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Hypertrophic pulmonary osteoarthropathy in Acquired Immunodeficiency Syndrome. Case Report and Review.

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Key words: Clubbing, hippocratic fingers, hypertrophic osteoarthropathy, HIV, AIDS, tuberculosis.

Abstract. We describe a case of hypertrophic pulmonary osteoarthropathy (HPOA) in an adult patient with acquired immunodeficiency syndrome (AIDS). This is the ninth case of HPOA associated with AIDS in adults, reported in the literature. The presence of pulmonary tuberculosis was also suspected, based on clinical grounds. Cases of clubbing associated with AIDS infection are reviewed.

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Palabras clave: Dedos palillo tambor, hipocratismo digital, osteoartropatía hipertrófica, HIV, SIDA, tuberculosis.

Resumen. Se presenta un caso de osteoartropatía hipertrófica pulmonar (OHP) en un paciente adulto infectado con el síndrome de inmunodeficiencia adquirida (SIDA). Este es el noveno caso de OHP asociado con SIDA registrado en la literatura. Se sospechó igualmente la presencia de tuberculosis pulmonar sobre la base de criterios clínicos. Se revisan los casos de dedos en palillo de tambor y SIDA reportados.

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INTRODUCTION

Digital clubbing, first described approximately 2400 years ago by Hippocrates, is one of the oldest and best-known physical signs in clinical medicine (1).

Simple clubbing of the fingers and toes has always been of interest to clinicians, but it was not until the nineteenth century when it received sufficient attention. Pigeaux in 1832 was the first to use the term "Hippocratic fingers" (2). Bamberger in 1889 and Marie in 1890 described clubbing of the fingers associated with general thickening and sclerosis of long bones and suggested the name of pulmonary hypertrophic osteoarthropathy (HPOA) to describe this condition (3, 4).

Since its recognition as a manifestation of systemic disease, a large number of entities including neoplasia, chronic inflammatory and fibrosing process (principally related to the lung) have been associated with clubbing. Pulmonary fibrosis, lung abscess, bronchiectasis, mesothelioma and bronchogenic carcinoma are all well known causes (5).

However, it is rare to find in the medical literature this condition, in adults, associated with Human Immunodeficiency Virus infection (HIV) or Acquired Immunodeficiency Syndrome (AIDS).

In this paper we present a case of an AIDS patient who developed clubbing of the fingers in the course of his illness, probably associated with the presence of pulmonary tuberculosis. A literature review of articles reporting pertaining cases of this association, was done using the MEDLINE database and the manual survey of bibliographies or the retrieved articles.

CASE REPORT

A 33 year old homosexual man with positive western blot assay for HIV antigens p17, p24, p31, gp41,p51-55, p65, gp 120 and gp 160 since 1991, was in control in our division because of perianal condylomata.

Since 1997 he had noted progressive enlargement of the tips of his fingers and toes, with occasional polyarthralgias and bilateral ankle swelling. He also reported a history of dry cough, progressive dyspnoea and intermittent fever of several months of duration.

He developed oral candidiasis in 1991, and cutaneous Kaposi's sarcoma lesions in legs and buttocks in 1996. The lesions spontaneously regressed without specific treatment. He never smoked and there was no history of abdominal pain, jaundice, nausea, diarrhea, hepatitis or family clubbing. He receives Zidovudine irregularly since 1995.

The physical exam disclosed clubbing of the fingers (Figs. 1a, 1b) and toes with no other abnormality. The hemoglobin was 12,3 g/dl, the glutamic oxalacetic transaminase (SGOT) 20 U/l, the lactic dehydrogenase (LDH) 89 U/l; and the alkaline phosphatase 42 U/l. The rest of laboratory tests were normal except

