Primary hypertrophic osteoarthropathy with anemia as assessed by ^{18}F-FDG PET/CT

Abstract

Primary hypertrophic osteoarthropathy (PHO), also known as pachydermoperiostosis, is a rare genetic disorder with autosomal inheritance. We present the case of a 31-year-old male with a disease onset at 12 years of age, initially presenting as digital clubbing of the hands and feet and ankle joint hypertrophy. The clinical phenotype progressed significantly by age 17, with the development of marked facial skin thickening, deepened centripetal skin folds, a corrugated scalp, hypertrophic alae nasi, acne, ptosis, and palmoplantar hyperhidrosis. Anemia was identified at age 19, accompanied by persistent fatigue, followed by the onset of bilateral knee joint pain two years later. Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) imaging revealed a constellation of findings that can be grouped into three categories: (1) skeletal: cortical thickening and periosteal reaction in the long bones of the lower limbs, along with extensively increased bone marrow density throughout the skeleton; (2) soft tissue: diffuse thickening of the cranial and facial skin, and multiple para-spinal soft tissue foci; and (3) systemic: cardiac findings suggestive of anemia-related adaptation. Genetic analysis confirmed the diagnosis by identifying heterozygous mutations in the SLCO2A1 gene (c.290G>A [p.R97H] and c.1295+1G>A), establishing PHO complicated by anemia.

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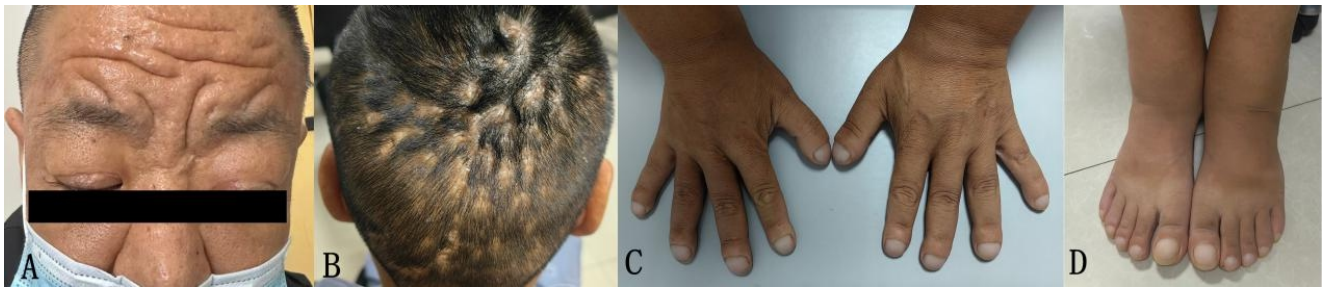

Figure 1. Physical examination revealed oily and coarse skin, deepened facial wrinkles, bilateral ptosis, broad and thickened nasal wings, and thickened forehead skin with deepened centripetal folds (A). The scalp exhibited a cerebriform appearance, accompanied by soft-textured nodules with alopecia on the surface (B). The patient presented with clubbed fingers and toes, pale nails on all digits, profuse sweating in the limbs, and bilateral ankle hypertrophy (C and D). Based on the above manifestations, hyper-trophic osteoarthropathy was clinically suspected.

