CASE REPORT

Paraneoplastic hypertrophic osteoarthropathy

Evaluation at 25 years after pneumectomy

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KEY WORDS

finger clubbing, hypertrophic osteoarthropathy, paraneoplastic syndrome

ABSTRACT

Finger clubbing, which involves distal phalanx thickening and nail convexity, has been known since antiquity. Observations made in modern times by Bamberger (1889), Pierre Marie (1890), and other investigators led to identification of various causes of this digital anomaly which can be the first manifestation of a severe organic disease. Undoubtedly, this somatic abnormality, often associated with arthralgia and bone pain (full-blown hypertrophic osteoarthropathy – HOA), is most often a harbinger of lung cancer. Paraneoplastic HOA is probably the best known and the most extensively studied paraneoplastic syndrome in human pathology. The familial or idiopathic HOA (pachydermoperiostosis) appears at puberty and is not associated with other underlying diseases. We present the case of a 58-year-old male with HOA, associated with spinocellular lung cancer, who survived 25 years after pneumonectomy.

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INTRODUCTION Finger clubbing, which involves distal phalanx thickening and nail convexity, has been known since antiquity. Observations made in modern times by Bamberger (1889) and Pierre Marie (1890), and subsequent investigators allowed to identify various causes of this digital anomaly, which can be a sign of a severe organic disease. Hypertrophic osteoarthropathy (HOA) is a clinical syndrome that causes clubbing of the fingers and toes, enlargement of the extremities, as well as joint pain and swelling. HOA is characterized by symmetric periostitis involving the long bones of the upper and lower limbs. The syndrome can be primary or secondary. Primary HOA, or pachydermoperiostosis, is a rare familial autosomal dominant disease. The majority of cases are secondary HOA, or hypertrophic pulmonary osteoarthropathy, which is associated with pulmonary disease, such as lung cancer.[1,2]

CASE REPORT In 1983, a 33-year-old patient was admitted to the Rheumatology Section of the County Hospital of Cluj for medical investigation. He presented with persistent cough associated with rheumatoid syndrome. However, joint pain was rather noninflammatory (only slight morning stiffness for <15 min, pain on joint movement and relief at rest, no swelling). The symptoms occurred about 2 years earlier, and the patient was initially diagnosed with acute rheumatic fever and then rheumatoid arthritis. Treatment with analgesics and non-steroidal anti-inflammatory drugs did not produce satisfactory relief, and the patient developed finger clubbing over the next few months. He reported persistent cough which has recently become more pronounced. He smokes 10 cigarettes a day on average. The patient's family history revealed three relatives diagnosed with cancer. He had a recent history of slight weight loss induced by loss of appetite during the preceding 3 months. Physical examination showed: excessive perspiration, seborrheic dermatitis, symmetrical edema of the large and small joints of the limbs, and finger clubbing (FIGURE). He presented dullness to percussion and diminished breath sounds over the middle lobe of the right lung.

Additional investigations led to detection of further pathologies. Chest radiogram showed right middle lobe atelectasis, which was confirmed by a classic tomography available at that time. The diagnosis of HOA was confirmed

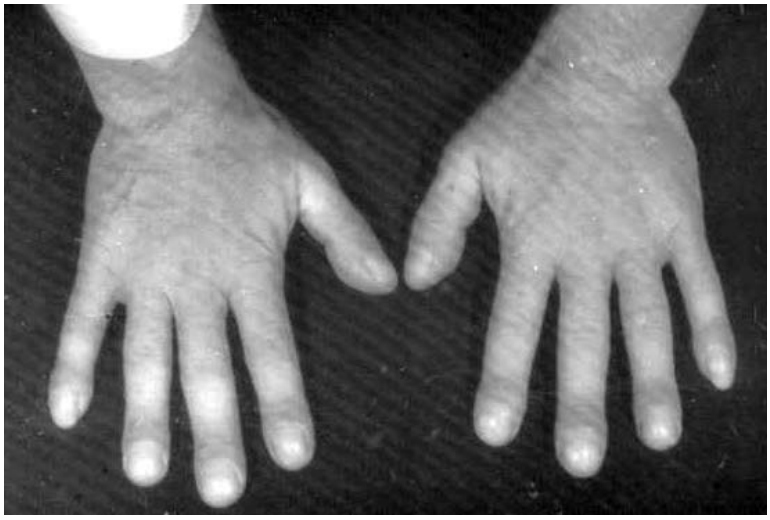

FIGURE Finger clubbing

by the radiograms of the long bones of the limbs, which showed periostosis.

The next diagnostic step was bronchoscopy that revealed a malignant lesion in the main bronchus of the right middle lobe. Histological examination of the tissue specimen showed a carcinoma with concomitant infection.

The patient underwent pneumectomy. About one month thereafter, his clinical condition was good and digital clubbing was reduced.

Seventeen years after the diagnosis had been established, the patient was again admitted to the hospital at the age of 50, because of critical ischemia of the left upper limb that was due to left subclavian artery thrombosis. Surgical treatment was administered. Three years later, he returned to our department with severe hepatic pain that was associated with jaundice, hepatomegaly, and abnormal liver test. Acute alcoholic hepatitis has been diagnosed based on all clinical manifestations. Abdominal ultrasound showed no signs of cirrhosis or abdominal tumor. Tests for hepatitis viruses were negative. The patient's condition gradually improved. The disease was self-limited. All the investigations performed at that time, particularly screening for potential recurrent malignancies were negative.

