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CLINICAL MEDICINE CASE REPORT

# HYPERTROPHIC OSTEOARTHROPATHY IN A PATIENT WITH HETEROZYGOUS MUTATION IN THE SLCO2A1 GENE: A CASE REPORT

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## Abstract
Hypertrophic osteoarthropathy (HOA) is a condition characterized by aberrant skin and osseous tissue proliferation in the distal extremities. Mutations in the 15-hydroxyprostaglandin dehydrogenase gene (HPGD) and the soluble carrier organic anion carrier family member 2A1 gene (SLCO2A1) were associated with primary HOA. Secondary HOA, which is also called as 'hypertrophic pulmonary osteoarthropathy' is responsible for 95-97% of cases. Herein, we present a 19-year-old female patient with primary HOA and heterozygous mutation in the SLCO2A1 gene.

**Keywords:** Arthralgia, arthropathies, Clubbed fingers, Hypertrophic osteoarthropathy, SLCO2A1 gene mutation, Synovial hypertrophy
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## INTRODUCTION
Hypertrophic osteoarthropathy (HOA) is a syndrome characterized by abnormal proliferation of skin and osseous tissue in the distal extremities. The etiology includes primary and secondary causes [1].

Primary HOA accounts for 3-5% of cases, its etiology is idiopathic and genetic factors are held responsible. It is a rare hereditary disease that usually starts in childhood/adolescence. Mutations in the 15-hydroxyprostaglandin dehydrogenase gene (HPGD) and the soluble carrier organic anion carrier family member 2A1 gene (SLCO2A1) were found to be associated with primary HOA. Since diffuse skin hypertrophy is more common in this form with a family history of 33-73%, it is also called 'pachydermoperiostosis' [1, 2].

Secondary HOA is responsible for 95-97% of cases and is also called 'hypertrophic pulmonary osteoarthropathy' since it is associated with underlying extraskeletal diseases. It may be localized to one to two extremities (localized form) or may be a generalized form. The most common secondary cause is non-small cell lung cancer. In addition, although pulmonary causes such as pulmonary fibrosis, chronic obstructive pulmonary disease (COPD), pulmonary infection/abscess are more

common in etiology, non-pulmonary causes such as hepatic, gastrointestinal, pleural/mediastinal causes and other malignancies may also be present [1, 3].

In this report, a case of HOA with heterozygous SLCO2A1 gene mutation is presented.

## CASE REPORT

A 19-year-old female patient applied to the Department of Physical Medicine and Rehabilitation with complaints of pain in the joints, swelling, limitation of movement, and decreased walking capacity. From her anamnesis, it was learned that she had complaints of pain and swelling in both knees and ankles for about ten years, and that she had received various biological agent treatments in the past with the diagnosis of juvenile idiopathic arthritis. She had a complaint of clubbing in her fingers and toes for about nine years. Her medical history included epilepsy, multiple type 1 arteriovenous malformations in both lungs, and polyposis coli.

On physical examination, signs of synovial hypertrophy in both knees, atrophy in the quadriceps, and clubbing in both fingers and toes were observed (Figure 1). Regarding laboratory tests, acute phase reactants were within normal limits; anti-cyclic citrullinated peptide (anti-CCP) antibody and rheumatoid factor (RF) were negative; there were signs of anemia in the hemogram.

