NON SMALL CELL LUNG CANCER: IS THERE A RELATIONSHIP BETWEEN BACTERIAL COLONIZATION OF THE TUMOUR PARENCHYMA AND POSTOPERATIVE INFECTIOUS COMPLICATIONS?

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The aim of the study was to investigate the influence of bacterial colonisation of a neoplastic lung tumour on the frequency of infectious complications after radical surgical treatment of the malignancy.

Material and methods. 49 patients operated on for non-small cell lung cancer (NSCLC) from 23rd January to 2nd November 2006 were included into the study. The analyzed group consisted of 39 men and 10 women, they were from 45 to 79 years old. Material for microbiological tests was collected in an operating theatre under sterile conditions directly after the resection of a tumour. A sample (5x5x5 mm) of the tumour was cultured for facultative anaerobes, obligate anaerobes and fungi. After the homogenisation of tumour tissues quantitative culture was also performed.

Results. Potentially pathogenic microbes were cultured from tumours in 14 patients (28.6%). The most frequent bacterium was Propionibacterium acnes. It was found in six out of 49 tumours (12.2%). In 13 cases (26.6%) postoperative infectious complications were observed. They were as follows: infection of the lower airways – 8 cases (16.3%), surgical wound infection – 3 cases (6.1%), pleurisy – 1 case (2%) and pleural empyema – 1 case (2%). In 12 patients (24.5%) pathogenic microbes were isolated from biological material obtained from other sources than a tumour. In remaining 36 patients (73.5%) no infectious postoperative complications were observed. In 13 patients in whom bacteria were cultured from a tumour there were no postoperative infectious complications. Only in one patient the same bacterium (Staphylococcus aureus) was identified in a tumour and 35 days later in pleural effusion where four other pathogenic bacteria were isolated, too. In 12 patients whose postoperative course was complicated by infections had no pathogenic microbes cultured from a resected tumour.

Statistical analysis showed no significant relations between the presence of pathogenic microbes within a lung malignant tumour and postoperative infectious complications in patients.

Conclusions. The most frequent microbe cultured from non-small cell lung carcinoma is Propionibacterium acnes. There is no relation between the colonisation of a malignant tumour by bacteria and postoperative complications in patients treated surgically for NSCLC.

Key words: lung carcinoma, postoperative complications, postoperative pneumonia

As more modern and effective diagnostic tools for early diagnosis of lung cancer become available, more patients can qualify for surgical treatment of this disease (1). Surgery is the best therapeutic method for patients with stage I or II non small cell lung cancer (NSCLC) (2, 3, 4). The outcome of such a treatment depends on the precise determination of the range of anatomical resection, proper preoperative qualification, and good postoperative care (5). Surgical treatment of NSCLC is fraught with numerous complications, including infectious ones. Some of these complications are directly caused by the treatment; others are the effect of pre-existing conditions, or the presence of increased risk factors for infections.
An important role is attributed to the colonization of the airways by pathogenic microorganisms that can appear in the natural course of lung cancer (6). Central cavitation is often observed in both primary and metastatic lung tumours. The most common reason for the cavitation is tumour necrosis, but cavitation can also be a result of the infection of a central necrotic part of a tumour (7). It seems likely that some postoperative infections may also be caused by pathogenic microorganisms that are present in the tumour (8).

The aim of this study was to analyze the influence of the presence of bacterial colonization of lung cancer parenchyma on the frequency of infectious complications after radical surgical treatment of the tumour.

MATERIAL AND METHODS

Forty-nine patients undergoing operations for NSCLC from 23rd January to 2nd November 2006 were included in the study. The analyzed group consisted of 39 men (79.6%) and 10 women (20.4%) with ages between 45 and 79 years (mean, 61.8 years). Squamous lung cancer was found in 36 cases (73.5%) and adenocarcinoma in 13 cases (26.5%). Twenty-seven tumours (55.1%) were localized in the right lung and 22 (44.9%) in the left lung. The tumour was found in the upper lobe in 23 cases (46.9%), in the lower lobe in 20 cases (40.8%), in the middle lobe in two cases (4.1%), and within the main bronchus in four cases (8.2%). Lobectomy was performed in 30 patients (61.3%), bilobectomy in one case (2%), pneumonectomy in 13 patients (26.5%), and wedge resection in five cases (10.2%). The postoperative staging of the patients was as follows: IA – 13 cases (26.5%), IB – 22 (44.9%), IIB – 4 (8.2%), IIIA – 5 (10.2%), IIIB – 1 (2%), and IV – 2 (4.1% – patients after earlier resection of brain metastases). T-stage in the analyzed group was as follows: T1 – 14 cases (28.6%), T2 – 32 (65.3%), T3 – 2 (4.1%), and T4 – 1 (2%). Eight patients underwent neoadjuvant chemotherapy before surgery.

