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Prikaz slučaja/
Case Report

MARIE- BAMBERGER SYNDROME: DESCRIPTION AND REVIEW OF THE LITERATURE

MARIE- BAMBERGER SINDROM: PRIKAZ SLUČAJA SA PREGLEDOM LITERATURE

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Ključne reči:

hipertrofična plućna osteoartropatija, Bambergerov sindrom, radiografija

Abstract

Introduction: Hypertrophic pulmonary osteoarthropathy (HOA, Marie-Bumberger syndrome) is a main skeletal manifestation of paraneoplastic syndrome in patients with non-small cell lung carcinoma (80%). It is also a phenomenon of cyanotic congenital heart diseases and suppurative lung diseases. Symmetric periostitis of diaphyseal and metadiaphyseal portion of tubular bones is radiographic hallmark of HOA, while painful and swallen joints are main clinicaly manifestations. **Purpose:** Present the importance of radiography in early diagnostics of lung carcinoma with initial signs of hypertrophic osteoarthropathy. **Methods**: 60-year-old patient with the progressive pain in the knees and ankles, has been treated from osteoarthrosis in period of one year. Within diagnostics was made radiography of the knees and ankles. **Results:** Radiography of the bone structures shows, bilateral and symmetric periosteal proliferation of the diaphysis of femur, tibia and fibula. Additional radiography of the thorax shows until now undiagnosed infiltrative mass in pulmonary parenchyma, behind the heart shadow. Pathohistological verification confirmed the squamous-cell carcinoma of the lung. **Conclusion**: Symmetric periostitis can be first sign or quite discrete change on the bone radiography in patientens with undiagnosed lung carcinoma. When it is presented as only sign on the bone radiography in the adults with painful joints, should be suspected in lung carcinoma and expand examination with chest radiography.

INTRODUCTION

Hypertrophic osteoarthropathy (HOA) represents main skeletal manifestation of paraneoplastic syndrome in lung adenocarcinoma(1). It was in 1889 first described by Bamberger and in 1890 Marie called this entity „hypertrophic pulmonary osteoarthropathy“(2). The term hypertrophic pulmonary osteoarthropathy emphasized pulmonary pathology as the main cause of periostitis, although many other conditions like colorectal and hepatocelular carcinoma, inflammatory bowel disease, cirrhosis hepatis, congenital heart diseases, Graves' disease, thalassaemia and many other rare conditions may cause it (3-5). For this reason, this disorder in the Western world has long been strongly linked to primary bronchial carcinoma caused by cigarette smoking(4).

The aim of this study is to present one case of a patient with Marie-Bumberger syndrome and examine the relevant literature.

CASE REPORT

A 60 year-old patient appears on a examination at rheumatologist due to pain in the knees and ankles which are increasing more often, despite the applied therapy as well as occasional subfebrile temperatures up to 37.5 ° C. A year ago was him diagnosed ostheoporosis and suggested therapy with NSAIDs he was taking as needed. Within the diagnostics was made radiographs of the knees and ankle joints in the standard projections. On radiographs of bones structures, along the distal diaphysis of the femur and proximal and distal diaphysis of the tibia and fibula beside diffuse osteopenia, reveals bilateral and symmetric proliferative periosteal reaction (Fig. 1 and 2).

