CASE REPORT

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Touraine Solente Gole Syndrome (Pachydermoperiostosis): Case Report and Brief Review

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ABSTRACT

Observation: Hypertrophic osteoarthropathy (HOA) is systemic disease characterized by periostosis, digital clubbing and arthritis. Touraine Solente Gole syndrome (TSGS), or pachydermoperiostosis - clinical variant of primary HOA, involving skeleton, soft tissues and cutis. The patents with TSGS may develop complications due to excessive growth in the soft tissues and bone tissues or develop serious associated diseases such as malignancies. Therefore, timely diagnosis of HOA and TSGS as a rare variant of it is important in aspect of prevention or early viewing of associated disease ad complications.

Keywords: Hypertrophic osteoarthropathy, Touraine Solente Gole syndrome, Pachydermoperiostosis, Malignancies

Introduction

Hypertrophic osteoarthropathy (HOA) is systemic disease characterized by periostosis, digital clubbing and arthritis. There are two variants of HOA: primary (idiopathic) and secondary (approximately 35% of cases) [1]. Touraine Solente Gole syndrome (TSGS), or pachydermoperiostosis (PDP). TSGS, or PDP - clinical variant of primary HOA - is rare inherited or idiopathic disease predominantly involving skeleton, soft tissues and cutis. In classical presentation the syndrome characterized by periosteal disorders, soft tissue hypertrophy and pachydermia (*cutis verticis gyrata*) most commonly involving the scalp and face. Facies leonina can develop in cases facial involvement.

Primary HOA was first described by Fredreich [2] in 1868 as a familial case of HOA. In 1830, Pierre Marie described it as "*osteoarthropathie hypertrophiante pneumique*" [3]. Touraine et al. [4] described TSGS as a form of primary HOA.

TSGS may be idiopathic or inherited. Although, an autosomal dominant inheritance with incomplete penetrance and variable expression has been confirmed, both autosomal recessive and X-linked inheritance has been suggested [5].

Case Report

We present the case of 13 years old white Caucasian male complained of skin thickening in the scalp (Figure 1A) and forehead (Figure 1B), digital clubbing, hypertrophy of soft tissues of digits and hyperhydrosis (Figure 2), manifestation of total hyperhidrosis (Figure 3), arthralgia, that had persisted nearly for four years.

Physical examination revealed skin thickening and folds formation in the face and forehead area, between the eyes, deep nasolabial folds, sebaceous gland hyperplasia, eyelids hypertrophy resulting in mechanical ptosis. This clinical feature resembled so-called *facies leonine*. Scalp examination revealed appearance consisting cutis

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verticis gyrata with deep folds in cerebriform distribution. Anomaly of fourth toe of both feet is also detected.

Body temperature of 36.6 ºC. PR: 70/min. BP: 120/60 mmHg. In other the physical examination revealed no pathologic signs.

Symptoms gradually progressed and there is no complete remission. Patient received treatment for different diagnosis of systemic rheumatic diseases such as rheumatoid arthritis, acute rheumatic fever etc with no or short term benefits: the symptoms recurred as soon as the treatment has been discontinued. Then the patient was referred to Department of Dermatology and Venerology of Azerbaijan Medical University by the rheumatologist due to skin changes.

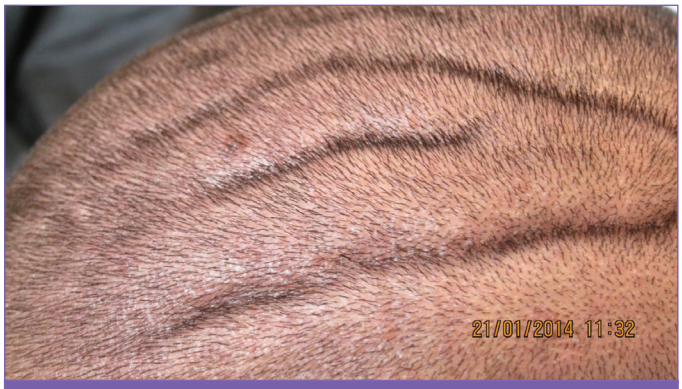

Figure 1A. Skin thickening and cutis verticis gyrata with deep folds in cerebriform distribution on scalp

