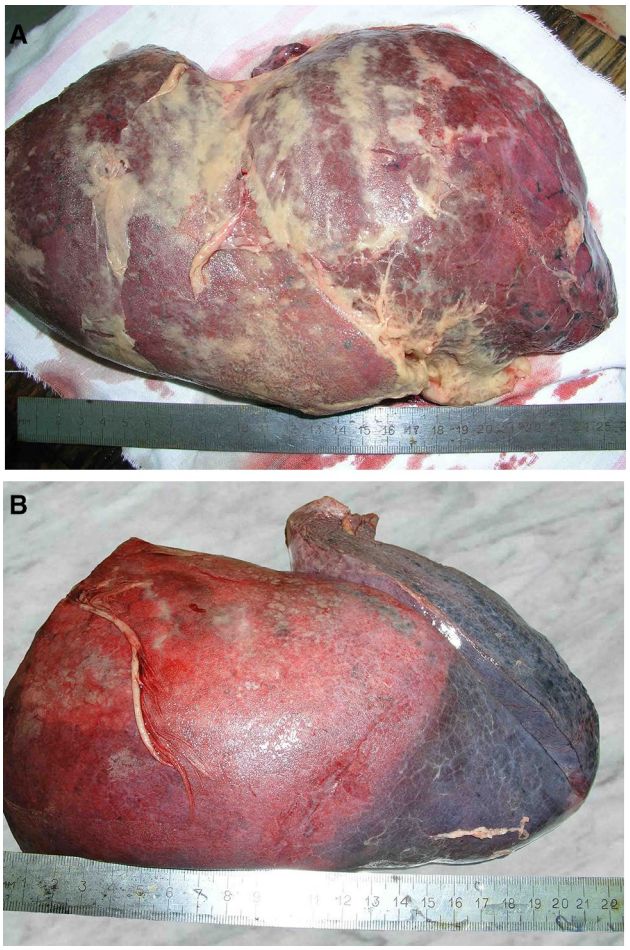

Fig. 1 Typical macroscopical changes in pneumonia. **A** "Lobar hepatization" with fibrinous pleuritis. **B** "Sublobar" pneumonia

types of inflammatory alterations in the affected lobes. For the entire group of 110 patients 417 different compositions of inflammatory changes were recorded, with a mean of 3.8 variants per patient.

Table 3 lists the pulmonary and extrapulmonary complications such as pleuritis, carnification, microabscesses, phlebitis and gangrene. Among the extrapulmonary complications, the most frequent were purulent meningitis, which also involved brain tissue and the ventricles in more than half of the cases. 46% of the patients showed myocardial changes. In 12.5% they were regarded as "disturbances of blood flow", in 25.5% as acute heart failure showing edema, hemorrhage and fiber fragmentation, and in 8% as myocardial infarction.

Twenty-one percent of the patients showed histological signs of acute renal failure, with anemia of the cortex, dilatation of the tubuli and swelling and necrosis of tubular epithelium. In spite of relatively early autopsies (1–2 day after death) it is impossible to exclude autolytic changes as well. Clinically these patients had oliguria and azotemia.

Lobar pneumonia was regarded as fatal disease in all patients because no other competing life-threatening disease detected. There were no cases with malignancies and chronic obstructive pulmonary diseases and atherosclerosis was only moderately expressed. Table 4 shows the immediate causes of death.

Out of 95 tests using the PCR technique, pneumococcal etiology was established in (30.5%) 29 cases (Fig. 3) (Table 5). It was possible to type the pathogen in 15 cases: 6 A/B/C-5, 3-4, 4-2, 23F-2 and 17F, 8, 19F were detected only once. 20 cases were typical lobar and 9—focal pneumonia.

20 cases of lobar lesions corresponded to the above described. During bacterioscopy (performed in 12 observations) typical lanceolate diplococci were constantly detected. The microbiological examination was performed in 13 observations: *Streptococcus pneumoniae* 1 case; Klebsiella 8 cases (in combination with Staphylococci and Streptococci 4, in combination with Acinetobacter-1); *E. coli*, *S. epidermidis*, *Candida glabrata-2*; *Candida albicans*, Pseudomonas-1. We consider that these pathogens did not play the etiological role, probably being contaminants.