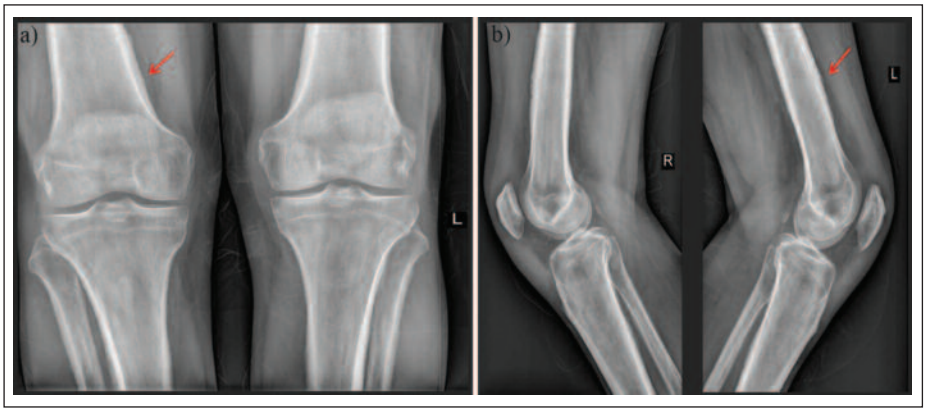

Figure 1. *Knee radiographs: a) AP and b) LL view*

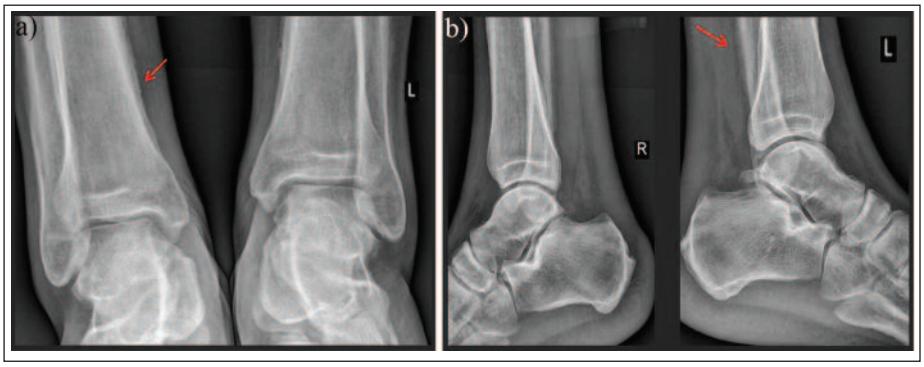

Figure 2. *Ankle radiographs: a) AP and b) LL view*

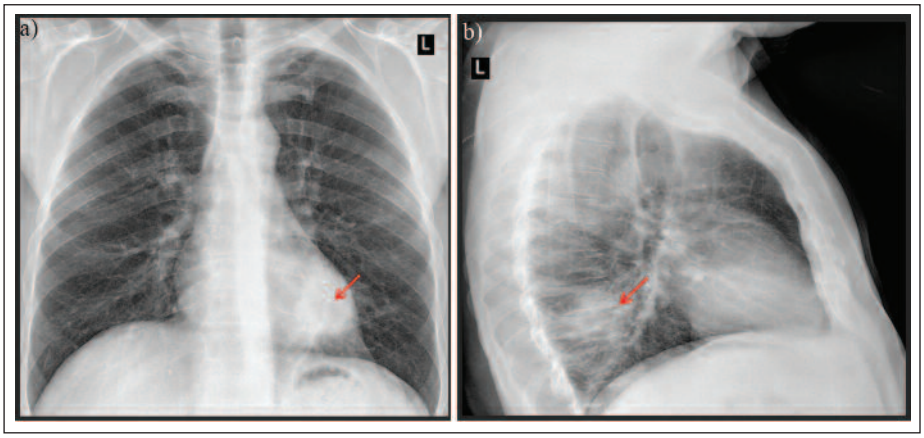

Figure 3*. Chest radiographs: a) PA and b) LL view*

Based on this radiographic finding, we suspected at hypertrophic pulmonary osteoarthropathy. Additional standards radiographic examination of thorax reveals until now undiagnosed 4x3 cm infiltrative mass in left pulmonary parenchyma, behind the heart shadow (Fig. 3).

Further diagnostics and pathohistological verification was confirmed the squamous cell carcinoma of the lung.

DISCUSSION

Hypertrophic osteoarthropathy is a clinical syndrome characterized by the appearance of clubbing of the digits, swelling of the extremities, painful and swolen joints, symmetric periostitis of diaphysis and metadiaphysis portion of tubular bones of the proximal and distal extremities [6]. The syndrome is classified in two category as primary (hereditary or idiopathic) and secondary HOA.

Primary HOA or pachydermoperiostosis (Touraine-Solente-Gole syndrome) is rare hereditary disease with autosomal dominance that occurs in 3-5% of all cases, more common in men in adolescence and as a familial form [7]. It is also characterized by skin changes with excessive sweating, which in secondary forms of the disease are not found.

Far more often is the secondary HOA or HPOA (Marie-Bumberger syndrome) most commonly associated with intrathoracic malignancies, supurative pulmonary diseases (bronchiectasis, empyema, abscesses, cystic fibrosis), and congenital cardiac diseases [8]. The secondary HOA is most commonly found in hormone-active tumours such as lung adenocarcinoma, ovary, breast carcinoma and lymphoma[9]. HOA occurs in 1-5% non-microcellular carcinoma and may precede the manifestation other signs of tumours. Often is HOA overlooked by a physician, because of mimicry with numerous rheumatologic and neurologic diseases [1]. However the secondary HOA is often associated with pulmonary malignancies, of which 80% refers to primary lung carcinoma [10], while in about 10% it is associated with pleural tumors [11]. It is described that HOA may be associated with neurofibrosarcoma of diaphragm [12]. Also can be associated with pulmonary metastasis of renal carcinoma [2]. As a rarity, cases of HOA have been reported in people with thymic carcinoma [13].

