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Malignant endobronchial lesions other than lung cancer

Anna Brzecka, Bożena Weryńska, Tomasz Dyła

Primary or secondary malignancies other than lung cancer may develop endobronchially. Both the clinical picture and the results of bronchoscopic examination may imitate primary lung cancer. Primary endobronchial malignancies may include extremely rare forms of Hodgkin's lymphoma, non-Hodgkin's lymphoma, plasmocytoma, chronic lymphocytic leukemia, as well as Kaposi's sarcoma (usually in immunosuppressed patients) and melanoma. Secondary (metastatic) endobronchial lesions usually develop lately in the course of neoplastic disease and constitute about 1-2% of tumors developing in the bronchial lumen. The most common endobronchial metastatic masses arise from such primary extrathoracic neoplasms, as colon, rectal, breast, uterine, renal, head-neck carcinomas, melanoma, and osteosarcoma.

Wewnątrzoskrzelowe zmiany nowotworowe inne niż rak płuca

Do wewnątrzoskrzelowych zmian nowotworowych, imitujących pierwotnego raka płuca, należą niezwykle rzadkie postacie nieziarniczego i ziarniczego chłoniaka, szpiczaka lub przewlekłej białaczki limfatycznej, a także mięsak Kaposi'ego (rozwijający się głównie u osób w stanie immunosupresji) i czerniak.
Przerzuty wewnątrzoskrzelowe guzów innych niż rak płuca powstają zwykle późno w przebiegu choroby rozrostowej i stanowią około 1-2% nowotworów stwierdzanych w świetle oskrzeli. Przerzuty wewnątrzoskrzelowe wywodzą się najczęściej z pierwotnego raka jelita grubego, odbytnicy, piersi, nerki, macicy oraz okolicy głowy i szyi, a także z mięsaka kości lub czerniaka.
W diagnostyce różnicowej guzów rozwijających się wewnątrzoskrzelowo należy brać pod uwagę rzadkie pierwotne lub wtórne nowotwory, inne niż drobnokomórkowy lub niedrobnokomórkowy rak płuca.

Key words: lymphoma, sarcoma, melanoma, endobronchial metastases
Słowa kluczowe: chłoniak, mięsak, czerniak, przerzuty wewnątrzoskrzelowe

A majority of endobronchial lesions are caused by primary lung cancer. In some cases, however, the endobronchial mass is, in fact, some other type of malignancy, which may be only imitating lung cancer. Endobronchial malignancies other than lung cancer may sometimes develop in the course of hematologic disorders, such as non-Hodgkin's lymphoma, Hodgkin's disease, plasmocytoma, and chronic lymphocytic leukemia [1-4]. Pulmonary Kaposi's sarcoma may form the endobronchial mass. This problem has gained importance in the era of the AIDS epidemic and in view of the increasing number of immunosuppressed patients after organ transplantation [5, 6]. Extremely rare primary pulmonary melanoma may occasionally manifest itself as an endobronchial malignancy [7]. Occasionally, extrathoracic neoplasms may metastasize into the bronchial wall creating diagnostic difficulties [8]. The differential diagnosis of these lesions from primary lung cancer is essential.

Department of Lung Diseases
Medical University in Wrocław

Lymphoma group of endobronchial lesions

Non-Hodgkin's lymphoma

In case of non-Hodgkin's lymphoma two patterns of involvement of lower airways have been described: diffuse submucosal infiltrates (occurring usually in the presence of lymphoma signs in other intra- or extrathoracic sites) and a mass obstructing the airway with or without the signs of disseminated disease [9-11]. Primary non-Hodgkin's lymphoma develops in B-cells in mucosa-associated lymphoid tissue [12]. Endobronchial masses may be solitary or multiple: unilateral or bilateral [1, 9, 10, 12]. The bronchoscopic examination reveals a polypoid tumor in the trachea and/or central or subsegmental bronchi [1, 12, 13]. The bronchial obstruction may be partial or complete and leading to atelectasis [1, 12]. Detailed radiographic studies, including computed tomography (CT), may not reveal lymphadenopathy or mediastinal involvement [12]. The cases of endobronchial non-Hodgkin lymphoma are extremely rare, but they also may be underestimated, and thus some authors suggest that endoscopic studies should be performed in patients

with lymphoma and symptoms indicating bronchial disease [14].