In 2008, the patient was again hospitalized due to another episode of critical ischemia of the right lower limb manifest a classic "blue toe syndrome". The Doppler ultrasound examination showed thrombosis of the superficial femoral artery and multiple arterial stenoses caused by atherosclerotic plaques. The ischemic episode subsided during conservative treatment. The patient does not show any signs of recurrence of lung cancer. However, he currently suffers from severe chronic obstructive pulmonary disease with the peak expiratory flow rate of 42% of the reference values.

All coagulation tests, including homocysteinemia, protein S and protein C levels, antiphospholipid antibodies, and factor VIII, yielded normal results. No source of embolic material was identified. However, he had high total cholesterol and he continued to smoke, which probably accounts for recurrent arterial thrombosis.

DISCUSSION We have reported this case because it documents a 25-year survival of a patient with lung cancer since the diagnosis. Another reason is the fact that paraneoplastic syndrome, but not signs or symptoms associated with the respiratory system, led to the final diagnosis of lung cancer. Joint and bone pains resolved quickly after tumor resection, which confirms its paraneoplastic nature. This link has been already observed in a few patients and described in the literature.[2] We did not confirm the provisional diagnosis of rheumatoid arthritis, as initially established in another medical center; on the other hand, paraneoplastic HOA is more common in subjects aged 50–70 years.[3] Risk factors for lung cancer in our patient included current smoking (10 cigarettes a day since adolescence) and a positive family history for cancer. A less extensive surgical resection would have been feasible, if endobronchial tumor had been detected earlier. However, the patient did not show any alarming symptoms for a long period of time. Periostosis can be detected by radiological examination or by scintigraphy.[4] However, scintigraphy was not widely available in Romania during the 1980s when the patient was first diagnosed.

Our patient developed HOA signs at an unusual age. The familial or idiopathic forms of HOA occur either in the first year of life or at puberty.[5]

Cases of paraneoplastic HOA concomitant with familial or idiopathic form have been observed and described in the literature. This fact may postpone establishing the diagnosis of an underlying disease.[5] Notably, some patients with primary HOA eventually develop disorders that are otherwise known to underlie secondary HOA many years after the onset of osteoarthropathy.[6] Skin changes are described especially in primary forms of HOA, but not exclusively.[1]

HOA occurrence is differently interpreted in the literature. Some authors[5] reported HOA as a harbinger of clinically overt lung cancer in over 20% of cases, with some patients self-reporting HOA as the only clinical sign of the disease. On the other hand, lung cancer accounts for almost 20% of isolated digital clubbing, and over 60% of HOA in adults.[6,7] HOA occurs more frequently in lung adenocarcinoma and extremely rarely in small-cell lung cancer. These data suggest that HOA or simple digital clubbing in adults must be considered as a warning and should prompt lung cancer screening, even in the absence of detectable respiratory symptoms, so that patients could benefit from early treatment ensuring better outcome.

Survival of patients with lung cancer is still poor despite recent advances in chemotherapy. Survivals after chemotherapy and surgical treatment ranges from 21–35% in the first year of treatment and 5–15% during the first 5 years.[8] To our knowledge, there have been no further cases of a 25-year survival after a positive diagnosis of spinocellular carcinoma, or separate analyses of the survival rate in patients

with paraneoplastic syndromes, including those with HOA.

In conclusion, over 90% of secondary HOA cases develop as a paraneoplastic syndrome or the anomaly associated with chronic suppurative infections[1,4], and can precede the diagnosis of an underlying disease. Therefore, a misdiagnosis could be made if the primary condition is overlooked. Because the diagnosis is essentially based on clinical grounds, a physician should study a patient's history thoroughly and perform physical examination, including evaluation of the musculoskeletal system, even in asymptomatic patients.

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OPIS PRZYPADKU

Paranowotworowa osteoartopatia przerostowa

Ocena po 25 latach od pneumonektomii

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SŁOWA KLUCZOWE

pałeczkowatość palców, osteoartropatia przerostowa, zespół paranowotworowy

STRESZCZENIE

Pałeczkowatość palców to objaw znany od czasów starożytnych, stanowiący pogrubienie paliczka dystalnego oraz uwypuklenie paznokcia. Obserwacje poczynione w czasach nowożytnych przez Bambergera (1889) oraz Pierre Marie (1890), jak również kolejne badania, pozwoliły określić różnorodne przyczyny tej anomalii palców, która może być objawem poważnej choroby organicznej. Niewątpliwie ta zmiana somatyczna, często skojarzona z bólem stawu i kości (pełnoobjawowa osteoartropatia przerostowa [*hypertrophic osteoarthropathy* – HOA]), jest najczęściej ostrzeżeniem przed obecnością raka płuc. Można powiedzieć, że paranowotworowa HOA jest najbardziej znanym i najlepiej przebadanym zespołem paranowotworowym w patologii. Z kolei rodzinna lub idiopatyczna HOA (*pachydermoperiostosis*) występuje w wieku dojrzewania i nie jest związana z występowaniem innych ukrytych chorób. W pracy przedstawiono przypadek 58-letniego mężczyzny z rozpoznaną HOA, powiązaną z kolczystokomórkowym rakiem płuc, który przeżył 25 lat po przeprowadzonej pneumektomii.

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