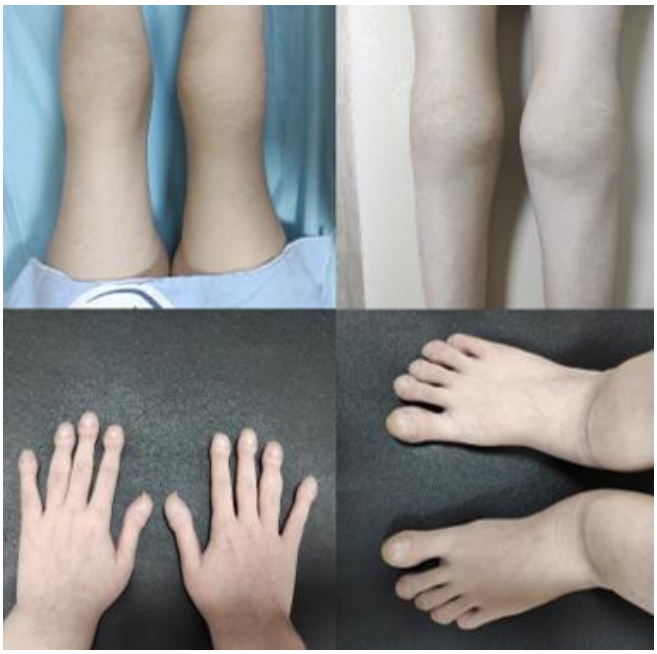

**Figure 1. Synovial hypertrophy in the knees, atrophy in the quadriceps, and clubbing in fingers and toes**

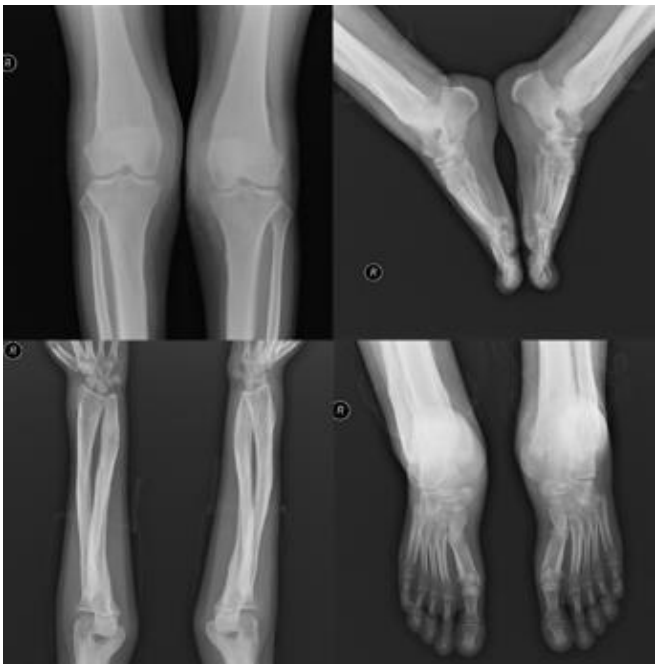

**Figure 2. Periostitis in both tibia and radius; periosteal thickening in both femurs, tibia, fibula, radius and metatarsal bones**

On radiographs, periosteal thickening was detected in the bilateral femur, tibia, fibula, radius, and metatarsal bones. An appearance compatible with periostitis was detected in the bilateral tibia and radius (Figure 2). On thorax computerized tomography (CT), there were multiple consolidated areas in both lungs (Figure 3). Genetic analysis revealed heterozygous SLCO2A1 gene mutation.

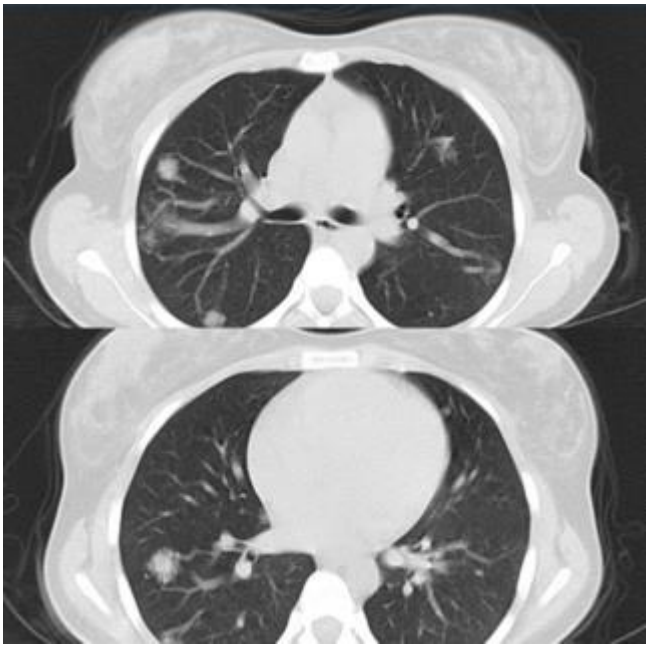

**Figure 3. Thorax CT: Multiple consolidated areas in both lungs**

Written informed consent was obtained from the patient for the publication of her clinical data, photographs, and radiographs.

## DISCUSSION

Hypertrophic osteoarthropathy is a syndrome characterized by digital clubbing, synovial effusions, and periosteal proliferation in tubular bones [1]. Primary and secondary causes are included in the etiology. Primary hypertrophic osteoarthropathy is idiopathic, covering 3-5% of cases. Genetic factors are held responsible for 1/3 of primary HOA (PHO). PHO is divided into two types: Type I and type II. PHO type I (autosomal recessive type 1) is associated with the HPGD gene and PHO type II (autosomal recessive type 2) is associated with the SLCO2A1 gene.