In all patients, perioperative antibiotic prophylaxis with four doses of a second generation cephalosporin was given intravenously. The first dose was administered approximately 30 minutes before surgery and next three doses after every six hours. In each of our patients, respiratory rehabilitation was employed before and after surgical treatment.

Material for microbiological examination was collected in the operating room according to the rules of sterility directly after the resection of a tumour, lobe, or lung. A specimen of 0.5x0.5x0.5 cm obtained from the central part of the tumour was placed into a sterile screw-cap cup and immediately (within 10-15 min.) sent to the Department of Microbiology. The specimen was cut into two parts, their internal surfaces were exposed to the media, and a touch preparation for Gram staining was prepared. A fragment of the material was also added to a liquid culture media. A quantitative analysis after the homogenization of the material was also performed. The material was cultured on commercial media for facultative anaerobes, anaerobes, and fungi according to routine procedures followed in microbiological laboratories. The identification of microorganisms was done by automatic system VITEK 60 (bioMérieux) or by manual API (bioMérieux) tests performed according to the manufacturer’s instructions.

Statistical analysis was carried out with STATISTICA 6.0 software (StatSoft, Inc. 2001). The correlations between clinical and pathological data and complications were evaluated by Spearman’s rank correlation coefficient and general regression model; p>0.05 was considered to be statistically significant.

RESULTS

Pathological examination of the tumour determined its histological type, the extension of necrosis and cavitation within the tumour, and inflammatory lesions and atelectasis in the lung parenchyma around the tumour. Necrosis was found in 14 tumours, destruction within the carcinoma in three cases, and inflammatory lesions in two tumours. Inflammation within the lung parenchyma was observed in seven cases, atelectasis was found in 17 cases, and both pathologies were present in nine cases. Lung abscess was diagnosed in one patient.

Potentially pathogenic microorganisms were found in tumours of 14 patients (28.6%). The list of positive cultures is presented in tab. 1. The most common microorganism was Propionibacterium acnes. It was isolated in six out of 49 (12.2%) tumours.

Thirteen patients (26.6%) were diagnosed with postoperative infections of the following sources: lower respiratory tract infections –
eight cases (16.3%), wound infections - three cases (6.1%), pleuritis - one case (2%), and pleural empyema - one case (2%). In 12 patients (24.5%), pathogenetic microorganisms were isolated from material other than the tumour. Infections caused by identified pathogens were treated with antibiotics selected on the basis of antibiogram. In the remaining 36 patients (73.5%), no infections were observed. In 13 patients whose tumours were positive for bacteria, none developed postoperative infection. In only one case were strains of Staphylococcus aureus isolated from a tumour and from a pleural effusion 35 days later. Four other strains of pathogenic bacteria were also cultured from the effusion. It cannot be claimed univocally that the same bacterial strains were isolated in the analyzed biological materials because no genetic analysis was conducted. In the 12 patients in whom postoperative infections were observed, no pathogenic microorganisms were isolated from the tumours.

Statistical analysis showed no significant correlations between the presence of pathogenic microorganisms in lung tumours and the frequency of postoperative infections.

DISCUSSION

The development of postoperative infections in patients undergoing surgery for lung cancer depends on certain risk factors, which include an impaired immunological system, damage to the lung caused by surgical resection, thoracic tubes and catheters responsible for ascending infections, impaired expectoration, shallow respiratory movements, and disorders of ventilation caused by postoperative pain (9). Preoperative risk factors for infections include poor nutritional status, obesity, and chronic diseases such as chronic obstructive pulmonary disease, diabetes mellitus, chronic bronchitis, and smoking (1, 10).