Focal pneumococcal pneumonia was diagnosed in nine cases. The pneumonic focus occupied from 1/4 to 1/3 of the lobe (5–7 cm), and was located more often closer to the central parts. It had a gray color, a slightly grainy surface of the incision, a typical pleural lesion was not observed in seven cases (without subpleural location), in two observations, the pleura in a limited area was dull, cloudy exudate flowed from the surface of the incision. The focus of infiltration was uniform. On the periphery in four observations there were additional small foci up to 1.5–2.0 cm, differing in morphological picture, azure staining revealed different flora (cocci, rods). During bacterioscopy (performed in 8 observations) typical lanceolate diplococci were found, in the mentioned four observations with mixed etiology in addition to typical pneumococci, different flora was found. Microbiological study in this group was performed in six cases, Klebsiella, Staphylococci, Edwardsiella, *Escherichia coli* were more frequently sown. In none of these observations pneumococci were detected. In the research group, no fungal pneumonias were observed.

In five cases (3 lobar and 2 focal) as a complication was detected purulent meningitis.

Discussion

Our study revealed that lobar ("croupous") pneumonia is still a frequently fatal disease. In several cases the typical symptoms of croupous pneumonia were associated with sublobar (focal) lesions. In addition, we found that the so-called stages of lobar pneumonia are usually occurring side by side and do not develop in a strictly sequential order in