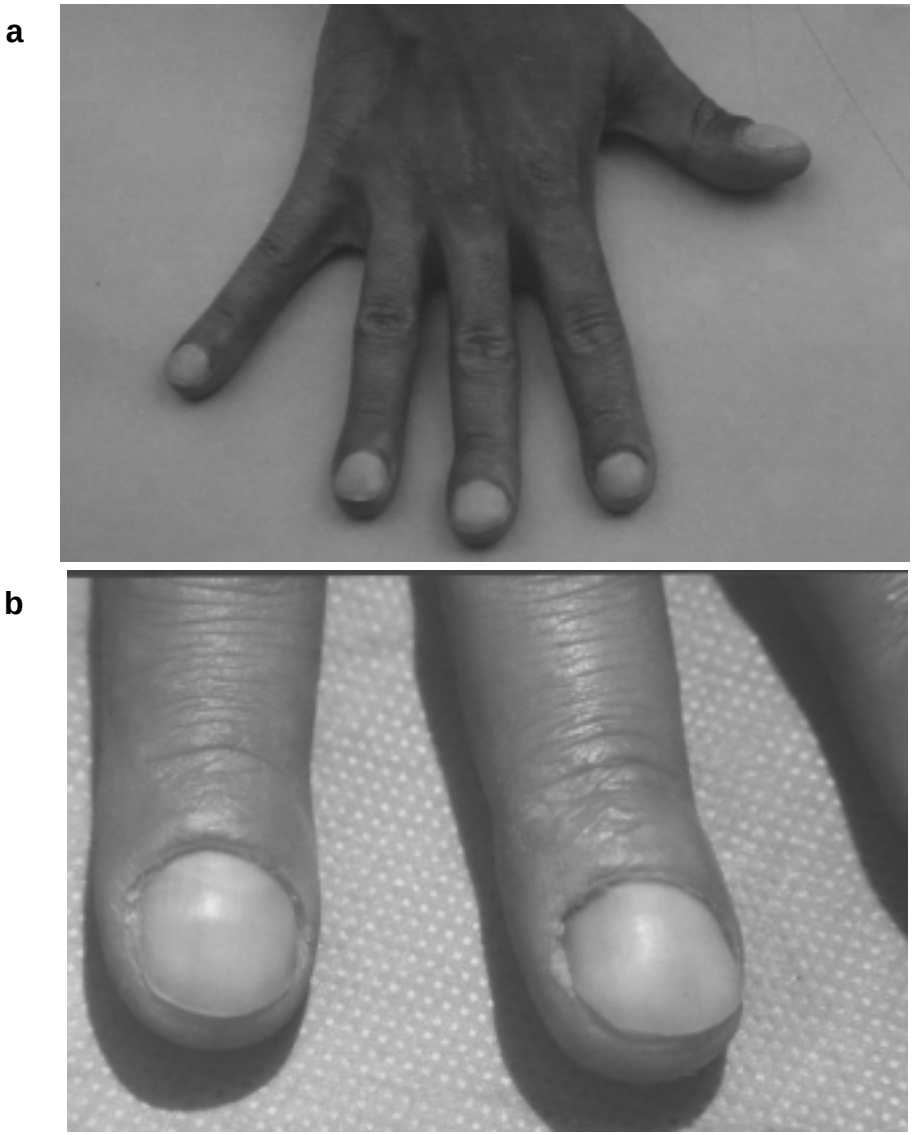

Fig. 1a,b. Clubbing of the patient's fingers.

for an elevated erythrosedimentation rate (110 mm/ h Westergren method) and a low number of CD4 positive lymphocytes (191 x 10^9/ l). The diameter of a PPD skin test was 26 mm (Fig. 2) and a chest X-ray showed a fine interstitial bilateral alveolar pattern (Figs. 3, 4). Periosteal elevation and subperiosteal new bone formation in the diaphysis of the tibia, fibula and metacarpals were noted in bone X-rays (Fig. 5).

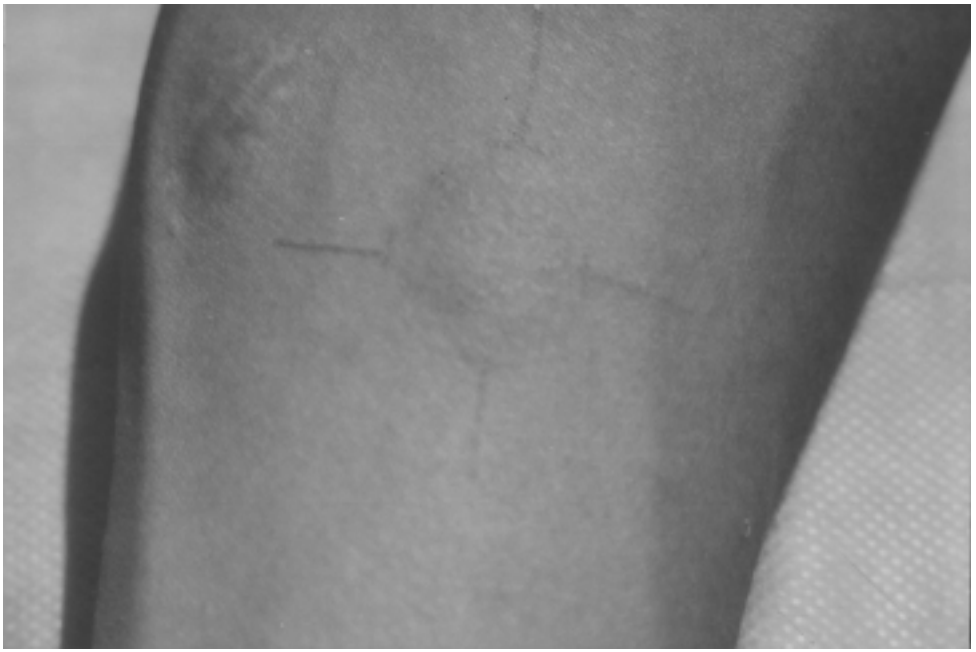

Fig. 2. A positive PPD skin test.

