SECONDARY HYPERTROPHIC OSTEOARTHROPATHY

AN UNUSUAL CAUSE OF ARTHRITIS IN CHILDHOOD

R. E. PETTY, J. T. CASSIDY, R. HEYN, A. G. KENIEN, and R. L. WASHBURN

Although an uncommon occurrence in childhood, hypertrophic osteoarthropathy secondary to tumors—most commonly to osteogenic sarcoma with pulmonary metastasis—may cause severe joint pain and swelling. The syndrome should be considered in the differential diagnosis of acute arthritis in childhood.

Hypertrophic osteoarthropathy secondary to chronic pulmonary suppuration or tumor is rare in childhood (1), although digital clubbing alone is common. When fully developed, the syndrome consists of terminal clubbing of digits, roentgenographic evidence of periosteal new bone formation at the distal ends of long bones, arthritis, and profuse sweating. The arthritis may precede clubbing (1) and is sometimes painless. The objective findings consist of soft tissue swelling of large joints, restriction of motion, and subcutaneous edema.

This paper reports 2 cases of acute osteoarthropathy in childhood associated with pulmonary metastases of osteogenic sarcoma.

From the Sections of Rheumatology and Hematology, Department of Pediatrics and Communicable Diseases and Department of Radiology, University of Michigan Medical School and C. S. Mott Children's Hospital, Ann Arbor, Michigan.

R. E. Petty, M. D.: Section of Rheumatology, University of Michigan Medical School; J. T. Cassidy, M.D.: Section of Rheumatology, University of Michigan Medical School; R. Heyn, M.D.: Section of Hematology, University of Michigan Medical School; A. G. Kenien, M.D.: Section of Rheumatology, University of Michigan Medical School; R. L. Washburn: Department of Radiology, C. S. Mott Children's Hospital.

Address reprint requests to R. E. Petty, M.D., Section of Pediatric Rheumatology, Department of Pediatrics and Communicable Diseases, University of Michigan Medical Center, Ann Arbor, Michigan 48109.

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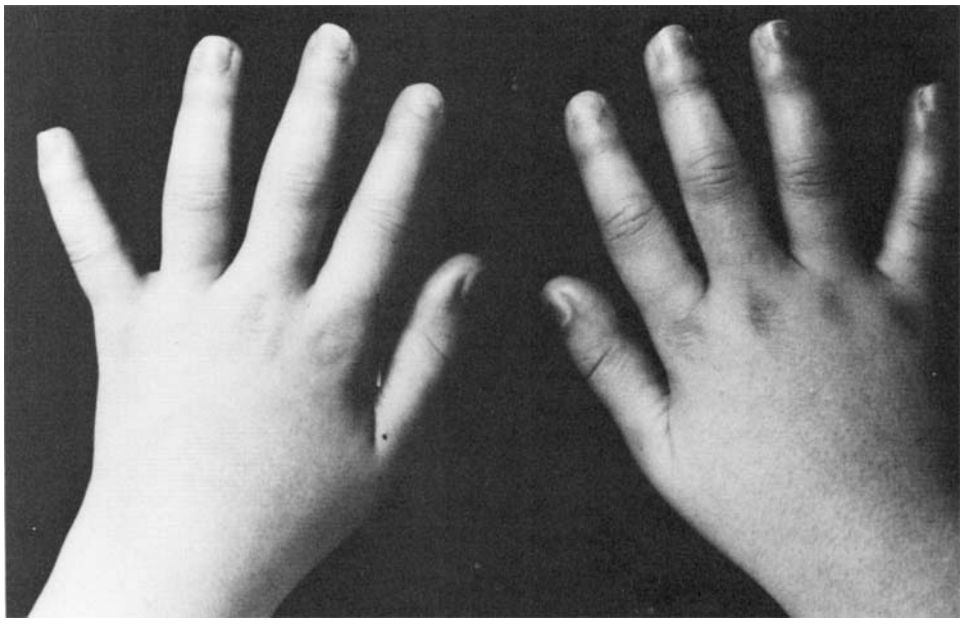
CASE REPORTS

Case 1

MF, an 11-year-old male Caucasian, was well until October 1973, when a limp and pain in the right leg led to a diagnosis of osteogenic sarcoma of the right femur. This condition was treated at another institution in March 1974 by amputation.