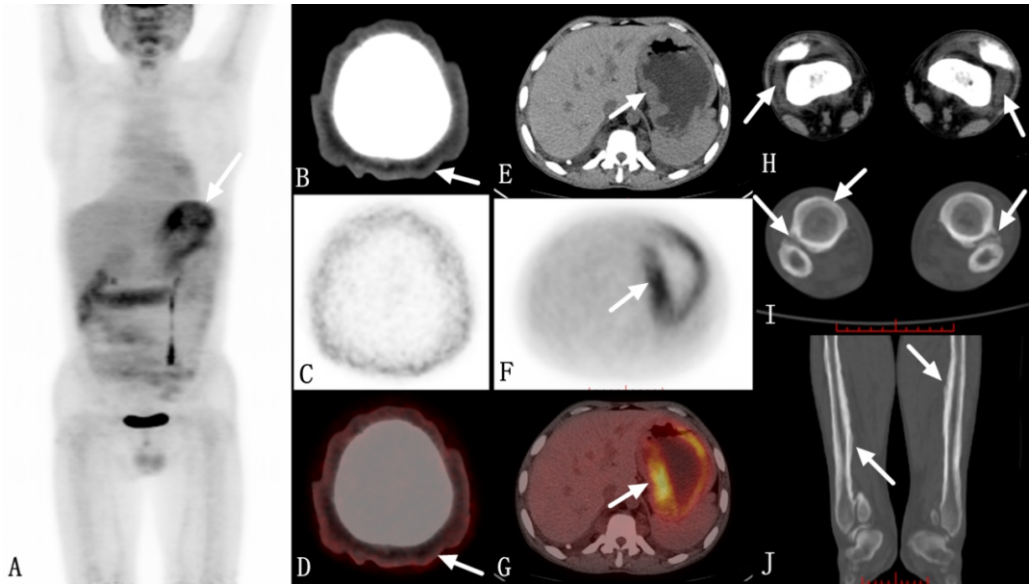

Figure 2. The patient underwent fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) to evaluate for underlying disease. Maximum intensity projection (MIP) images showed no significant ^{18}F-FDG uptake in the lungs but revealed diffusely heterogeneous ^{18}F-FDG uptake in the stomach (A, arrows). Axial CT, corresponding PET, and fusion images (B-D and E-G, arrows) demonstrated undulated scalp morphology and thickened gastric walls with heterogeneously increased ^{18}F-FDG uptake (maximum standardized uptake value (SUVmax) 4.79 and 5.18, respectively). Knee joint CT showed synovial fluid accumulation (H, arrows), while long bone CT revealed cortical thickening with irregularity and intense periosteal proliferation along the diaphysis (I-J, arrows). Based on these characteristics, along with skin thickening and digital clubbing, complete PHO was initially suspected. The diagnosis was confirmed by whole-exome sequencing.