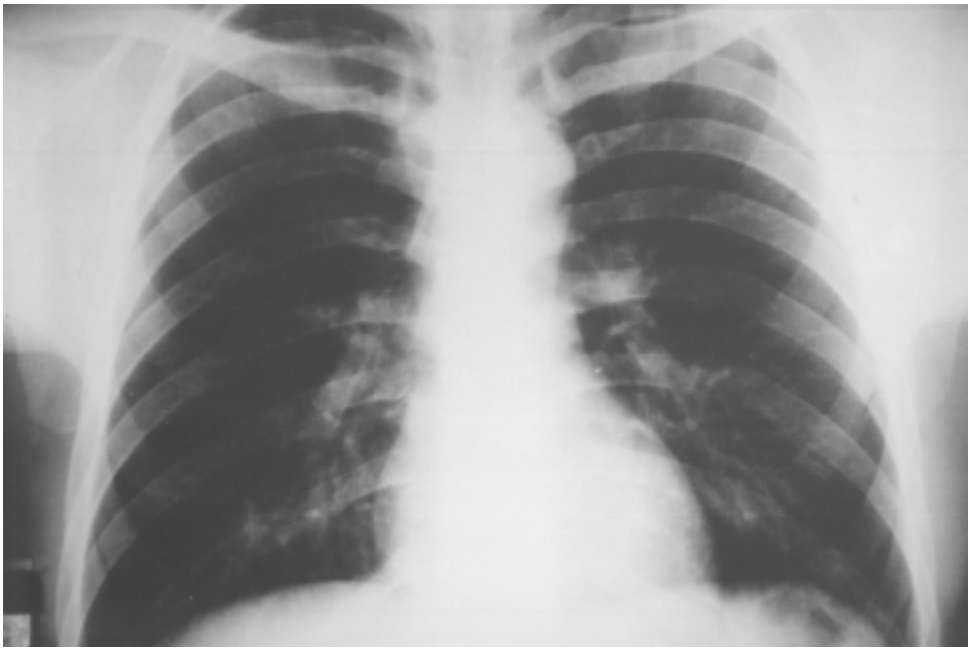

Fig. 3. Pulmonary X-ray showing bilateral alveolar infiltrates.

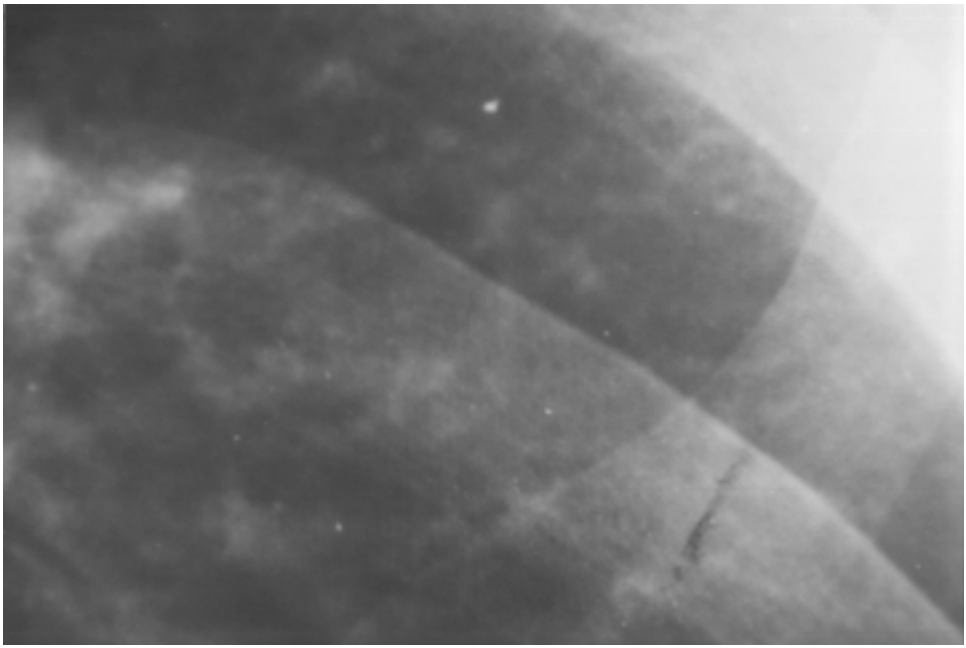

Fig. 4. Detailed view of the alveolar infiltrates in the left inferior third.