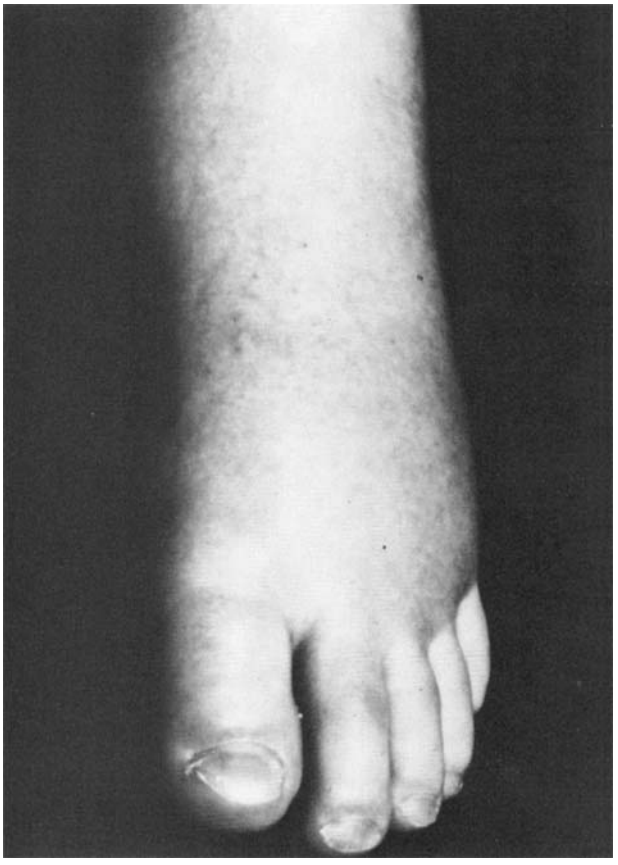
The patient remained well until February 1975, when he developed acute pain and swelling in joints of his hands, wrists, elbows, ankle, and knee and fevers to 103°F. He appeared acutely ill and was sweating profusely. Blood pressure was 108/72 mm Hg, pulse 128/minute, and respirations 76/minute. There was marked swelling over the dorsa of both hands and wrists, the elbows, dorsum of the foot, ankle, and knee (Figure 1). These areas were exquisitely tender to touch and movement. The pretibial swelling pitted. There were several petechiae on the left ankle and foot and a faint macular erythema on the inner aspects of the arms and forearms. There were palpable fluid and warmth in the metacarpophalangeal and proximal interphalangeal joints, wrists, and knee.

Pertinent laboratory studies included a hemoglobin of 11.8 g/100 ml, white blood cell count of 11,400/cm^3 with 86% segmented neutrophils, 8% lymphocytes, and 6% monocytes. There were 392,000 platelets/cm^3. Erythrocyte sedimentation rate was 56 mm/hour. Urinalysis was normal. Total serum



A

Fig 1. A. *Moderate clubbing of the digits and soft tissue swelling of the proximal interphalangeal joints of the hands.* **B.** *There is marked pitting edema of the dorsum of the foot.*



B

protein was 6.7 g/100 ml: 46% albumin, 6% alpha-1, 20% alpha-2, 12.3% beta, and 14.2% γ-globulins. Tests for antinuclear antibody, the serologic test for syphilis, and the Coombs' test were negative. Total hemolytic complement and immunoglobulins were normal. X-ray films showed periosteal elevation on the distal ulnar shafts (Figure 2), the fifth metacarpals, and the first left metatarsal. Chest films showed a rounded lesion in the left hilum which laminograms revealed to be a 3 × 6 cm oval mass adjacent to the main stem bronchus of the left lower lobe. Liver and spleen scans with 99-Technetium were normal. A bone scan with 99-Technetium revealed increased uptake compatible with secondary hypertrophic osteoarthropathy (Figure 3) in forearms, clavicles, sternum, and tibia. There was no uptake of the isotope in the pulmonary metastases. Bone marrow examination was normal.

Treatment with acetylsalicylic acid was instituted in a dose of 60 g/day with rapid marked improvement in joint pain, swelling, and fever. During the next week the joint findings disappeared. A metastasis was resected subsequently from the left lung. Recurrence of lung metastases 3 months later was accompanied by a return of hypertrophic osteoarthropathy of severe degree (Figure 4). This episode was not controlled clinically by acetylsalicylic acid or indomethacin.