Hodgkin's disease

Endobronchial tumors may be found in 1,9% of cases of Hodgkin's disease [15]. They usually develop in the late course of the disease and are rarely seen at presentation [15]. In autopsy studies endobronchial lesions can be found in 15% of cases [16]. Endobronchial Hodgkin's disease develops from mucosa-associated lymphoid tissue [16]. The endobronchial masses which appear in the course of Hodgkin's disease cause coughing, wheezing and hemoptysis [15]. They may present as intermittent multilobar atelectases [2, 16]. Concomitant pneumomediastinum has been described [16]. Mediastinal (anterior and middle) involvement (with or without disease in the hili) is common [2, 15, 16]. Clinically, endobronchial Hodgkin's disease can be confused with small cell carcinoma [2]. Thus, it is important to include Hodgkin's disease in the differential diagnosis of endobronchial masses, especially in relatively young patients [16].

Plasmocytoma

Extramedullary plasmocytoma usually develops in the upper respiratory tract, but in some cases may form endobronchial masses [3]. Primary endobronchial plasmocytoma is a very rare disease [17]. Endobronchial lesions may occur as solitary plasmocytoma of the lung [18] or in the course of multiple extramedullary plasmocytoma confined to the lung [3]. Endobronchial lesions in the course of extramedullary plasmocytoma may be unilateral or bilateral [3, 17]. Severely hemorrhagic endobronchial tumors have been described in the course of extramedullary plasmocytoma [3]. The occurrence of multiple extramedullary plasmocytoma confined to the respiratory system may be caused by an endobronchial metastatic process or by a multicentric autochthonous process [3].

In the case of solitary plasmocytoma of the lung histopathological studies of the tumor reveal sheets of well-differentiated plasma cells and large extracellular deposits of amorphous Congo red negative material [18]. Immunohistochemical studies of biopsy specimens may reveal monoclonal kappa chains [17].

Solitary extramedullary plasmocytoma may develop in the absence of abnormal proteinuria, with no monoclonal spike in the serum electrophoresis, with no plasmacytosis in the bone marrow biopsy specimen, and with no other signs of multiple myeloma [18, 19]. In the case of multiple extramedullary plasmocytoma Bence-Jones proteins in the urine and IgA (kappa) components in the serum may be present [3].

The best treatment for endobronchial plasmocytoma has not been established. Long-term survival has been observed in the case of primary endobronchial plasmocytoma after complete surgical resection [17]. In the case of extramedullary plasmocytoma laser treatment of endobronchial lesions can be performed [19].

Chronic lymphocytic leukemia

Pulmonary parenchymal involvement in chronic lymphocytic leukemia is characterized by lymphocytic infiltrates in the peribronchial and perivascular interstitium, as well as in the alveolar walls and septa [4]. These changes are reported to occur in approximately one-third of patients with chronic lymphocytic leukemia [20, 21]. The development of endobronchial infiltration in the course of chronic lymphocytic leukemia is distinctly uncommon [22]. The endobronchial infiltrates can be considered as the extension of a peribronchial infiltrative process [22]. Endobronchial infiltrates may occur several years after the diagnosis of chronic lymphocytic leukemia [22]. In these rare cases submucosal infiltration by malignant lymphocytes may lead to endobronchial narrowing [22]. Multiple foci of endobronchial leukemic infiltrates may cause atelectasis [4, 20]. Massive peribronchial lymphadenopathy may be present [20]. In the course of chronic lymphocytic leukemia the histopathologic examination of endobronchial mass may demonstrate the presence of anaplastic large cell lymphoma consistent with Richter's transformation [4].

The treatment of endobronchial lesions caused by infiltration by malignant lymphocytes in the course of chronic lymphocytic leukemia can be effectively palliated with local irradiation and steroid therapy [22]. A resolution of the endobronchial mass developing in the course of Richter's transformation after bronchoscopic Nd-YAG laser therapy while the patient underwent chemotherapy has been described [4].

It has to be noted that in patients with chronic lymphocytic leukemia there is an increased risk of developing secondary malignancies, including lung cancer, laryngeal cancer, melanoma, and Kaposi's sarcoma [23].