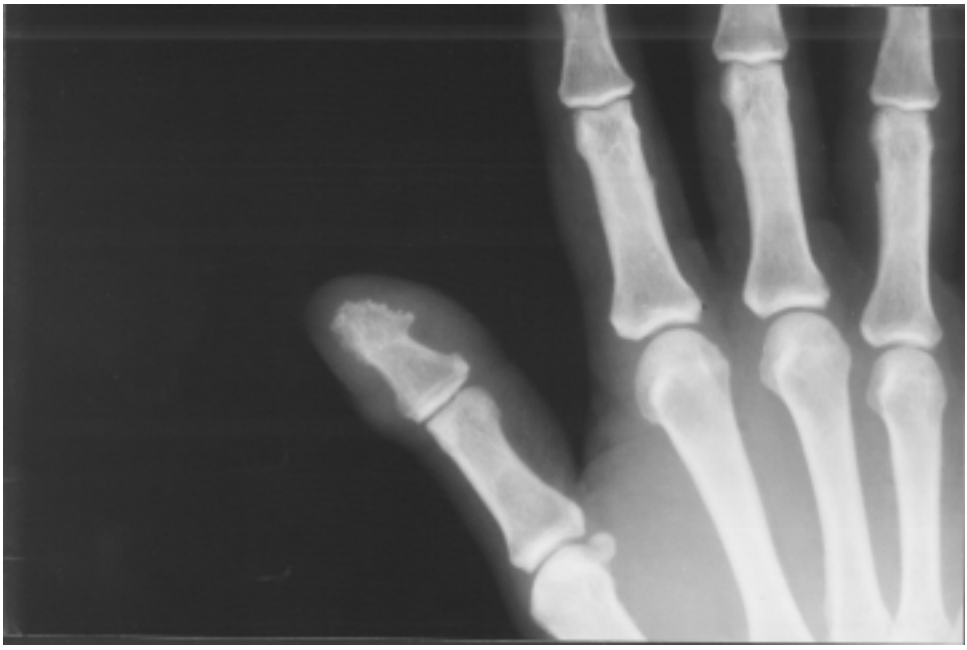

Fig. 5. Classical bulbous deformity of the fingertip with periosteal apposition.

Efforts were made to obtain sputum samples without success. Hystoplasmosis, paracoccidiodomycosis, coccidiodomycosis and aspergylosis serologies were all negative. VDRL was negative and an arterial gasometry was normal. A sigmoidoscopic examination to 25 cm disclosed no lesion. The patient refused bronchoscopic examination or transbronchial biopsy.

On the basis of the rapid development of clubbing, the absence of a family history of this disorder, the arthralgias and the subperiosteal bone formation, a diagnosis of (HPOA) was done. A presumptive diagnosis of tuberculosis was also done based on clinical criteria. The patient received a 2 months course of antituberculous therapy with isoniazid (INH), rifampicin (RIF), ethambutol (EMB) and pyrazinamide (PZA) followed by (INH) and (RIF) for 4 months. The constitutional symptoms mentioned above rapidly resolved when the treatment was started. A permanent relief of arthralgia, and ankle enlargement were also achieved. Clubbing however did not regress until the date of this report.

DISCUSSION

The term “clubbing of the fingers” is used to denote an increase in the phalangeal soft tissue and nail convexity, enlargement of nailbed area and thickness with loss of the normal nail angle. The diagnosis is made when the normal angle of 15-20 between the nail bed and the cuticule is lost. (6)

Hypertrophic pulmonary osteoarthropathy or secondary hypertrophic osteoarthropathy (HPOA) occurs in the course of various chronic conditions and is characterized by a general and symmetrical hypertrophy of the distal phalanges and toes with clubbing (acropachy). This alteration is frequently accompanied by enlargement of some of the others bones in the hands and feet or by hypertrophy of the bones of the forearms and legs, and in late stages by involvement of the joints, and polyarthralgia (2).

