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Unusual symptoms of lung cancer — a case report

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ABSTRACT

Lung cancer remains a major oncological problem, both in Poland and worldwide. A quick and accurate diagnosis is the key element in improving survival outcomes in oncology. Unusual and uncharacteristic signs and symptoms hinder adequate diagnostic proceedings. The case report presented below is an example of diagnostic difficulties arising from an unusual constellation of symptoms and their effect on patient's outcomes. Additionally, we shortly discuss the potential medical conclusions that might be drawn from the described case. A 56-year-old male patient, a long-time smoker, was consulted by a primary care physician due to persistent abdominal pain. Initial proceedings provided no decisive diagnosis. The patient was referred to hospital for an extended diagnostic work-up. However, the additionally performed procedures added no further evidence and no insight into the diagnosis. Unfortunately, neither chest X-ray nor abdomen ultrasonography was performed. After four months the patient presented with a generalised metastatic spread to skin, along with a clear deterioration of performance status. Finally, the diagnosis of large-cell neuroendocrine carcinoma of the right lung was made. The patient received two courses of a palliative cisplatin-based chemotherapy, shortly after which he progressed. Further treatment included only palliative radiotherapy and hospice care.

Improvement in both the diagnosis and treatment of lung cancer require adherence to the current guidelines and close cooperation with a primary care physician. When possible, the least uncomfortable procedures should be undertaken to preserve the patient's quality of life. However, if no clear diagnosis is obtained despite a suspicion of neoplastic diseases, repeating of a full diagnostic work-up may be considered. Further attention should be given to the development of effective preventative programmes and the creation of work-groups devoted to dealing with rare symptoms of neoplastic diseases.

Key words: lung cancer, rare symptoms, diagnosis, neuroendocrine cancer

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Introduction

Lung cancer remains a major oncological challenge in Poland and worldwide. The number of newly diagnosed lung cancer diagnoses in 2015 in Poland reached 7503 cases in women and 14,460 cases in men, with mortality numbers of 7475 and 16,238 cases, respectively [1]. One of the key elements of improving both cure rates and survival outcomes is a timely diagnosis, which allows prompt initiation of treatment. Common signs and symptoms of lung cancer allow a quick referral to units specialised in lung cancer diagnosis, such us pulmonology or thoracic surgery departments. However, in cases of unusual or uncommon symptoms, usually seen in advanced disease, the diagnosis might be delayed. The case report presented herein is an example of both unusual symptomatology of lung cancer and a typical course of disease with delayed diagnosis.

Case report

A 56-year-old male was referred to a hospital by a primary care physician due to persistent abdominal pain that was not responsive to an initial analgesic treatment. The patient's comorbidities included arterial

hypertension and low back pain disorder. In an internal medicine department of the local hospital gastroscopy and colonoscopy were undertaken, both showing no evident pathology. The results of a laboratory work-up (including: complete blood count, liver enzymes, amylase in serum and urine, electrolytes, glycaemia, urea, and creatinine) were within normal limits. Electrocardiography showed only partial right bundle branch block. Physical examination was unremarkable, with the exception of mild pain in the upper abdomen. No radiological imaging of the chest or abdomen were done. The patient was discharged with a prescription for a spasmolytic drug and a recommendation to perform additional stool analyses for parasites and lamblia.

After four months the patient was admitted to the pulmonology department as a result of abnormal chest radiograph. Radiological examination was done by a primary care physician due to the presence of night sweats and cough, both slowly progressing for a period of six weeks. Bilateral enlargement of supraclavicular nodes and numerous subcutaneous chest wall nodules were found on physical examination. The body temperature was within normal limits. Bronchoscopy and spirometry demonstrated no abnormalities. The laboratory results revealed mild anaemia (haemoglobin concentrations of 13.0 g/dL) and elevated CRP level (46.9 mg/L). Computed tomography of the thorax showed the presence of the inhomogeneous nodal masses in the mediastinum measuring up to 45 mm, a small amount of fluid in the left pleural cavity, small singular infiltrates in the apex of the right lung, similar solitary lesions in the subcutaneous tissue of chest and epigastrium, changes in the right renal capsule and in the liver, and enlargement of the retroperitoneal lymphatic nodes by up to 27 mm. Additionally, the presence of osteoarthritic changes in the vertebrae was confirmed. The patient was referred to the thoracic surgery department with the intention of obtaining material for a pathological examination.