Patients undergoing pulmonary resection for lung cancer have a high risk of developing respiratory infections that ranges from 2% to 20%. The mortality rate in these patients is 22-67%, especially if postoperative pneumonia develops (3, 6), and infection is the most common cause of death (1). Postoperative pneumonia makes the prognosis in cancer patients less favourable (5). Severe and life-threatening postoperative infections extend the hospital stay and increase therapy costs (9). Many authors report a significant decrease in median survival in patients with lung cancer and postoperative pulmonary infections. Effective treatment for infection in these patients can potentially improve their survival (11). In our study, respiratory infections were diagnosed in eight patients (16.3%) and infections of another localization in four cases (8.2%). No patient had postoperative pneumonia. We had no postoperative deaths in our group. Only in one case was a severe postoperative complication observed - pleural empyema after right pneumonectomy. This was the only case in which strains of Staphylococcus aureus were isolated from a tumour and then from pleural pus. Other pathogenic microorganisms were also cultured from the pus (Acinetobacter baumannii, Streptococcus spp., Candida glabrata) as a result of the hospital-acquired infection.

Infections are a basic part of the natural course of lung cancer. There have been only infrequent reports demonstrating clinical and microbiological documentation of infections in this group of patients (11, 12). There are many different factors that predispose patients with lung cancer to infections, including depression of the immunological system, neutropenia, and disturbances of endogenous microflora. Multidirectional treatment of these patients may promote the development of opportunistic infections. Lung cancer is often complicated by respiratory infections, which are documented in 9.5-84% of cases. The differential diagnosis is usually difficult because signs and symptoms are atypical and X-ray imaging shows lesions such as pulmonary infiltration, atelectasis, or pleural effusion that are hard to differentiate between. Streptococcus pneumoniae is considered to be the main pathogen causing pulmonary infections. On the other hand, Gram-negative bacteria such as Haemophilus influen-
zae, Klebsiella pneumoniae, Enterobacter cloacae, and Pseudomonas aeruginosa were isolated in more than 68% of cases (11).

Other authors estimate the frequency of infections to be 53-70%. These authors are of the opinion that the infections are caused in equal proportions by Gram-negative (Haemophilus and other Enterobacteriaceae and Pseudomonas aeruginosa) and Gram-positive bacteria (Staphylococcus, Streptococcus pneumoniae, and other Streptococcus) (12). Of the eight patients in whom respiratory infections were observed in our study, cultures were positive in only one case, and several pathogens were isolated, including Haemophilus influenzae, Moraxella catharrhalis, Klebsiella pneumoniae, Candida albicans. The infection was mild and cured by guided antibiotic therapy.

Pre-existing colonization of the airways by pathogenic microorganisms is highlighted as an important risk factor for the development of postoperative respiratory infections after lung resections for lung cancer (6). The source of pathogens responsible for the complications is not clearly defined. A significant relationship was found between the presence of Haemophilus influenzae in the preoperative culture of sputum, pharyngeal swabs, and the colonization of the trachea at the time of intubation. According to Sok and colleagues, pathogenic bacteria cultured from bronchoalveolar lavage obtained from resected lung and intraoperative bronchial aspirations were a significant predictor of postoperative chest infections (9). Ioanas and colleagues report that the colonization of the respiratory tract by potentially pathogenic microorganisms is found in approximately 41% of patients with operable lung cancer. Risk factors of such colonization were found to be central localization of the tumour and high body mass index (BMI) (1).

In our study, we isolated pathogenic bacteria in 13 (26.5%) out of 49 resected lung tumours. Zając-Lenczewska found anaerobic bacteria in 46 (58.2%) out of 79 resected specimens of lung cancer. In this study, however, not only the tumour, but also the pulmonary parenchyma surrounding it was subjected to microbiological examination. Overall, authors found no significant relations between the isolation of microorganisms from tumours and the frequency of postoperative infectious complications, a similar finding to our results (13). Liao and colleagues examined material obtained by aspiration from a cavity in the central part of malignant tumours. In seven out of 22 (31.8%) cases, cultures were positive and nine microorganisms were isolated in total. Only one of them was a Gram-positive anaerobic bacillus. Klebsiella pneumoniae was a dominating pathogen. Administration of guided antibiotic therapy caused patients to become afebrile and improvement in their general state (7).

The most common microorganism isolated from tumours in our study was the anaerobic Gram-positive rod-shaped bacterium Propionibacterium acnes, which was cultured from six out of 49 tumours (12.2%). Similar results were observed in the study by Zając-Lenczewska, in which Propionibacterium was isolated in 19 out of 79 (23.0%) tumours and was also the most common microorganism found (13).

CONCLUSIONS

1. The most common microorganism isolated from NSCLC is Propionibacterium acnes.
2. There is no significant correlation between the bacterial colonization of NSCLC and infectious complications after its surgical treatment.

REFERENCES


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