When a clinician is confronted with individual who acutely develops any of the manifestations of this syndrome, a through search for an underlying illness should be undertaken with special attention directed to the chest where the most frequent causes (malignant primary or metastatic tumors) are located. However the clinician must be aware to exclude disorders of the gastrointestinal tract (esophageal, small bowel, or colon cancer, inflammatory bowel disease), liver (cirrhosis, carcinoma) and other rare causes, as Graves disease, thalassemia and diverse malignancies (5).

Since the first cases of acquired immunodeficiency syndrome (AIDS) were identified in 1981, this syndrome has been associated with a wide variety of clinical abnormalities, especially opportunistic infections and cancers. Rheumatic syndromes reported in individuals infected with HIV are diverse and include: oligoarthropathy, polymiositis, Sjögren syndrome, vasculitis and septic

arthritis; however, HPOA associated with HIV infection or AIDS has rarely been described (7).

Since the first report by Harris in 1988 (8), only eight additional cases have been described (Table I). All cases occurred in young homosexual men with a mean age of 29,37 years (range between 28 to 39 years). In most cases (62,5%), the time between positive HIV diagnosis and clubbing appearance was unknown. When this data could be ascertained, six years was approximately the time elapsed. Our patient fit this pattern.

In the cases reported, pneumonia were related to clubbing in four patients. Pneumocystis carinii was the cause in three of these patients and *Bacteroides melaninogenicus* was identified in the last one (9-12). Boonen *et al* (13) found two additional cases of clubbing and HIV infection. One of their patients was HBs-Ag positive, and the other showed a polymerase chain reaction positive for hepatitis C. Although they could not certainly exclude chronic hepatitis B or C as the cause of the disorder, they though HIV infection was the primary cause. The last patient (14) had disseminated tuberculosis and Visceral Leishmaniasis as recurrent concomitant infections.

In areas where HIV infection is frequent, the situation is different in children. Graham *et al* (15) reported a high rate of HIV infection and pulmonary tuberculosis associated with digital clubbing in Malawian children. However they did no mention the number of HIV positive patients or AIDS cases associated with tuberculosis they found. Smyth *et al* (16) in a similar area, found finger clubbing in one HIV positive child who had a persistent right-sided empyema.

We believe that our patient represents a new case of HPOA in an dult with AIDS and probably, se - condary to pulmonary tuberculosis. Tuberculosis diagnosis was based on the clinical history, radiological pattern, elevated ESR, high positivity of the PPD skin test and the response to treatment.

In the immunocompromised patient *Mycobacterium tuberculosis* remains a constant concern and diagnosis relies on a high level of suspicion. In spite of unreliability of the tuberculin skin test in these patients, because of anergy, a positive test identifies patients with tuberculosis infection and therefore, risk of clinical disease (17).

P. carinii pneumonia can cause a similar clinical picture of weight loss and fever in AIDS patients, however, the low level of lactate dehydrogenase, the normal blood oxygen content, and the rapid response to antituberculosis treatment, made this diagnosis improbable in this setting.

As Bezunegui *et al* (14), we must conclude that the potential relationship between clubbing and HIV infection is difficult to ascertain in cases reported so far. Physicians treating HIV-infected patients must carefully search for an opportunistic infection such as *Pneumocystis cari-*

TABLE I
CLUBBING FINGERS AND HIV INFECTION IN ADULTS (CASES REPORTED)

AUTHOR	YEAR	AGE	SEX	EVOLUTION TIME SINCE HIV POSITIVITY	ASSOCIATED INFECTIONS	TYPE INFECTION	CHEST X RAY
Harris (7)	1988	33	M	Not known	NO	-	Normal
Bhat *et al* (8)	1989	37	M	Not known	YES	*Pneumocystis carinii* pneumonia	Bilatelar alveolar-interstitial infiltrates
Lena *et al* (9)	1991	33	M	Not known	YES	*Pneumocystis carinii* pneumonia	Bilateral alveolar interstitial involvement
May *et al* (10)	1993	29	M	6 years	YES	*Pneumocystis carinii* pneumonia	Alveolar infiltrate in right lower lobe with right sided pleural reaction
Gil-Garcia *et al* (11)	1993	29	M	Not known	YES	*Bacteroides melaninogenicus* pneumonia	Consolidation. Multiple cavitations Pneumonitis necrotising
Boonen *et al* (12)	1996	36	M	6 years	YES	HBs-Ag positive Hbe-Ag negative	Increased interstitial density of both lower lung fields
Boonen *et al* (12)	1996	39	M	Recently ?	YES	PCR positive for Hepatitis C	Normal
Belzunegui *et al* (13)	1997	28	M	6 years	YES	Past disseminated tuberculosis and visceral leishmaniasis	Normal

nii pneumonia or pulmonary tuberculosis when clubbing is found.

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