Case 2

PL was a 13-year-old female Caucasian who experienced pain and swelling of her left knee following minor trauma. A diagnosis of osteogenic sarcoma was made and femoral disarticulation was performed. Three months later

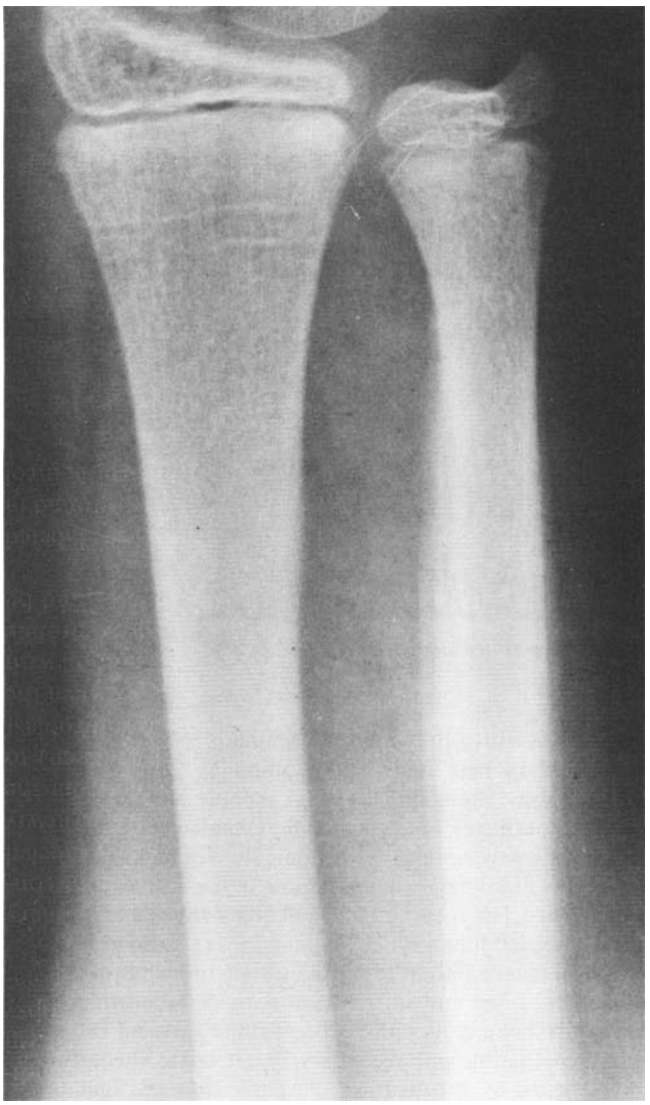


Fig 2. *Subperiosteal new bone formation along the shaft of the ulna.*

multiple pulmonary nodules appeared coincident with the development of fever and arthralgias. She was treated with x-irradiation, dactinomycin, vincristine, and cyclophosphamide. The patient was essentially asymptomatic except for persistent pain, limited range of motion, and swelling of her right knee.

Physical examination revealed profuse sweating, total alopecia of the scalp, and a left femoral disarticulation. There was clubbing of all digits, swelling of the small joints of the hands, and moderate pitting edema of the right leg. There were swelling and an effusion, increased warmth, and marked limitation of flexion of the right knee. A chest film showed a large mass within the right hemithorax and nodular lesions at the left base and in the left upper lung field. X-ray films of the hands and wrists showed subperiosteal new bone formation along the lateral aspects of the proximal phalanges of the fingers and similar changes about the distal radii and ulnae. X-ray films of the right knee revealed a moderate degree of soft tissue swelling and generalized demineralization.

An arthrocentesis yielded 15 ml of yellow fluid of moderate viscosity. Synovial fluid analysis showed 45 red