Endobronchial Kaposi's sarcoma

Kaposi's sarcoma is a recognized complication of solid organ transplantation [5, 24]. It is also the most common malignancy occurring in AIDS patients [6, 25]. In AIDS patients infected with human herpes virus-8 (called Kaposi's sarcoma associated virus) pulmonary Kaposi's sarcoma usually develops as an extensive mucocutaneous disease [5, 26]. In some cases, however, solitary endobronchial Kaposi's sarcoma develops without cutaneous involvement [6, 27]. CT findings may be completely normal despite endobronchial isolated Kaposi's sarcoma [6] or may reveal coexisting typical signs, such as tumor masses, numerous nodules, bronchovascular pathway thickening, and bilateral pleural effusions [28, 29].

Early recognition of pulmonary Kaposi's sarcoma is essential, because chemotherapy, radiation therapy, and highly active retroviral therapy may provide palliation or improve survival in AIDS patients [25, 26], while the

modification of immunosuppressive therapy in organ transplant patients may bring on disease remission [5].

Pulmonary melanoma

Primary pulmonary endobronchial malignant melanoma is an extremely rare tumor [30, 31]. More frequent are pulmonary melanoma metastases, including their endobronchial form [8, 32, 33]. Melanoma in the lung probably arises from residual melanoblasts [7]. Endobronchial melanoma has a tendency to present as a central polypoid growth [30, 31]. It may closely resemble carcinoid tumors or poorly differentiated non-small-cell carcinoma of the lung [31]. In the biopsy samples melanin may be present on hematoxylin and eosin staining [31]. Immunohistochemical staining may help in establishing the diagnosis of primary pulmonary endobronchial melanoma [30, 31].

Endobronchial metastases

Endobronchial metastases from extrathoracic primary malignancies usually represent a late manifestation of the primary disease with generally poor prognosis [34]. In a group of over 1000 patients with histologically verified endobronchial lesions, endobronchial metastases made up some 1.5% of cases [35]. However, in some large series of patients with proven pulmonary metastases this type of lesion has been found in up to 46% [36] – 50,4% [37] of cases.

There are four developmental modes of endobronchial metastases from non-pulmonary neoplasms [38]. These are: direct metastasis to the bronchus, bronchial invasion by mediastinal or hilar lymph node metastasis, peripheral lesion extending along the proximal bronchus, and – rarely – bronchial invasion by a parenchymal lesion [38].

Endobronchial metastatic tumors may present as polypoid or nodular lesions covered with necrotic material [36]. In case of direct extension to the bronchi from adjacent metastatic foci submucosal swelling with an irregular margin and narrowing of the bronchial lumen can be seen [36].

Symptoms and radiological/endoscopic signs in endobronchial metastatic carcinoma are indistinguishable from those of primary lung cancer [11, 34]. The most common clinical manifestations include coughing, haemoptysis, dyspnea, and recurrent pulmonary infections; the course of the disease may also be asymptomatic [8]. A common radiologic finding in CT in case of endobronchial metastasis is an atelectasis [39, 40]. CT, and especially spiral CT, may help in the identification of endobronchial lesions and occasionally reveal the other metastatic lesions: pulmonary nodules, *lymphangitis carcinomatosa*, and pleural involvement [41].

Immunohistochemical techniques using different antibodies may help to find the primary tumor which has metastasized into the lung [42] – thyroid or prostate carcinomas, melanomas, sarcomas, lymphomas – all of those are known to form endobronchial metastatic masses – can be reliably differentiated with immunohistochemical methods [42].

In different series of patients with endobronchial metastatic lesions the most frequent primary tumors are: thyroid, head-neck and breast carcinoma [37], colon, rectal, breast, uterine carcinoma and osteosarcoma [38]; colon, breast and renal carcinoma [34]; colon, rectal and renal carcinoma [11]; breast and colon carcinoma [8, 36]. In some cases endobronchial metastatic lesions may develop in the course of melanoma [8, 32, 33], basal cell carcinoma, bladder carcinoma, gastric carcinoma [34, 43], pheochromocytoma [44], and prostatic carcinoma [45].

In some cases of endobronchial metastases causing dyspnea and/or hemoptysis, photodynamic therapy may help in alleviating the symptoms, although the mortality is high [46].

Conclusion

Rare primary and secondary malignancies other than small cell lung cancer or non-small cell lung cancer have to be included in the differential diagnosis of endobronchial neoplastic lesions.

Anna Brzecka MD, PhD
Department of Lung Diseases
Medical University
53-439 Wrocław,
ul. Grabiszyńska 105
e-mail: aniabrz@box43.pl

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