The surgical biopsy of supraclavicular lymph node was performed and one subcutaneous nodule from the chest wall was excised.

The tissues obtained were insufficient to determine appropriate diagnosis in the pathomorphological examination. As a result, the patient required diagnostic right-sided thoracotomy, which was undertaken three weeks later. The final pathology report identified the presence of large-cell neuroendocrine carcinoma with CD30 (–) and CD117 (–) immunophenotypes in the excised lung parenchyma. The patient was referred to the oncology department with the intention of receiving systemic therapy.

Two weeks later, on the day of admission to the oncology department, the patient presented several new symptoms: exertional dyspnoea, asthenia, weight loss and pain in the lower left extremity. Massive and generalised metastatic spread to the subcutaneous tissue, including all limbs, was present. Additionally, signs of venous thrombosis in the left lower extremity were noted. The laboratory examination showed anaemia (haemoglobin 10.2 g/dL), hypercalcaemia (3.19 mmol/L) and increased concentrations of serum creatinine (1.39 mg%). The patient started chemotherapy consisting of cisplatin and vinorelbine (PN scheme) in full doses according to the body surface area. Supportive treatment included buprenorphine, bisphosphonate, low molecular weight heparin and diuretics. Unfortunately, the computed tomography performed after two full cycles of chemotherapy showed disease progression, with enlargement of the chest lesions and the development of new metastases in the thoracic vertebrae and in the pelvis. Due to the unequivocal disease progression chemotherapy was stopped. Subsequently, the patient was referred for palliative radiotherapy to the bone lesions and then to home-based hospice care.

Discussion

The case report described herein represents a good example to contemplate on the possibilities of lung cancer diagnostic work-up optimisation, with additional emphasis on therole of unusual symptoms. Usually, the most important part of diagnostic evaluation for lung cancer is performed in pulmonology departments or, less commonly, in thoracic surgery departments. Specialists at such facilities are capable of utilising the most important procedures: bronchoscopy, ultrasonography-guided or tomography-guided transthoracic biopsies, video-thoracoscopy, functional tests and others. Ambiguous cases often require even more sophisticated technologies such as a positron emission tomography (PET-CT). However, as some initial signs and symptoms of lung cancer might arise from systems other than respiratory, different medical specialties might initially encounter such cases. This includes signs and symptoms such as: inguinal or axillar adenopathy, hepatomegaly, jaundice, pain in abdomen, vertebrae, long bones, ribs, head, shoulder, with or without paraesthesia and muscular atrophy, apathy, asthenia, weight loss leading to cachexia, night sweats, vitiligo, nausea and vomiting, imbalance, speech impairment, loss of consciousness, paresis and paraparesis, paraplegia, abnormal results of radiological imaging such as presence of metastases in liver, central nervous system or bones, arterial and/or venous thrombosis and laboratory abnormalities such as elevated liver enzymes, elevated CRP, leucocytosis, hypercalcaemia, anaemia, electrolyte imbalances, elevated D-dimer or elevated serum creatinine.

Many specialists (internal medicine specialist, neurologist, haematologist, orthopaedic surgeon, neurosur-

geon and others) should cooperate in the establishment of the diagnosis of lung cancer, despite the fact they are seldom involved in such patients. As a result, in some cases, the diagnostic work-up might be delayed. Additionally, medical literature regarding lung cancer published in Poland rarely brings up symptomatology other than that arising from the respiratory system [2, 3]. It is worth noting that more attention is given to different kinds of paraneoplastic syndromes accompanying lung cancer, despite their scarcity [4, 5]. Special attention should be given to the role of the primary care physician. In the records of the presented patient there is no information regarding abdominal ultrasonography, chest radiography, or history of smoking. Knowledge of a high risk of lung cancer in the patient would probably have led to performing a chest radiogram sooner. One may also speculate that currently ultrasonography is a basic diagnostic tool for a primary care physician and, in the case of the presented patient, it should have been obtained more promptly.