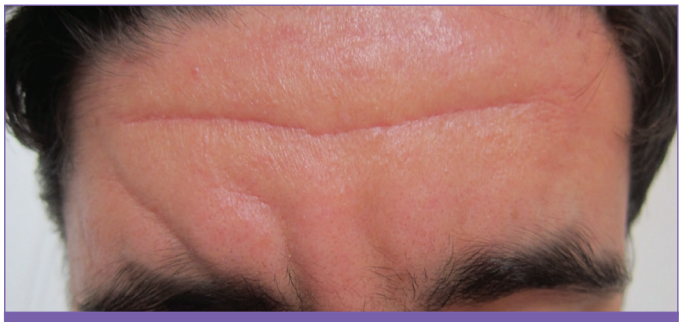

Figure 1B. Skin thickening and furrowing on the face and forehead

A blood work up including a hemoglobin, hematocrit, red blood cell, white blood cell and blood biochemistry resulted (glucose, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, serum creatinine, urea) in the normal ranges. An acute phase markers slightly elevated: erythrocyte sedimentation rate (ESR): 30 mm/h and C-reactive protein (CRP): 20 mg/L. P-ANCA, C-ANCA, ANA, RF, cryoglobulins were all negative. A serology for sexually transmitted diseases, viral hepatitis (VDRL, TPHA, HBsAg, anti-HIV, anti-hepatitis C virus), TORCH, antibodies against streptococcus, Epstein-Barr virus and Write test for brucellosis was negative. A urinalysis revealed no changes. Abdominal ultrasound and chest X-ray examination revealed no pathology. Electrocardiogram and electrocochleaography revealed no heart pathology.

The patient's medical history is remarkable for four surgical interventions for femoral bone fracture four years ago.

His parents are consanguineous. The patient has a brother. Al the family members are healthy. No history of TSGS present in father's or mother's relatives, but there is a history of anomaly of fourth toe of both feet.

Diagnosis of TSGS (PDP) was made basing on clinical, radiological and laboratory data.

Therapy with isotretinoin 20 mg/day, nimesulid 100 mg b.i.d. was started with mild clinical efficacy: arthralgia resolved, skin folds became less prominent.

Discussion

TSGS is related to mutations of the gene encoding for 15-hydroxyprostaglandin dehydrogenase [6]. TSGS patients have

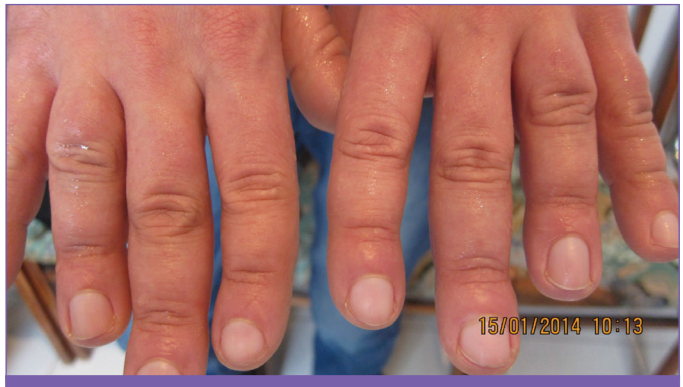

Figure 2. Skin thickening on hands, digital clubbing, hypertrophy of soft tissues of digits and hyperhydrosis

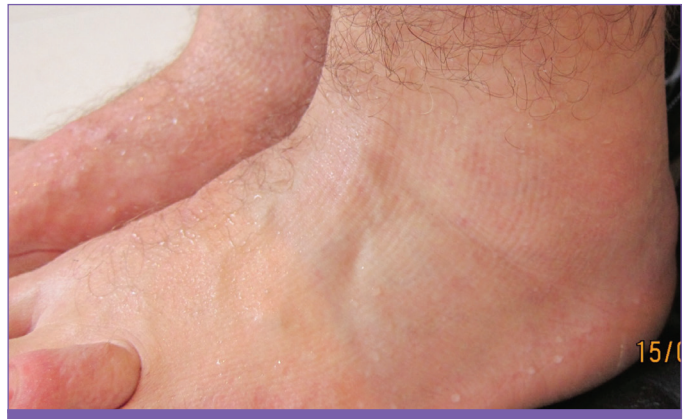

Figure 3. Skin thickening on foots and marked hyperhydrosis

high levels of PGE2 and decreased levels of PGE-M (the metabolite of PGE2). PGE2 can mimic the activity of osteoblasts and osteoclasts, which may be responsible for the acro-osteolysis and periosteal bone formation [7]. PGE2 also has vasodilatory effects, which may be responsible for prolonged local vasodilation resulting in digital clubbing [7].

