Bronchial Carcinoma Mimicking Rheumatic Disease; Hypertrophic Pulmonary Osteoarthropathy (HPOA) or Pierre Marie-Bamberger-Syndrome

Jeppe Faurholdt Lauridsen, Maria Kverneland Kavli, Anders Thomassen, Soeren Schifter

Department of Nuclear Medicine, Odense University Hospital, 5000 Odense C, Denmark.
Department of Nuclear Medicine, Vejle Hospital, 7100 Vejle, Denmark
Department of Lung Medicine, Odense University Hospital, 5000 Odense C Denmark.
Department of Anesthesiology Levanger Hospital, 7600 Levanger, Norway

Abstract: Hypertrophic pulmonary osteoarthropathy (HPOA) or Pierre Marie-Bamberger-syndrome is a paraneoplastic syndrome often associated with bronchial carcinoma. A 60-year-old previously healthy man, with swelling and pain in multiple joints, underwent a chest x-ray and bone scintigraphy. The x-ray raised suspicion of a lung tumor and the bone scan showed increased activity in the periostea of the tubular bones in the upper and lower extremities suggesting HPOA. A 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) scan disclosed a FDG-avid right lung mass, a mediastinal lymph node but no FDG uptake in the periostea of the tubular bones. The patient was timely treated for his bronchial carcinoma ensuring a curative outcome.

Keywords: FDG-PET/CT; bronchial carcinoma; paraneoplastic syndrome; bone scan; Hypertrophic pulmonary osteoarthropathy; Pierre Marie-Bamberger-syndrome.

INTRODUCTION

HPOA, also known as Pierre Marie-Bamberger syndrome, is a relatively rare syndrome characterized by digital clubbing, painful periostitis of the long tubular bones and arthritic symptoms, especially in the lower extremities, including non-inflammatory arthrits of the large joints in a bilateral and symmetrical fashion. The syndrome is frequently related to lung neoplasms and due to its various degrees of symptomatic expression doctors in various specialties must be attentive to such patients.

CASE PRESENTATION

In May 2012 a 60-year-old previously healthy man, but former heavy smoker, was referred to our hospital for a rheumatological evaluation due to swelling and pain of the ankles, knees, fingers and wrists developing over a 3 month period. The pain was refractory to paracetamol and glucosamine. Furthermore, the patient presented digital clubbing and nails convexity of the fingers and toes (Image I). He presented no cardiopulmonary symptoms and had an inconspicuous medical and surgical history.

Laboratory investigations showed an increase in sedimentation rate (60 mm, normal range 2–20 mm), blood alkaline phosphatase (188 U/L, normal range 55-105 U/L), lactate dehydrogenase (222 U/L, normal range 105-205 U/L), thrombocytes (498 x 10^9/L normal range 120-400 x 10^9/L), C-reactive protein (81 mg/L, normal range < 10 mg/L), anemia (6-9 mmol/L, normal range 8-11 mmol/L ) and normal levels of specific rheumatic blood components. His chest X-ray revealed a 4·3 x 3·6 cm lung tumor in the lower right lobe. A bone scan showed symmetrical, diffuse linear uptake in the femoral, tibial, radial and ulnar bones consistent with HPOA (Image II). [1,] A PET/CT-scan demonstrated a FDG-avid solid 12un tumor in the right lower lobe and a FDG-positive ipsilateral hilar lymph node. There was no periosteal FDG-uptake as detected on the bone scan of the tubular bones of the upper extremities (Image III). Finally a CT-guided biopsy of the tumor revealed a pulmonary adenocarcinoma, subsequently staged T2N1M0 by surgery. The patient underwent an uncomplicated lobectomy and subsequent out-patient chemotherapy. Five years after surgery the patient is completely alleviated of symptoms and remains without any sign of recurrence.
Image I: Digital clubbing and nail convexity of the fingers and toes (A-D)

Image II: Tc-99m MDP uptake in the periostea of the femoral, tibial (A-B), radial and ulnar bones (C).
DISCUSSION

In about 80% of HPOA cases, the syndrome is secondary to pulmonary neoplasms, most frequently adenocarcinoma and squamous cell carcinoma, although the differential diagnoses are ample. According to various reports, 0.2-17% of patients with pulmonary cancer develop signs of HPOA. Studies have indicated that the prevalence of patients presented with the complete HPOA triad of clubbing, arthritis and periostitis is less than 1%. The prevalence of patients presented with periostitis and typical scintigraphy findings without clubbing or arthritis is reported to be slightly higher [3,4]. The pathophysiology of HPOA is not yet fully known. Several mechanisms have been suggested, and recent reports indicate that growth factors may contribute to the clinical picture seen in HPOA. Serum levels of vascular endothelial growth factor (VEGF) are reported to be elevated in patients with lung cancer and HPOA [5-7]. One important theory is derived from the fact that many large circulating molecules, growth factors and platelets are cleared from the circulation in the pulmonary capillary bed. Structural abnormalities in the lung may cause a right-to-left shunt thereby increasing levels of growth factors in the systemic circulation. Growth factors, including VEGF, are angiogenic, and cause osteoblast and fibroblast proliferation. Increased levels of growth factors can thus explain all the features of HPOA, including clubbing and periostitis. A second potential mechanism includes ectopic production of hormone-like substances, such as VEGF by the tumor, resulting in elevated levels of circulating angiogenic substances [5-8]. A recent retrospective study by Qian et al. [9] showed prompt improvement of symptoms in 91.1% of surgically resected patients and in 77.4% of non-resected patients. The reported patient presented with the rare complete triad of HPOA, received the correct and timely diagnostic workup ensuring curative treatment with following alleviation of symptoms. The lack of FDG-avidity in the periostea of the tubular bones, having high uptake on the bone scan, has to our knowledge not been reported previously.

CONCLUSION

HPOA is a rare syndrome that frequently is related to lung neoplasms. It is of pivotal importance that clinicians encountering patients with a history of smoking presenting with clubbing, bone and joint pain ensure a rapid work-up including diagnostic imaging. This to disclose possible underlying malignancy, which caught in time, can be curatively treated. It is equally important that physicians at imaging departments keep this syndrome and its variations in mind when interpreting examinations.

REFERENCES


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