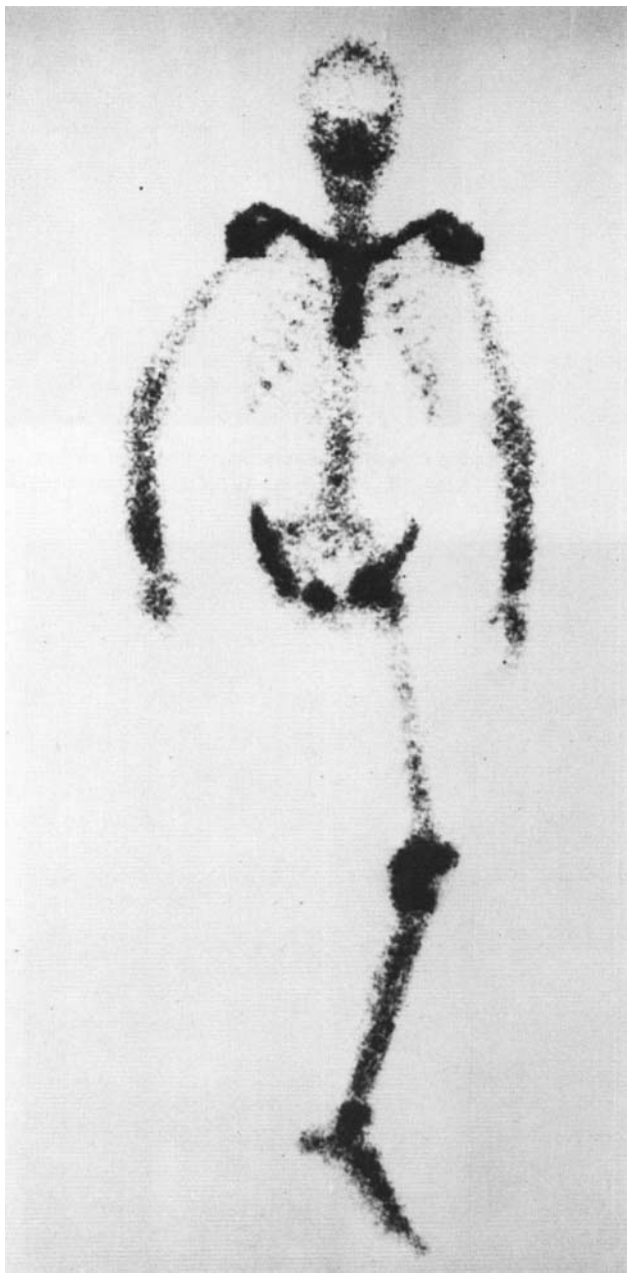


Fig 3. *Bone scan shows disarticulation of the right lower extremity and increased accumulation of the isotope in the clavicles, glenohumeral articulations, sternum, forearms, and left tibia. There is no uptake of the isotope in the pulmonary metastases.*

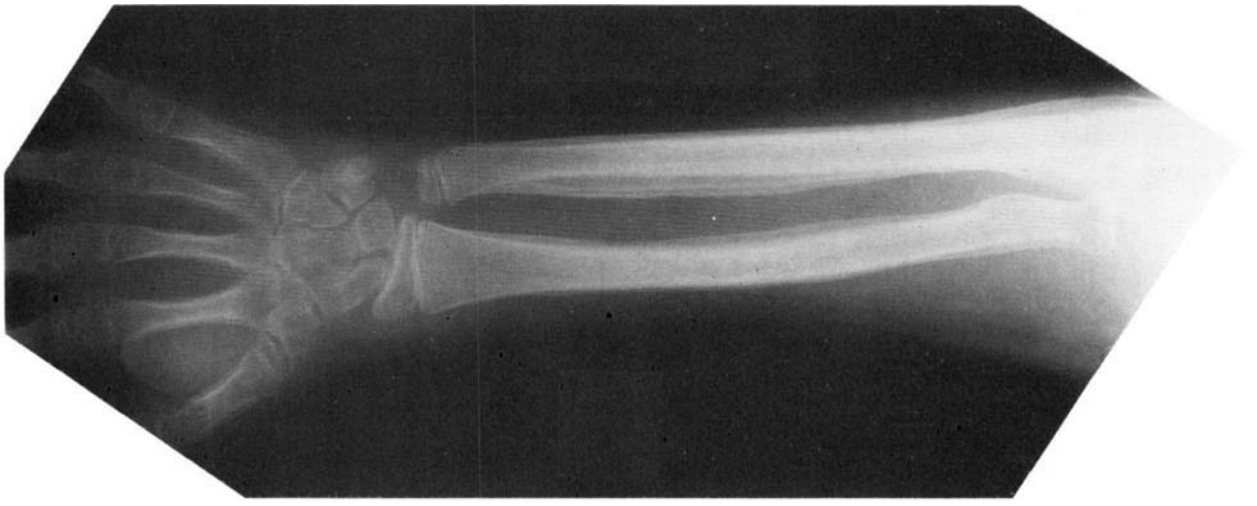


Fig 4. *Marked subperiosteal new bone formation along radius, ulna, metacarpal shafts, and phalanges.*

blood cells and 1354 white blood cells consisting of 98% mononuclear cells and 2% segmented neutrophils. Inclusions were not seen. Rheumatoid factor as measured by the latex tube dilution method of Singer and Plotz was absent. The gram stain and cultures were negative. No tumor cells were seen on a cytocentrifuged specimen. A bone scan with 99-Technetium revealed increased uptake in both wrists, in the right knee, and in the right side of the chest.

