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Case report

Hypertrophic osteoarthropathy and intrathoracic Hodgkin's disease in children

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Abstract

Background: Hypertrophic osteoarthropathy (HOA) is a syndrome characterized by clubbing of the fingers and toes, periosteal new bone formation of the long bones and polyarthritis.
Case report: In this report, two children with intrathoracic Hodgkin's disease and HOA are presented.
Conclusions: Intrathoracic neoplasms are one of the major causes of HOA in adults; however HOA is rarely associated with intrathoracic malignancies in children. HOA associated with intrathoracic Hodgkin's disease is even more rare, but should be kept in mind.

Keywords: Hypertrophic osteoarthropathy; Hodgkin's disease; Childhood

1. Introduction

Hypertrophic osteoarthropathy (HOA) is a syndrome characterized by clubbing of the fingers and toes, periosteal new bone formation of the long bones and polyarthritis [1,2]. Although, intrathoracic neoplasms are one of the major causes of HOA in adults; HOA is rarely associated with intrathoracic malignancies in children [3–14]. HOA associated with intrathoracic Hodgkin's disease is even more rare [7–10,12,13]. We had published such a case previously [12] and in this report, we present two more children with intrathoracic Hodgkin's disease and HOA.

2. Case report

2.1. Case 1

A 12-year-old white male was admitted to the hospital in November 2000 with 4 months history of pain and swelling of the fingers, tenderness of the wrist, fingers and toes; 4 months history of abdominal pain; 4 months history of brassy cough, hoarseness of voice, dyspnea. He had lost 12% weight in the last 2 months, had fevers and night sweating. He had been diagnosed with Guillain Barre syndrome after being paralytic when he was 5 years old, and it had resolved completely. Family history revealed an aunt who had expired due to lung cancer. On physical examination he was well developed. His respiration and pulse rate were 24/min and 100/min, respectively. There was clubbing and severe pain of the fingers and toes bilaterally. His voice was hoarse. There was 1 cm × 1 cm cervical lymphadenopathy on the right. Laboratory studies were noncontributory except an elevated erythrocyte sedimentation rate (ESR) (42 mm/h) and serum β_2 microglobulin level (3 mg/dl). Chest X-ray films showed a mediastinal widening and computerized axial tomography (CT) of the chest revealed multiple mediastinal enlarged nodes, the largest being 4 cm × 4 cm in the left hilar area. X-rays of bones and Tc^{99} whole body bone scan was normal. Bone marrow biopsy was normal. Cervical CT demonstrated bilateral lymphadenomegalies the largest being 1 cm × 1 cm on the right. CT and ultrasound of the abdomen were normal.

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Indirect laryngoscopy revealed paralysis of the left vocal cord (left nervus recurrens paralysis), most probably due to compression of mediastinal enlarged nodes. Nasopharynx was normal on endoscopic examination. Cardiac functions and anatomy were normal on echocardiography. Microscopic and culture examinations of the urine and stool done for abdominal pain were normal.

A biopsy from the hilar lymph node was done under mediastinoscopy. Histopathological evaluation revealed mixed cellular type Hodgkin's disease. The patient was clinically staged as II_B and treated according to our stage-adapted institutional protocol [15] by four courses of ABVD chemotherapy regimen (adriamycine 25 mg/m^2 i.v., bleomycine 10 mg/m^2 i.v., vinblastine 6 mg/m^2 i.v, dacarbazine 375 mg/m^2 i.v. all days 0 and 14). This cycle was repeated every 28 days and followed by involved field radiotherapy of 25 Gy. A partial response was attained after two courses of chemotherapy. The pain and swelling of the fingers and toes diminished, abdominal pain decreased and the hoarseness of the voice regressed after the second course of chemotherapy. A complete response was attained both clinically and radiologically after four courses of chemotherapy which continued after radiotherapy. The patient is alive with no evidence of disease 55 months after diagnosis.