The pathophysiological mechanism has not yet been fully clarified, but rheumatic syndromes associated with carcinoma may occur by one of following mechanism: direct tumour invasion of bones, joints or muscles; altered immune surveillance causing both the rheumatic and neoplastic diseases; or adverse reactions to anticancer therapy [14]. The pathogenesis of secondary HOA remains poorly understood. Hormonal disturbances, cytokine and autoimmune dysfunction are some of the factors leading to manifestation of HOA. Studies showed that vascular endothelial growth factor (VEGF) may have a key role in pathogenesis [14]. It was reported as well that platelet-derived growth factor (PDGF) and TGF-beta can be cause of fibroblast growing and collagen synthesis. A gene that defines prostaglandin E2 degradation, as cause of inflammation, can play a role in etiopathogenesis of HOA [10]. It was showed that HOA, even in the context of arthropathic aspects, can regrade after vagotomy, which implies vasovagal stimulation in the formation of HOA [2]. It is important to mention the role of hypoxia in stimulating the proliferation of periostal cells

with subsequent periostal thickening and clubbing [15-17]. Also, roles of neurogenic stimuli, toxic substances, chemical irritants, hypervascularity and increased deoxygenated blood cannot be excluded [18].

Skeletal manifestation is first manifestation of a paraneoplastic syndrome which can precede the manifestation of a tumor. Symptoms of HOA can be diveded into pulmonary and extrapulmonary symptoms. Pulmonary symptoms mainly include pleural pain, cough and haemoptysis [8], while extrapulmonary symptoms include clubbed fingers, pain and swelling of the extremities, pain in bones und joints, subfebrility, thickening of the face skin, so it arises asymmetrical convolutions of the forehead, hypertrophy of the eyelids and prominent nasolabial folds. Sinovial fluid is viscous without signs of inflammation [4].

Skeletal manifestation of HOA are primarily detected radiographically, folowed by the other radiological diagnostic procedures such as CT, MRI and scintigraphy [19].

Skeletal radiography is usually sufficient to raise suspicion of HOA. In the presented case, based on the skeletal findings, it is suspected of the tumor of the lungs, which prove it by chest radiography, although it is most often described in the literature that changes in the bones were seen after a diagnosed lung tumor [6].

Differential diagnosis of secundary HOA included numerous intrathoracic and extrathoracic diseases (tumours, infections, inflamatory diseases, endocrine disorders such as acromegaly, vascular diseases) [20,17].

Complete resolution of HOA had been seen with cure of the primary disease, especially after removal of primary tumour with chemotherapy and/or radiotherapy with the resection and/or adjuvant chemotherapy of operable lesions [17]. The most communly used therapy for HOA includes atropine sulfate which leads to chemical vagotomy, as well as subcutaneous octreotide, high dose Colchicine, bisphosphonates. Indomethacin, as prostaglandin synthetase inhibitor, leads to significant pain reduction, and the study has been shown that can also inhibit new bone formation [16]. It is important that that symptomes of this disease are mostly self-limiting lasting for 5-10 years and completely disappear, if it is a primary form, whereas in the case of a secondary form, symptomes disappear with cure of the primary disease [18].

CONCLUSION

Malignant neoplasms are associated with a wide range of rheumatic diseases. Symmetric periostitis can be a first or quite discrete change on the X ray of the bones in patients with undiagnosed lung carcinoma. With this example, we want to point out the importance of correct performance and interpretations of classical radiography of the skeletal system, which, as in this case, can be of crucial importance for establishing accurate and complete diagnosis of malignancy of remote localizations.

Sažetak

Uvod: Sekundarna hipertrofična osteoartropatija (HOA, Marie-Bumberger sindrom) predstavlja glavnu skeletnu manifestaciju paraneoplastičnog sindroma primarnih nemikrocelularnih karcinoma pluća (80%), a propratni je fenomen kongenitalnih srčanih i supurativnih plućnih oboljenja. Karakteriše je simetrični periostitis na dijafizama i metafizno-dijafiznim prelazima dugih kostiju gornjih i donjih ekstemiteta, batičasti prsti i otok ekstremiteta. **Cilj:** prikazaćemo značaj klasične radiografije u ranom dijagnostikovanju karcinoma pluća sa početnim znacima hipertrofične osteoartropatije. **Materijal i metode:** pacijent starosti 60 godina, godinu dana se leči od osteoartroze, a kako su se bolovi intenzivirali, ponovo se javlja na pregled kod reumatologa koji indikuje RTG kolenih i skočnih zglobova u dva pravca. Rezultati: na prikazanim koštanim strukturama osim difuzne osteopenije, uočava se izražena proliferativna reakcija periosta obostrano i simetrično duž distalnih dijafiza femura i proksimalnih i distalnih dijafiza tibije i fibule. Na osnovu radiografija koštanih struktura postavljena je sumnja na HOA. Pregled je dopunjen standardnom radiografijom srca i pluća, na kojoj je uočena do tada nedijagnostikovana infiltrativna promena u plućnom parenhimu. Nakon dopunske dijagnostike i pato-histološke verifikacije, dokazano je da se radi o skvamocelularnom karcinomu pluća. **Zaključak**: simetrični periostitis nekada može biti prva i sasvim diskretna promena na radiografijama skeleta kod pacijenata sa nedijagnostikovanim karcinomom pluća. Kada se ove promene uoče na kostima kod pacijenata u odrasloj populaciji, uvek treba posumnjati na karcinom pluća i pregled dopuniti radiografijom srca i pluća.

