

Tropical fever

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CASE REPORT

A 58-year-old Caucasian woman with no medical history presented with diarrhoea and fever after a short visit to the North-Western region of Thailand. She complained of pain in her lower legs and joints and altered fingers, toes and nails. A positive history for smoking (40 pack-years) was present. Physical examination showed clubbed fingers and toes with eye-glass shape of the nails, painful joints with no signs of arthritis (*figure 1A*). Body temperature was 38.5 °C; no haemodynamic and respiratory instability was found. Additional laboratory investigation showed an erythrocyte sedimentation rate of 42 mm/U, leucocytes of $13.6 \times 10^9/l$, platelet count of $419 \times 10^9/l$ and a C-reactive protein of 48 mg/l. Because of her recent visit to the tropics, infectious disease was suspected, but blood and stool cultures were negative. No parasites were found in the stools. Serological and endoscopic examination for Whipple's disease, Yersinia and HIV were negative. An X-ray of her lower legs was performed which revealed a periostitis (*figure 1B*).

WHAT IS YOUR DIAGNOSIS?

See page 200 for the answer to this photo quiz.

Figure 1A. Clubbed fingers with eye-glass shape of the nails



Figure 1B. Periosteal reaction in the proximal tibia and fibula and the distal femur



DIAGNOSIS

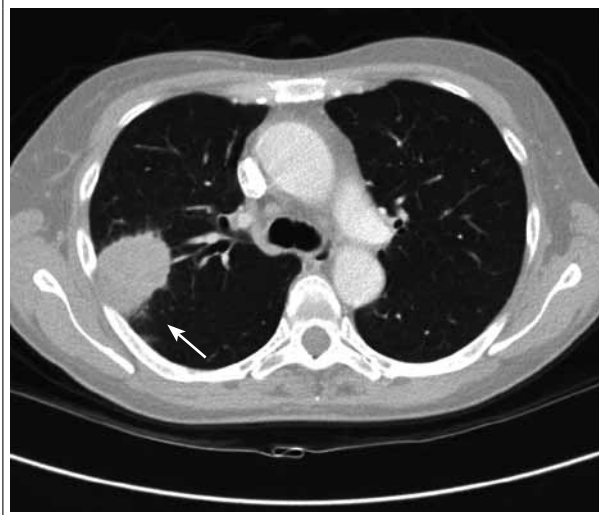
The symptoms and clinical signs of the patient were caused by a paraneoplastic sign called hypertrophic pulmonary osteoarthropathy (HPOA), also known as the Pierre-Marie-Bamberger syndrome. Additional investigation by chest X-ray and subsequent CT thorax revealed a mass in the right upper lung (*figure 2*). A lymph node biopsy confirmed adenocarcinoma of the lung. Typical signs of HPOA are symmetric periostoses on the diaphyses of the long tubular bones, clubbed fingers and toes with eye-glass shape of the nails, neuro-vegetative disturbances and dysproteinaemia. HPOA is strongly associated with lung carcinoma, but may also occur in a primary form, which is often familial and more common in males. Other secondary forms include carcinomas of the liver and gut, inflammatory bowel disease, liver cirrhosis, congenital cyanotic heart disease, pulmonary fibrosis, Graves' disease, thalassaemia and many other rarer conditions.¹ The incidence of HPOA associated with lung carcinoma is reported between 0.8 and 10%.^{2,3} The prevalence is higher in non-small cell lung carcinoma

(NSCLC) than in small cell lung carcinoma (SCLC).⁴ HPOA is associated with arteriovenous shunting, but the exact cause of HPOA is still unclear. Besides arteriovenous shunting humoral factors may play a role in HPOA. Production of growth factors such as platelet-derived growth factor and vascular-endothelial growth factor (VEGF), leading to angiogenesis, endothelial hyperplasia and clubbing may contribute to the onset of HPOA. Production of growth factor by malignant cells is the main source of endothelial stimulation and development of distal changes, although shunting due to local tissue destruction may contribute. Treatment is based on expert opinion as no clinical trials have been performed.⁵ Treatment is primarily focused on eliminating the aetiology of the HPOA (e.g. resection of the malignancy) and secondarily on treatment of symptoms of HPOA with NSAIDs, bisphosphonates, octreotide, vagotomy, and even chemotherapy with VEGF antagonists.⁵

This patient was treated for her adenocarcinoma with concurrent chemotherapy and radiotherapy and subsequently underwent surgery for lobectomy of the right upper lobe.

In conclusion, patients with a history of smoking and signs of HPOA should be screened for primary or secondary lung cancer.

Figure 2. CT scan of chest, showing right upper lobe tumour (arrow) with involvement of right hilar nodes



REFERENCES

1. Armstrong DJ, McCausland EM, Wright GD. Hypertrophic pulmonary osteoarthropathy (HPOA) (Pierre Marie-Bamberger syndrome): two cases presenting as acute inflammatory arthritis. Description and review of the literature. *Rheumatol Int.* 2007;27:399-402.
2. Izumi M, Takayama K, Yabuuchi H, Abe K, Nakanishi Y. Incidence of hypertrophic pulmonary osteoarthropathy associated with primary lung cancer. *Respirology.* 2010;15:809-12.
3. Segal AM, Mackenzie AH. Hypertrophic osteoarthropathy: a 10-year retrospective analysis. *Semin Arthritis Rheum.* 1982;12:220-32.
4. Sridhar KS, Lobo CF, Altman RD. Digital clubbing and lung cancer. *Chest.* 1998;114:1535-7.
5. Nguyen S, Hojjati M. Review of current therapies for secondary hypertrophic pulmonary osteoarthropathy. *Clin Rheumatol.* 2011;30:7-13.