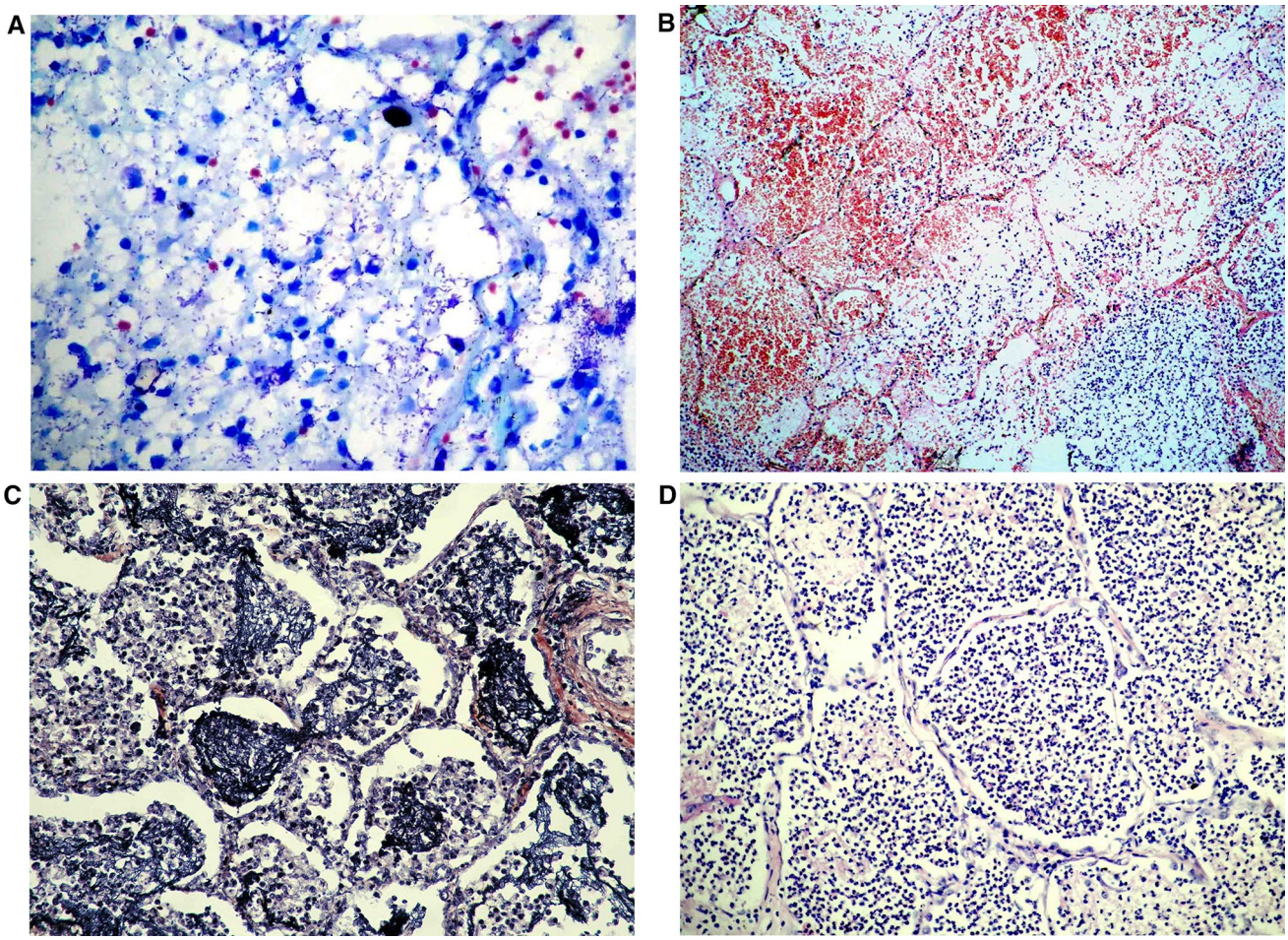

Fig. 2 Different histologic changes in lobar (croupous) pneumonia. **A** Congestion (microbeous edema). Numerous diplococci in the serous alveolar exudate. Stained by azur-eosin. ×1000. **B** "Red hepatization" Blood vessel congestion. In the lumen of alveoli erythrocytes, fibrin, several neutrophils. Stained by h-e ×100. **C** "Gray hepatization" with equal quantity of neutrophils and fibrin in alveolar exudate. Fibrin in the pore of Kohn. Staining by aniline violet according to Gram. ×200. **D** "Gray hepatization" with the predominance of neutrophils in alveolar exudate. Stained by h-e, ×200

Table 2 Correlation between the histological type of lung lesion and the duration of the disease in lobar pneumonia ($n=159$)

Type of the changes	Time after beginning of the disease (in days)									
	1	2	3	4–5	6–7	8–9	10–11	12–14	> 14	In total
E	1	4	9	12	16	6	2	8	3	61
RH	1	4	11	8	20	8	–	9	2	63
GH	1	5	13	21	22	7	3	10	4	86
GHL	1	4	11	18	20	6	3	9	5	77
GHF	–	4	9	18	16	5	2	8	3	65
GHM	–	3	12	17	18	4	1	7	3	65
In total	4	24	65	94	112	36	11	51	20	417

E engorgement (microbeous edema), *RH* red hepatization, *GH* gray hepatization with equal quantity of neutrophils and fibrin, *GHL* gray hepatization with predominance of leucocytes, *GHF* gray hepatization with predominance of fibrin, *GHM* gray hepatization with predominance of fibrin and macrophages

Table 3 Pulmonary and extrapulmonary complications ($n = 152$)

N	Type of complication	Number of cases	Percentage	CI 95%
1	Exudative pleuritis	29	19.1	12.9–25.3
2	Carnification	12	7.9	3.6–12.2
3	Gangrene	1	0.65	0–1.8
4	Formation of microabscesses	47	30.9	13.6–38.2
5	Vascular lesions	32	21.1	14.6–27.6
6	Acute coronary insufficiency	27	17.8	11.1–23.9
7	Early myocardial infarction	12	7.9	3.6–12.2
8	Hemorrhages in the adrenals	7	4.6	1.3–7.9
9	Purulent meningitis and meningoencephalitis	17	11.2	6.2–16.2
10	Purulent-fibrinous pericarditis	5	3.3	0.5–6.1
11	Acute renal failure	32	21.1	14.6–27.6
12	Liver steatosis[a]	118	77.6	71.0–84.2

[a]Regarded as manifestation of chronic alcohol abuse

Table 4 Immediate death causes

N	Leading clinical syndrome[a]	Number of cases	Percentage	CI 95%
1	Heart failure	39	25.7	18.8–32.6
2	Respiratory failure	35	23.0	16.3–29.7
3	Brain coma	17	11.2	6.2–16.2
4	Adrenal failure	7	4.6	1.3–7.9
5	Acute circulatory failure[b]	23	15.1	9.4–20.8
6	Combined respiratory and circulatory failure	31	20.4	14.0–26.8
	In total	152	100	

[a]In 32 cases, additionally, clinically and morphologically were noted the signs of renal insufficiency

[b]The signs of acute vascular insufficiency (critical decrease of arterial pressure) has been noted in 133 cases (87.5%)

the affected lobe. Finally, our data confirm the frequency and clinical importance of extrapulmonary complications such as purulent meningitis and heart and kidney failure, and also clearly indicate that the main risk group are men between 40–50 years of age with low social status and alcohol abuse. Infants and elderly persons who are thought to be mainly lethally affected by pneumonia [9, 14] did not prevail in our study, we consider it to be a real phenomenon.