LITERATURA

1. Lomatzsch M, Julius P, Luck W, Bier A, Virchow JC. Hypertrophic pulmonary osteoarthropaty as a cue for NSCLC: four cases in the light of the current literature. Pneumologie. 2012; 66 (2): 67-73.

2. Goldstraw P, Walbaum PR. Hypertrophic pulmonary osteoarthropathy and its occurrence with pulmonary metastases from renal carcinoma. Thorax. 1976; 31: 205-211.

3. Khalid A, Baqai MT. Primary hypertrophic osteoarthropathy. J Pak Med Assoc 2014; (7):843-5.

4. 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(4):399-402.

5. Niu J, Gelbspan D, Chong L, Birdsall S, Weitz D, Weiss GJ. Lung Adenocarcinoma Presenting with WDHA Syndrome and MarieBamberger Syndrome: A Case Report. J Clin Exp Oncol 2013, 2:3.

6. Ito T, Goto K, Yoh K at all. Hypertrophic pulmonary osteoarthropathy as a paraneoplastic manifestation of lung cancer. J Thorac Oncol. 2010; 5 (7): 976-80.

7. Martínez-Lavín M, Pineda C, Valdez T, Cajigas JC, Weisman M, Gerber N, Steigler D. Primary hypertrophic osteoarthropathy. Semin Arthritis Rheum. 1988;17(3):156-62.

8. Serafinella PC, Guarneri C, Borgia F, Vaccaro M. Pierre- Marie- Bamberger syndrome (secondary hypertrophic osteoarthropathy). Int J Dermatol. 2005; 44 (1): 41-2.

9. Aggarwal R, Oddis CV. Paraneoplastic myalgias and myositis. Rheum Dis Clin North Am. 2011; 37 (4) : 607-21.

10. Perković D et al. Paraneoplastična hipertrofična osteoartropatija. Reumatizam. 2013; 60 (1) : 29-31.

11. Mito K, Maruyama R, Uenishi Y, Arita K, Kawano H, Kashima K, Nasu M.Hypertrophic pulmonary osteoarthropathy associated with non-small cell lung cancer demonstrated growth hormone- releasing hormone by imunohistochemical analysis. Internal Med. 2001; 40(6): 532-5.

12. Parish C. Complications of mediastinal neural tumours. Thorax. 1971; 26 :392.

13. Kim SJ, Seo JH, Choi CW, Lee ES, Seo BK, Kim JS. Unusual presentation of thymic carcinoma: hypertrophic osteoarthropathy. Korean J Intern Med. 2003; 18(2):125-8.

14. Nahar I, Al-Shemmeri M, Hussain M. Secondary hypertrophic osteoarthropathy : new insights on pathogenesis and management. G. J. O. 2007; 1 (1): 71-76.

15. Carroll DG Jr. Curvature of the nails, clubbing of the fingers and hypertrophic pulmonary osteoarthropathy. Trans Am Clin Climatol Assoc. 1972;83:198-208.

16. Leung FW, Williams AJ, Fan P. Indomethacin therapy for hyperthrophic pulmonary osteoarthropathy in patients with bronchogenic carcinoma. West J Med. 1985; 142: 345-347.

17. Yao Q, Altman RD, Brahn E. Periostitis and hypertrophic pulmonary osteoarthropathy: report of 2 cases and review od the literature. Semin Arthritis Rheum. 2009; 38 (6): 458-466.

18. Cannavò SP, Guarneri C, Borgia F, Vaccaro M. Pierre Marie-Bamberger syndrome (secondary hypertrophic osteoarthropathy). Int J Dermatol. 2005;44(1):41-2.

19. Donald Resnick, Diagnosis of bone and joint disorders, Fourth edition, vol. 5, 3565-3584p.

20. Sadikot RT Johnson J, Loyd JE, Christman JW. Respiratory bronchiolitis associated with severe dyspnea, exertional hypoxemia, and clubbing. Chest. 2000;117(1):282-5.

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