2.2. Case 2

A 16-year-old boy was admitted to the hospital with 3 months history of swelling of bilateral cervical lymph nodes, fatigue, weight loss (23%), 1 month history of fever and night sweating, 1 week history of cough, dyspnea and arthralgia. On physical examination he was dyspneic, tachypneic, tachychardic. His respiration and pulse rate were 36/min and 128/min respectively. A 10 cm × 8 cm conglomerate lymphadenopathy on the left cervical area extending to the left supraclavicular area was present. Additionally, lymphadenopathies, on the right cervical area, on the right and on the left axillary areas, on bilateral inguinal areas could be palpated. There was severe pain of the wrist, fingers, knees, ankles and toes. Laboratory studies were noncontributory except an elevated ESR (77 mm/h) and serum β_2 microglobulin level (4 mg/dl) [5]. Chest X-ray films showed a mediastinal widening (bulky mediastinum) and computerized axial tomography (CT) of the chest revealed lymphadenomegaly in the preaortic, internal jugular chain, paratracheal, bronchomediastinal, precaval, tracheobronchial, subcarinal, paraoesophageal, and hilar areas, the largest being 7.5 cm × 5.5 cm in the preaortic area. There was slight compression of the trachea due to the enlarged nodes in the internal jugular chain, and compession of two main bronchus due to hilar lymphadenomegalies. There were multiple enlarged lymph nodes on bilateral cervical and supraclavicular areas on cervical CT. CT and ultrasound of the abdomen revealed paraaortic 3 cm × 3 cm lymphadenopathies. Bone marrow biopsy, X-rays of bones, whole body bone scintigrapy and echocardiogram were normal.

A biopsy from the supraclavicular lymph node was done. Histopathological evaluation revealed nodular sclerosis type Hodgkin's disease. The patient was clinically staged as III_B and treated according to our institutional protocol [15] by six courses of COPP/ABV hybrid chemotherapy regimen (cyclophosphamide 600 mg/m^2 i.v. day 1, vincristine 1.4 mg/m^2 i.v.day 1, procarbazine 100 mg/m^2 p.o. day 1–7, prednisolone 40 mg/m^2 p.o. day 1–14, adriamycine 35 mg/m^2 i.v. day 7, bleomycine 10 mg/m^2 i.v. day 7, vinblastine 6 mg/m^2 i.v. day 7) every 28 days, followed by involved field radiotherapy of 25 Gy. The severe pain of the wrist, fingers, knees, ankles and toes completely diminished, the mediastinal widening on chest X-ray was significantly reduced (>70%) after the second course of chemotherapy. A partial response was attained after two courses and complete response after six courses of chemotherapy which continued after radiotherapy. The patient is alive with no evidence of disease 24 months after diagnosis.

3. Discussion

Hypertrophic osteoarthropathy (HOA) was first described by Marie in 1890 [16] and Bamberger in 1898 [17] in association with intrathoracic inflammatory lesions. HOA syndrome can be either primary or secondary [1,18,19]. Primary HOA and secondary HOA are two distinct clinical entities. Primary familial HOA is extremely rare, and is not associated with an underlying disease. The prognosis of primary HOA is good and the changes may resolve spontaneously [4,17,19]. Secondary HOA has been associated with various underlying pulmonary and nonpulmonary causes, including intrathoracic tumors [2,3]. Neoplastic disorders are among these intrathoracic tumors and account for 92% of the HOA cases in adults, whereas only 12% of HOA in childhood has been associated with neoplasia [3,5].

From 1890 to 2003 only 32 children, including our cases, under age of 18 years with malignancy and associated HOA have been reported [3,6–14]. All but three were over 10 years of age and 26 (80%) were males. The diagnosis were: nasopharyngeal carcinoma in 11, osteosarcoma in 8, Hodgkin lymphoma in 8, thymus carcinoma in 3, sarcoma in 1, and pleural mesothelioma in 1 patient. Table 1 demonstrates the characteristics of the eight cases of childhood Hodgkin's disease that were associated with HOA.

Radiologic findings of HOA are usually characteristic. Periosteal new bone formation is seen as a thin opaque line of new bone formation separated from the bony cortex by a narrow translucent band. Later, the two layers of bone gradually fuse and lamellar patterns of periosteal new bone may be seen [1,9]. Periosteal new bone formation may also be seen as a radiologic manifestation of Hodgkin bone disease, but cortical bone destruction is also evident in those cases [9,15]. In the two cases in this report, despite severe arthralgia and swelling of the joints, there was no radiological findings char-