Impaired degradation of prostoglandin E2 (PGE2) is responsible for the clinical findings [4]. The gender distribution ratio in PHO is male/female: 9/1 [5]. There are clinical differences between the two PHO types, one of which is the male gender predominance in PHO type II [6]. Although our patient also had the SLCO2A1 mutation, her gender was female. Being heterozygous for the mutation can be suggested as a reason for this difference.

There are case reports in the literature regarding the coexistence of juvenile polyposis, HOA, and pulmonary arteriovenous malformation [7, 8]. In one case, the association of juvenile polyposis and HGPD gene mutation was mentioned [8]. In addition, in the clinical picture defined as chronic enteropathy (CEAS) associated with SLCO2A1 mutation, there are gastrointestinal findings such as chronic gastritis, peptic ulcer, Crohn's Disease, abdominal pain, diarrhea, and bleeding [9]. The literature review found no association between SLCO2A1 mutation and juvenile polyposis.

As a result, HOA is classified as primary and secondary according to etiology. Secondary causes constitute the majority of cases. HPGD and SLCO2A1 gene mutations are responsible for primary cases. The genetic component should be considered in patients presenting with HOA. Patients with heterozygous mutation in the SLCO2A1 gene might present with diverse signs and symptoms. Future research is needed to examine this diversity.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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## SLCO2A1 ГЕНІНІҢ ГЕТЕРОЗИГОТАЛЫ МУТАЦИЯСЫ БАР НАУҚАСТАҒЫ ГИПЕРТРОФИЯЛЫҚ ОСТЕОАРТРОПАТИЯ: КЛИНИКАЛЫҚ ЖАҒДАЙ

**Түйіндеме**

Гипертрофиялық остеоартропатия (ГОА) - дистальды аяқ-қолдардағы тері мен сүйек тінінің аберранттық пролиферациясымен сипатталатын ауру. 15-гидроксипростагландиндегидрогеназа (HPGD) геніндегі және 2A1 (SLCO2A1) еритін тасушының органикалық аниондардарын тасымалдаушылар тұқымдастар мүшесінің геніндегі мутациялар біріншілей НОА-мен байланысты болды. "Гипертрофиялық өкпе остеоартропатиясы" деп те аталатын екіншілей ГОА 95-97% жағдайлардың себепшісі болып табылады. Мұнда біз SLCO2A1 генінде біріншілей ГОА және гетерозиготалы мутациясы бар 19 жастағы науқас ә йелді ұсынамыз.

**Түйінді сөздер:** артралгия, артропатиялар, саусақтардың маймақ тығ ы, гипертрофиялық остеоартропатия, SLCO2A1 генінің мутациясы, синовиальдық гипертрофия.

**Дәйексөз үшін:** Бенлайда И.К., Тунцер К., Сарпель Т. SLCO2A1 генінің гетерозиготалы мутациясы бар науқастағы гипертрофиялық остеоартропатия: клиникалық жағдай. Медициналық гипотеза мен этиканың Орта Азиялық журналы 2023:4(3):159-162. https://doi.org/10.47316/cajmhe.2023.4.3.03

## ГИПЕРТРОФИЧЕСКАЯ ОСТЕОАРТРОПАТИЯ У ПАЦИЕНТА С ГЕТЕРОЗИГОТНОЙ МУТАЦИЕЙ ГЕНА SLCO2A1: КЛИНИЧЕСКИЙ СЛУЧАЙ

**Резюме**

Гипертрофическая остеоартропатия (ГОА) — заболевание, характеризующееся аберрантной пролиферацией кожи и костной ткани в дистальных отделах конечностей. Мутации в гене 15-гидроксипростагландиндегидрогеназы (HPGD) и гене члена семейства переносчиков органических анионов растворимого носителя 2A1 (SLCO2A1) были связаны с первичной НОА. Вторичная ГОА, которую также называют «гипертрофической легочной остеоартропатией», является причиной 95-97% случаев. В статье описывается случай 19-летнюю пациентки с первичной ГОА и гетерозиготной мутацией в гене SLCO2A1.

**Ключевые слова:** артралгия, артропатии, косолапость пальцев, гипертрофическая остеоартропатия, мутация гена SLCO2A1, синовиальная гипертрофия.

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