TSGS as a form of primary HOA has been described by Touraine et al. [4] in 1935 in their paper entitled: *Un syndrome osteo-dermopathique: La pachydermia plicaturee avec pachyperiostose des extremites.* HOA characterized by *triad* of symptom including digital clubbing, periostitis and swollen limbs. TSGS accounts for only 3-5% cases of HOA0020 [8]. Touraine et al. [4] distinguish *three* clinical forms of TSGS: *complete* (pachydermia, clubbing and periostosis), *fruste* (pachydermia with minimal skeletal changes) and *incomplete* (skeletal changes with no pachydermia) TSGS.

Diagnostic criteria TSGS include *major* (pachidermia, periostosis, finger clubbing) and *minor* (hyperhidrosis, arthralgia, gastric ulcer, cutis verticis gyrate, blepharoptosis, joint effusion, column-like legs, edema, seborrhea, acne, hyperhidrosis, flushing) one.

The clinical diagnosis of TSGS may be easily confirmed by radiography of the long bones viewing characteristic periosteal changes and absence of any underlying pulmonary or cardiac disease, which must be carefully ruled out.

As in our case report the symptoms of TSGS often begin at the adulthood, progress during several years and become stable. According to Kerimovic-Morina and Mladenovic [9] family history exists in about a 25-38% of the cases and so it is important to consider close relatives.

TSGS is more common in men with men-to-women ratio 9:1 [1,10].

There is no racial predisposition.

Patients with PDP may present to multiple clinical specialist like orthopedist, rheumatologist, endocrinologist and dermatologist. The general physician is very occasionally confronted with such a case in a lifetime. Such cases are intriguing, challenging to diagnose and difficult to treat [2].

A diagnosis of primary HOA can be made only after carefully exclusion of secondary PDP with rapid bone changes and painful clubbing which may occur as a manifestation of severe pulmonary diseases such as adenocarcinoma of bronchus, pleural mesothelioma, bronchiectasis, gastric carcinoma or cyanotic heart diseases [11], because TSGS accounts for only in minority of cases of HOA.

The presence of nonspecific arthralgia or arthritis sometimes erroneously suggests systemic connective tissue diseases such as rheumatoid arthritis, or systemic infectious diseases (acute or chronic) - brucellosis, Lyme disease, viral hepatitis etc. Nevertheless, it is advisable to check for these diseases as comorbidities.

Other differential diagnoses include - acromegaly, thyroid acropachy, rhematoid arthritis etc. Patients with predominantly cutaneous manifestations may also have to be differentiated from the rare hyperelasticity disorders such as Ehler Danlos syndrome, cutis laxa, Meretoga's syndrome, Marfan's syndrome and pseudoxanthoma elasticum, which may cause forehead furrows [3].

Osteonecrosis of the femoral head [12], carpal and Tarsal Tunnel syndrome [13] are the *complications* of TSGS occurring with different rate.

No specific laboratory findings of TSGS available in routine clinical practice. Nevertheless, Zhang et al. [10] state elevated ESR and CRP with synovitis might be found in patients with PDP, yet it is fairly rare to note a two-fold elevation of ESR and a 10-fold elevation of CRP.

Non-steroidal anti-inflammatory drugs, pamidronate, isotretinoin for skin disorders. Surgical treatment may be required in some cases of prominent skin changes.

Finally, it needs to be underlined that patients with primary HOA require regular monitoring as, in the long term, they may develop malignancies and complications due to excessive growth in the soft tissues and bone tissues [1]. Therefore, timely diagnosis of HOA and TSGS as a rare variant of it is important in aspect of prevention or early viewing of associated disease ad complications. It is also important to check for malignancies at the time of diagnosis.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Concept: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Design: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Data Collection or Processing: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Analysis or Interpretation: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Literature Search: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B., Writing: Z.H.F., I.A.A., I.Z.B., N.Z.V., P.Z.B., H.Z.B.

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