Lobar pneumonia is known to be caused by *S. pneumoniae*, however, other causes have also been discussed [1, 7]. Our data suggest that all patients were infected with *S. pneumonia*. Although the frequency of positive pneumococcal cultures only ranged between 24 and 34%, comparable with the data of other investigators [6], the results of our cytologic and bacterioscopic studies in smears and tissue sections, based on the detection of typical lancet-shaped diplococci in the involved lung tissue, strongly indicated that *S. pneumoniae* is the etiological factor in our lobar pneumonia cohort. The negative results of *S. pneumoniae* cultures may be explained by the effect of the antibiotic treatment on the growth of the bacteria, even if the treatment was clinically ineffective. Another reason is probably the property of pneumococcus to easily undergo autolysis [1] or due to temperature-sensitive nature of the pathogen. The conclusion that *S. pneumoniae* is the main etiologic factor was strongly supported by the results of the PCR studies. Our bacteriological studies also revealed other bacteria, but these were not regarded as causes of lobar pneumonia, because they were not constantly found and the majority of these agents are not known to possess the necessary properties to cause pneumonia. Therefore, we regard these bacteria as contamination. The only exception seems to be *Staphylococcus aureus*. Correlations of some of our histological and bacteriological findings let us assume (data not shown) that superinfection with this bacterium might play a role in the formation of microabscesses and vasculitis.

The pneumococci that were histologically identified as lancet shape diplococci were mainly detected in alveoli filled with serous exudate, where many of them were found to be dividing. Zinserling [5, 6] described this scenario as the

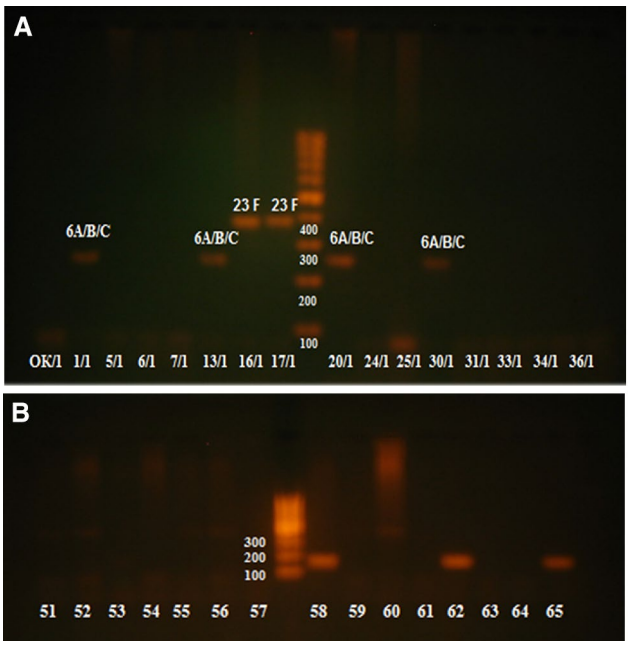

Fig. 3 Results of PCR. **A** Electrophoregram of PCR products using a primer on cpsA (locus of bacterial DNA involved in the biosynthesis of capsular polysaccharide). The PCR product is detected as a band corresponding to a size of 160 bp. Positive samples: 58, 62, 65. **B** Results of multiplex PCR typing of *S. pneumoniae*. Figure shows the results of multiplex PCR with the indication of the numbers of samples and sets (nominator—sample number, denominator—set number). Set 1: detectable serotypes—6 A/B/C, 19A, 23F

Table 5 Detection of pneumococcus in the second study group ($n = 95$)

