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Adenocarcinoma of the colon in a patient with systemic sclerosis

Gruczolakorak jelita grubego u chorego na twardzinę układową

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Key words: systemic sclerosis, adenocarcinoma of the colon, risk of cancer.

Słowa kluczowe: twardzina układowa, rak jelita grubego, ryzyko wystąpienia nowotworu.

Summary

Systemic sclerosis is a chronic connective tissue disorder characterised by progressive fibrosis of the skin and subcutaneous tissue, occurrence of Raynaud's phenomenon and other vascular abnormalities as well as internal organ involvement due to fibrosis, especially within the alimentary tract, lungs, heart and kidneys. Malignant tumours are also found in the patients but it remains unclear whether the disease is associated with higher incidence of malignancy. Some authors provide evidence of an increased incidence of cancer in patients with scleroderma, while others do not confirm this correlation. Most of the studies report a statistically significant relation of systemic sclerosis to increased risk of lung cancer. The paper reviews a patient suffering from systemic sclerosis for a few years with recent diagnosis of adenocarcinoma of the colon.

Streszczenie

Twardzina układowa jest przewlekłą chorobą tkanki łącznej charakteryzującą się postępującym twardnieniem i włóknieniem skóry, występowaniem objawu Raynauda i innymi zmianami naczyniowymi, a także zmianami narządowymi związanymi z włóknieniem, które dotyczą szczególnie przewodu pokarmowego, układu oddechowego, serca i nerek. Główną przyczyną zgonów chorych na twardzinę układową są zmiany płucne, niewydolność serca i nerek, nadciśnienie płucne, nadciśnienie tętnicze i zespół złego wchłaniania. U chorych na twardzinę opisywane są przypadki rozpoznania nowotworów, jednak nie jest do końca jasne, czy twardzina układowa wiąże się ze zwiększonym występowaniem nowotworów w porównaniu z populacją osób zdrowych. W literaturze związek między twardziną układową a wystąpieniem nowotworu badano wielokrotnie. Część autorów wykazuje zwiększoną częstość występowania nowotworów w przebiegu twardziny, inni autorzy nie potwierdzają tej zależności. Większość autorów publikowanych obecnie prac wskazuje na znamienną statystycznie korelację twardziny układowej ze zwiększoną częstością występowania raka płuc. W pracy przedstawiono chorego z kilkuletnim wywiadem twardziny układowej, u którego przypadkowo rozpoznano nowotwór jelita grubego.

Systemic sclerosis or scleroderma is a chronic connective tissue disorder characterised by progressive fibrosis of the skin and subcutaneous tissue, occurrence of Raynaud's phenomenon and other vascular abnormalities as well as internal organ involvement due to fibrosis, especially within the alimentary tract, respiratory system, heart and kidneys [1]. The major cause of death in patients with systemic sclerosis is pulmonary involvement, pulmonary hypertension, cardiac and renal failure, and malabsorption [2, 3]. Malignant tumours are also found in the patients but it remains unclear whether the disease is associated with higher incidence of malignancy.

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The aim of the paper is to describe a patient suffering from systemic sclerosis for a few years with recent diagnosis of colon cancer.

Case description

A 60-year-old patient with systemic sclerosis diagnosed in 2003 was admitted to the Department of Internal Medicine and Rheumatology due to significant worsening of the health condition. He was treated with cyclophosphamide – at the beginning as intravenous pulses and then orally from October 2006 to September 2007. Additionally, in the past, he was treated with avocado and soya oil, cyclosporin and vasodilators.

On admittance, he suffered from weakness, dyspnoea, pain of the hip and knee joints, dysphagia, progressive thickening of the skin, and recurrent digital ulcers. The physical examination revealed thickening of the skin of the face, chest, hands, forearms and shins (modified Rodnan skin score – 33), limitation of the joint mobility of the hands, elbows, shoulders, knees as well as crepitations at the base of the right lung. The laboratory tests revealed a positive test for antinuclear and Scl 70 antibodies, erythrocyte sedimentation rate of 15/70 mm/1/2 h, and increased serum creatinine kinase activity (223 U/l). Occult blood stool test was positive. Other laboratory tests were normal (full blood count, urine analysis, 24-hour protein excretion, plasma electrolyte, serum glucose, iron, creatinine, uric acid, urea nitrogen, transaminases, serum protein fractions, C-reactive protein, coagulation tests).

Nailfold capillaroscopy performed in October 2006 revealed reduced capillary density, increased number of Raynaud loops, megacapillaries, shortening of the capillaries and microbleeding (active scleroderma). The histopathological analysis of a biopsy specimen of the skin and muscles performed in 2004 was characteristic for scleroderma. Barium radiography revealed a slightly dilated oesophagus. High resolution computed tomography of the chest revealed progression of pulmonary fibrosis compared to the examination performed in April 2004 (additionally there were inactive tuberculosis changes at the apex of the left lung – history of tuberculosis in 1979). Evaluation of the lung function tests (DLCO, spirometry, vital capacity) did not reveal abnormalities. Ejective fraction evaluated with echography was 60-65%. 24-hour electrocardiographic monitoring did not reveal any abnormalities.