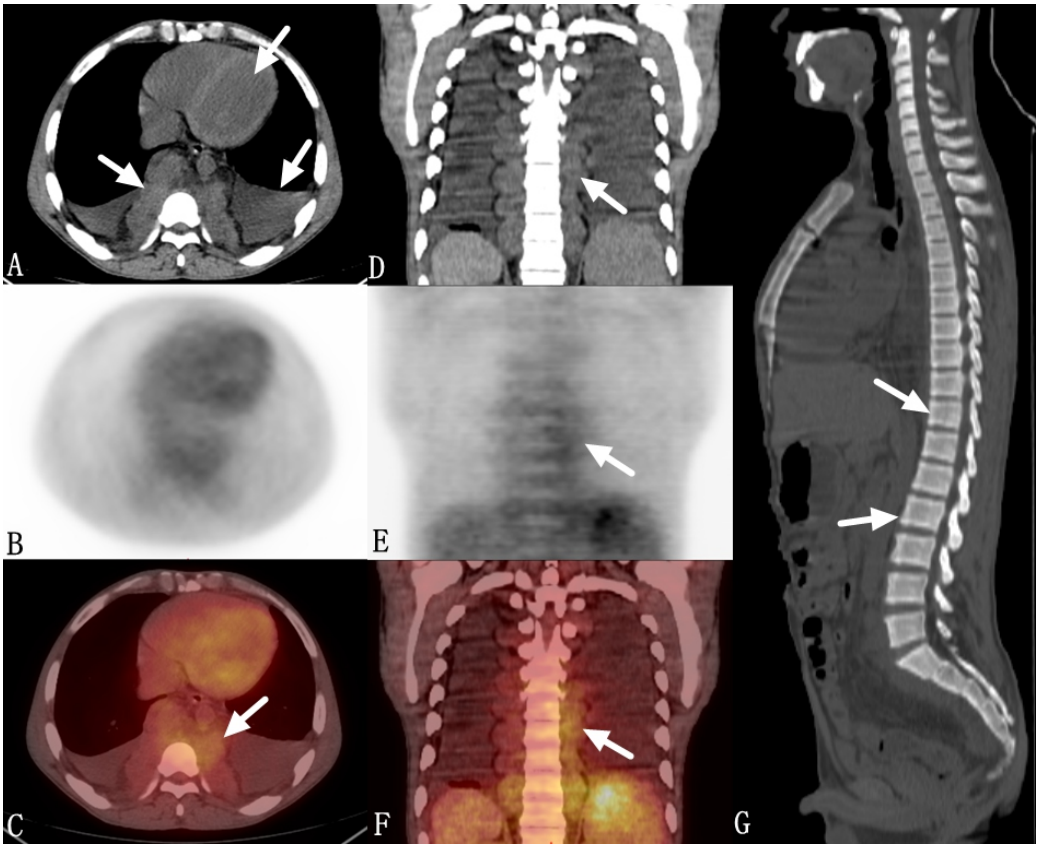

Figure 3. Axial and coronal PET/CT images revealed multiple, segmentally distributed paraspinal (T2-T11) soft-tissue nodules and masses exhibiting a clumped and beaded morphology. Some lesions showed fusion with ill-defined borders and mild ^{18}F-FDG uptake (SUVmax 1.64) (A-C, D-F, arrows). The CT component demonstrated diffusely increased bone density throughout the skeleton, with blurred trabeculae or a ground-glass opacity pattern (G, arrows).

Primary hypertrophic osteoarthropathy is a rare genetic disorder characterized mainly by pachydermia, digital clubbing, and periostitis with subperiosteal new bone formation [1, 2]. The pathogenesis of pachydermoperiostosis remains unclear [3]. Onset typically occurs around puberty, and definitive diagnosis relies on genetic testing [4]. Diagnostic criteria include major features-pachydermia, periostosis, and digital clubbing-and minor features such as hyperhidrosis, arthralgia, hypertrophic gastritis, ptosis, joint effusion, seborrhea, acne, and facial flushing [5]. In this context, ^{18}F-FDG PET/CT serves as a valuable "one-stop" imaging modality, providing comprehensive whole-body assessment of cutaneous, skeletal, and gastric involvement while helping exclude secondary causes such as malignancy or chronic inflammatory conditions. It thus offers essential diagnostic clues facilitating timely genetic confirmation and appropriate management of PHO.

Primary hypertrophic osteoarthropathy is primarily a benign disorder; however, it can result in clinically significant anemia [6]. Anemia typically develops gradually and parallels disease progression. Recent analyses indicate that patients with SLCO2A1 mutations-affecting the prostaglandin transporter-are more susceptible to developing anemia and even myelofibrosis [7]. In this case, it was anemia accompanied by fatigue that prompted clinical presentation and led to the eventual diagnosis of PHO. This association is explained by SLCO2A1-encoded prostaglandin transporter dysfunction, which impairs prostaglandin E_2 clearance, thereby leading to chronic inflammation, bone marrow fibrosis, and ultimately anemia. Implementing periodic monitoring of hematologic parameters in genetically confirmed PHO patients, particularly those with SLCO2A1 mutations, is recommended to detect anemia promptly. This case highlights the role of modern imaging in revealing the systemic involvement of PHO, especially when accompanied by hematologic abnormalities. Integrating phenotypic features with metabolic and genetic findings allows for timely diagnosis and comprehensive management of the condition.

In conclusion, this case highlights the critical role of PET/CT in providing comprehensive metabolic and structural evidence that aids in diagnosing PHO and guiding subsequent genetic testing by excluding secondary causes. The teaching point is that PHO with anemia, particularly in SLCO2A1 mutation carriers, requires symptomatic management addressing inflammation, bone metabolism, and gastrointestinal support; our patient received corticosteroids, an NSAID, calcium/vitamin D supplements, and gastroprotective agents, with planned long-term hematologic follow-up.

The authors declare that they have no conflicts of interest.

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