Final pathological diagnosis	N of cases	Results of PCR	Results of bacteriological study [c]	Results of histobacterioscopy [c]
Lobar pneumonia	20	20/20	1/13	12/12
Focal pneumonia [a]	75[b]	9/75	0/6	8[d]/8

- [a]Was considered as complication of tumors, liver cirrhosis, cardiomyopathy et al.
- [b] In 2 cases with clinics of croupous pneumonia
- [c] Results related to focal pneumonia are presented only for cases with positive PCR results
- [d] in 4 cases with admixture of other types of microorganisms

"microbeous edema", thereby criticizing the usually used term engorgement. He also pointed out that the diplococcus-containing exudate easily spreads through the pores of Kohn. This spread from one alveolus to the other may be one explanation for the rapid involvement of the entire lobe. Another reason for the spreading of the pneumococci seems to be a lack of neutrophils. Why there is a blockade of the neutrophils` chemotaxis in the first hours after infection, is not known. However, it may be speculated that alcohol intoxication and overcooling (as for instance after bathing in the cold water of the Baikal lake near Irkutsk, where the water temperature remains as 10^0C even on hot summer days) might be factors that propagate the unhindered spread of pneumococci in lung tissue. Another factor may be an individual susceptibility to pneumococcal infections based upon gene polymorphism [14], production of IL-1 [11] and galectin3 [7].

In the course of the *S. pneumoniae* infection the lungs show "hepatization", characterized by infiltrates composed of neutrophils, fibrin and erythrocytes. The presence of these inflammatory components can be explained by the production of peptidoglycans, pneumolysin, and hydrogen peroxidase by pneumococci [7, 12]. PcpA (pneumococcal choline-binding protein A) may also play a certain role [10]. Recent studies also demonstrated the ability of the pathogen to induce apoptosis, necroptosis and pyroptosis [15].

Hepatization has been divided into two stages that follow each other and are called "red" and "gray" hepatization [1, 2]. Our study clearly revealed that the inflammatory infiltrates characterizing "read" and "gray" hepatization at the histological level occur next to each other and, in addition, that in "gray" hepatization the composition of the infiltrate may be very variable. Thus, the inflammatory process in lobar pneumonia does not follow a sequential course marked by histologically defined stages but is characterized by the juxtaposition of various inflammatory patterns and it is possible to speak about overlapping pathological changes in lobar pneumonia. The mechanisms of the development of different patterns of inflammatory changes remain unclear. It is also noteworthy that "gray" hepatization occurred much more frequently than "red". The phenomenon, that there may be different ratios between neutrophils and fibrin has never been described before, and it is worth to note that predominance of fibrin over neutrophils was typically associated with leucopenia.

We found acute heart failure and shock to be the most important complications of lobar pneumonia. These complications were often rapidly fatal and led to an improper clinical diagnosis. Among the patients who survived for some days there were many with severe purulent meningitis, and the frequency of this complication was higher than that reported in earlier investigations (11–24.3% versus 6%) [5].

In summary, lobar pneumonia was found to be a pulmonary disease associated with *S. pneumoniae* infection. The disease typically affects an anatomical unit of the lung, usually a lobe, in which variably composed inflammatory infiltrates develop. We were unable to confirm the postulate that "red" and "gray" hepatization are sequential changes in the course of lobar pneumonia. The disease usually affects men of low social status and alcohol abuse, and is still a frequently fatal disorder because of its severe and rapid complications. The role of genotypes of S. *pneumoniae* and individual properties of the strains in the development of different histological changes in pneumonia (variants of "gray" and "red" hepatization) and several other aspects of pathogenesis have still to be evaluated.

Exact knowledge of the etiology and course of lethal pneumonias is of particular value in the current COVID-19 pandemic, but any information on the cause of pneumonia can be only considered reliable if an autopsy with detailed histological investigation flanked by bacteriological and PCR tests has been performed [16, 17].

Author contributions All authors made a significant contribution: VS and AM collected the specimen, LS provided PCR studies, VS, VZ and AM did histopathological studies, VZ, VS and AB elaborated the concept of the study, VZ and VS wrote the draft, VZ and AB critically revised the text.

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Declarations

Conflict of interest There is no conflict of interest.

Ethical approval The work was done on autopsy material with the concordance with Russian regulations of such studies and ethical principles.

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