Colonoscopy was performed despite a lack of anaemia and subjective signs because the result of the occult blood stool test was positive. The examination revealed a pedunculated polyp – diameter 20 mm. Polypectomy was performed and on the basis of histopathological examination the diagnosis of adenoma tubulo-villosum high grade in adenocarcinoma vertens (Ca foci found in the pedicle) was established. The altered part of the colon (30 cm long) was removed surgically. The postsurgical period was without complications. Pathological examination of the removed part of the colon did not reveal distant foci or nodal involvement. The wound healed and the patient was discharged from the surgery ward in good condition.

Discussion

Adenocarcinoma of the sigmae was found four years after diagnosis of systemic sclerosis in this patient. There were no signs or symptoms of intestinal carcinoma apart from the positive result of the occult blood stool test. He had no anaemia, weight loss, fever, abdominalgia or bowel emptying disturbances. The performed colonoscopy allowed for early diagnosis of cancer and its management.

In the literature, the coexistence of scleroderma and cancer has been studied frequently. Some authors provide evidence of an increased incidence of cancer in patients with scleroderma [4–8], while others do not confirm this correlation [9]. The development of cancer in patients with scleroderma might be influenced by genetic factors and immunosuppression [4, 10]. The analysis of Swedish scleroderma patients [5] revealed that systemic sclerosis (both limited and diffuse) but not localised scleroderma is associated with a higher rate of cancer. None of the performed studies have confirmed the correlation between cancer and serum Scl 70 antibodies [4, 9, 11, 12]. Jacobsen et al. [13] provide evidence that fatal malignancy in scleroderma patients occurs more often in men than in women and is more common in patients with late age onset disease than in patients with early onset disease.

It is still not easy to evaluate whether the incidence of the reported cancers in systemic sclerosis patients is comparable to the incidence in the healthy population. In the literature, the risk of cancer is expressed as standardised incidence ratios (SIRs). This is an equivalent to relative risks, which are calculated by dividing the number of observed cases of cancer in patients with systemic sclerosis by the number of expected cases, allowing for the age and sex of patients in the general population occurring during the same period of follow-up [10].

In the recent studies describing occurrence of cancer in patients with systemic sclerosis the most frequently reported were: lung cancer [2–4, 13, 15], breast cancer [2, 6, 14], skin cancer [5], non-Hodgkin's lymphoma [6, 16], oesophageal cancer [17], and hepatic cancer

[5, 9]. In a study of 441 patients with scleroderma [4], apart from lung carcinoma and breast cancer, which were the most commonly found ones, cases of cancer of other locations were observed in only a few patients, i.e. in the oesophagus, stomach, skin, prostate, urinary bladder, rectum, ovary and haematopoietic system. Colorectal cancer was diagnosed only in four individuals.

Recent studies provide evidence of a statistically significant relation of systemic sclerosis with increased risk of lung cancer only [5, 7–9, 18]. In a study of 538 patients [9] the most frequently observed sites of cancer in patients with scleroderma were the lungs and breast, but the incidence of cancer was similar to the incidence in the healthy population. A study of 917 systemic sclerosis patients reported an increased incidence of lung cancer, non-melanoma skin cancer and primary hepatic cancer [8]. In the previous studies no evidence of an increased risk of intestinal carcinoma in patients with systemic sclerosis was found.

It is possible that pulmonary fibrosis, a common feature of patients with systemic sclerosis, may be a crucial risk factor of lung cancer [2, 5, 7, 10, 19]. Roumm et al. [19] reported that in 62% of scleroderma patients lung cancer had been preceded by pulmonary fibrosis, and only 28% of them had had no lung changes before cancer diagnosis. Other authors do not support the concept of increased risk of lung cancer in scleroderma patients with pulmonary fibrosis [11]. They indicate that the only risk factor of lung cancer in scleroderma patients is smoking. Some investigators point to the increased incidence of lung cancer in scleroderma patients with pleural effusion and elevated serum Ca125 level [2, 20].

Although there is no evidence that cancer itself increases the risk of systemic sclerosis, there is evidence that some of the treatments used in cancer patients (such as radiation therapy or chemotherapy) induce scleroderma or scleroderma-like reactions [10]. On the other hand, Corner et al. [21] presented a case of a scleroderma patient with concomitant lymphoma with remission of scleroderma after chemotherapy for lymphoma.

To conclude, the diagnosis of adenocarcinoma of the sigmae which was diagnosed in the above-described patient is not commonly observed in patients with systemic sclerosis. Perhaps it is an incidental observation, not related to the diagnosis of scleroderma. Long-term immunosuppressive therapy might have had an impact on the occurrence of cancer. Additionally, late onset of the disease and the fact that he was a male might be risk factors of malignancy [13]. Nevertheless, this case confirms the need for oncological surveillance and careful observation of patients with systemic sclerosis, particularly those who are treated with immunosuppressive therapy, in order to early diagnose and manage cancer in these patients.

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