However, the referral to the internal medicine department can be considered appropriate. The two invasive and cost-generating procedures undertaken — gastroscopy and colonoscopy — led to no additional insights. At this point, abdominal ultrasonography should have been performed, especially considering the diagnostic tests taken to evaluate the function of the liver and pancreas because a pathology within the abdomen was suspected. The lack of chest radiogram is unexpected, as this procedure is low-cost and clearly advisable considering the difficulties with obtaining diagnosis. In effect, the patient was discharged from the hospital without diagnosis. Considering the patient's further fate, it might be suspected that the abdominal pain was due to the enlargement of abdominal lymph nodes. Even if we assume an isolated functional abdominal pain syndrome, chest radiogram and abdominal ultrasonography might have shown pathology within the lungs and the abdomen.

When the patient was again admitted to the hospital four months later, the presented symptoms where typical for metastatic lung cancer and metastatic spread to the subcutaneous tissue was visible in physical examination. The diagnostic work-up was performed in the pulmonology department and the tissue was obtainment in thoracic surgery department. The biopsy specimen was firstly collected without invasive procedures. The further decision regarding diagnostic thoracotomy is questionable because an additional diagnostic sample might have been obtained from subcutaneous or lymphatic lesion without the risk associated with thoracotomy.

Finally, nearly six months since the occurrence of initial symptoms, the patient was admitted to the oncology department, where systemic treatment was initiated. At this point, with extensive metastatic spread, concomitant cachexia and several other abnormalities in laboratory examination, the patient could only receive two cycles of chemotherapy with platinum and vinorelbine before he progressed and developed new bone metastases. The choice of chemotherapeutic agents also can be debated because the presence of anaemia and elevated creatinine concentration might suggest carboplatin use instead of cisplatin. However, the outcomes achieved with carboplatin might not be equal to those achieved with cisplatin. Nevertheless, considering rapid progression after only two cycles of chemotherapy without treatment toxicity, it is probable that the fate of the patient was inevitable regardless of the type of systemic treatment. The decision about limiting further treatment to palliative radiotherapy and hospice care is respectable. Management of the patient was complicated by the presence of a rare pathomorphological subtype of lung cancer (large-cell neuroendocrine carcinoma). Unfortunately, large-cell neuroendocrine carcinoma of the lung is often resistant to chemotherapy and no widely accepted standard-of-care exists [6, 7].

The presented case of unusual lung cancer symptomatology suggests several important considerations. Because the primary care physician plays a key role in the initial diagnosis, prompt diagnosis of neoplastic diseases might rely on his/her knowledge, commitment and diagnostic capabilities. Taking that into consideration, it might be beneficial to support primary care practices with tools necessary for the initial work-up. Additionally, current guidelines, preferably in a printed form rather than conference lectures, regarding rare symptoms of the most common malignancies might be beneficial.

Another important issue is the necessity of compliance with current diagnostic and therapeutic guidelines. Lack of lung radiogram or even abdominal ultrasonography at both primary care level and internal medicine department level should be considered as a suboptimal diagnostic work-up. However, it should be emphasised that the proper diagnostic process focuses not only on the disease, but also on the burden generated with each procedure. Performing invasive procedures, such as gastroscopy and colonoscopy, before obtaining simple abdominal USG or undertaking diagnostic thoracotomy when other source of tissue is available, are good examples.

A practical aspect of every medical subspecialty includes the need for prompt re-examination or incorporation of additional procedures, whenever the symptoms persist and previous tests are inconclusive. This should enable the detection of previously unnoticed findings, preventing irreversible damage. The case described above lacked such promptness.

Prophylaxis, both primary and secondary, remains of the utmost importance in every form of cancer. Therefore, in the presented case of a 56-year-old life-long smoker, it might be suggested that a common chest radiogram should be obligatory, despite the lack of

evidence on its effect as lung cancer prophylaxis. Finally, considering the example of working groups devoted to diagnostics and treatment of rare tumours, the uncommon symptomatology of common malignancies should also bring more scientific attention. If unnoticed, this problem will surely result in inadequate cancer care and unchangeably high cancer-associated mortality in Poland.

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