During the next 3 months the patient continued to experience pain and swelling of the aforementioned joints, developed increasing dyspnea and pleuritic chest pain, and had marked increase in the size of her pleural effusions and pulmonary metastases.

DISCUSSION

Clubbing of the fingers in the presence of chronic lung disease was first described by Hippocrates (2). The full clinical syndrome of secondary hypertrophic osteoarthropathy was presented by Marie in 1890 (3). These syndromes should be differentiated from primary osteoarthropathy or pachydermoperiostosis (4). Although a rare occurrence in childhood, hypertrophic osteoarthropathy secondary to pulmonary metastatic disease must be considered in the differential diagnosis of the child with painful joints. However, in a recent review of 10 children in whom arthritis was the initial manifestation of malignancy, secondary hypertrophic osteoarthropathy was not found (5). In the 2 patients with secondary osteoarthropathy presented here, the diagnosis of osteogenic sarcoma had been made 1 year or more previously. The initial manifestation of pulmonary metastases in the first patient was painful swollen joints.

There are 61 documented cases of secondary hypertrophic osteoarthropathy in childhood (17 years of age or younger). Thirty-nine cases were reviewed by Cavanaugh and Holman (1), who reported 8 additional cases. Five other cases were reviewed by Yacoub *et al* (6), and others have been reported by Trever (1 case) (7), Neale *et al* (2 cases) (8), McLaughlin *et al* (2 cases) (9), Shapiro and Zvaifler (1 case) (10), Adler and Sharma (1 case) (11), Barclay *et al* (1 case) (12), and Kay *et al* (1 case) (13). In these patients the underlying disease most commonly was pulmonary infection (28 cases) or congenital heart disease with occasional osteoarthropathy associated with biliary atresia (3 cases) or Crohn's disease (1 case). In 11 of the 61 cases, the underlying lesion was a lung tumor (Table 1), primary in 2 cases and metastatic in 9 cases. Nine of the 11 patients were male and all were over 11 years of age. As with the 2 patients reported here, the tumor type was osteogenic sarcoma in 4 cases.

Clinical evaluation of the joint symptoms in these 2 patients was remarkable in several ways. The pain, which was present at night as well as during the day, was very severe, to the extent that even gentle palpation or the slightest movement of the joint elicited extreme discomfort. Additionally, pain was present along the ends of the bones as well as over joint surfaces. Although there was palpable fluid in several joints, the swelling was much more extensive and extended beyond the usual demarcations of intraarticular fluid alone. The

Table 1. *Review of Reported Cases of Hypertrophic Osteoarthropathy Secondary to Tumors in Childhood*

Author	Date	Tumor Type	Primary Site	Age	Sex
Hall*	1905	Parosteal osteogenic sarcoma	Femur	14	M
Palugyay*	1934	Osteogenic sarcoma	Femur	13	M
Miller†	1939	Thymic cancer	Thymus	14	M
Barta*	1939	Parosteal sarcoma	Femur	13	M
Martin*	1939	Transitional cell sarcoma	Nasopharynx	15	M
Stol'ser†	1962	Schwannoma	Lung	13	M
Alexander*	1962	Osteogenic sarcoma	Tibia	17	F
Diner*	1962	Lymphoepithelioma	Nasopharynx	17	M
Adler (11)	1970	Hodgkin's disease	Cervical nodes	12	M
Shapiro (10)	1973	Hodgkin's disease	Abdomen	16	F
Kay (13)	1974	Hodgkin's disease	Chest	11	M

* Reviewed by Yacoub *et al* (6).
† Reviewed by Cavanaugh and Holman (1).

synovial fluid analysis in Patient 2 was consistent with a noninflammatory arthropathy.

Although the pathogenesis of hypertrophic osteoarthropathy is unknown, it is generally postulated that the stimulus to new bone formation is increased local blood flow possibly related to an endocrine mechanism (14) or neurogenic reflex arc (15). It has been reported in adults that the signs and symptoms of this syndrome disappear following removal of the causative pulmonary lesion or after intrathoracic vagotomy (15,16). Therapeutic doses of salicylate markedly improved discomfort and swelling after only a few days in Patient 1, although with recurrence of pulmonary tumor the symptoms could no longer be controlled by antiinflammatory medication.

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