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Single Case

Comprehensive Treatment of a Rare Case of Complete Primary Pachydermoperiostosis with Large Facial Keloid Scars: A Case Report and Literature Review

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Pachydermoperiostosis · Keloid · Comprehensive treatment · Botulinum toxin · Touraine-Solente-Gole syndrome

Abstract
Introduction: Pachydermoperiostosis (PDP), or primary hypertrophic osteoarthropathy, is a rare autosomal dominant disease with primary clinical features of pachydermia (thickening of skin) and periostosis (new bone formation). Keloid scar formation is also rather obscure, and some scientists have claimed that keloid scars contain an excessive amount of fibroblasts compared with normal skin as well as a dense mass of irregularly deposited connective tissues. ***Case Presentation:*** A 25-year-old man exhibited extensive skin folding on his face, a gyrus-like scalp, depressed nasolabial folds, and keloids. Symptoms began at 18 years of age, progressing insidiously. Additionally, he experienced clubbing of fingers and toes, joint pain, muscle soreness, and hyperhidrosis. Radiographic examinations revealed thickened bone and cystic regions. Diagnosed with complete primary PDP and facial keloid scars, he underwent skin dermabrasion, biopsies, and a comprehensive treatment involving, botulinum toxin injections, 5-fluorouracil, and a carbon dioxide lattice laser. ***Conclusion:*** PDP presents challenges due to its unclear etiology but stabilizes over time in most cases. Comprehensive treatment strategies, including dermabrasion and a combination of intralesional therapies, are effective in managing keloids in PDP patients. This case contributes to

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the understanding of managing rare diseases and underscores the importance of personalized approaches to improve therapeutic outcomes in patients with complete primary PDP and concurrent keloids.

Introduction

Pachydermoperiostosis (PDP) or primary hypertrophic osteoarthropathy (PHO) is a rare autosomal dominant disease characterized by primary clinical features of pachydermia (thickening of skin) and periostosis (new bone formation) and is also known as primary PDP and Touraine-Solente-Gole syndrome. This condition was first described by Friedrich in 1868 and called "hyperostosis of the entire skeleton" [1–3]. In 1907, Unna termed this disease "cutis verticis gyrate" because of the thick, transversely folded skin of the scalp and the forehead [4]. In 1935, three French dermatologists, Touraine et al. [5], recognized this condition as a familial disorder with three forms: complete (periostosis and pachyderma), incomplete (without pachyderma), and the forme fruste (pachydermia with minimal skeletal changes) [2]. PDP is reportedly related to mutations in the *HPGD* (encoding 15-hydroxyprostaglandin dehydrogenase) or *SLCO2A1* (encoding solute carrier organic anion transporter family member 2A1) genes [6–10], which lead to impaired prostaglandin E2 degradation, thus elevating prostaglandin E2 levels [11]. However, the other causes of PDP are still unclear. As a result, clinicians generally provide treatment that can effectively improve patients' quality of life.

Keloid scar formation is still a rather obscure process, and some scientists have claimed that keloid scars contain an excessive amount of fibroblasts compared with normal skin as well as a dense mass of irregularly deposited connective tissues [12]. Therefore, it is extremely difficult for clinicians to treat keloid scars.

In this report, we describe the comprehensive treatment of a 25-year-old man exhibiting complete primary PDP with facial keloid scars. The CARE Checklist has been completed by the authors for this case report and attached as online supplementary material.

Case Report

A 25-year-old man was referred to the dermatology department with extensive skin folding on his forehead and face, along with a gyrus-like scalp and depressed nasolabial folds. He also complained of bilateral joint pain, muscle soreness, and hyperhidrosis. These symptoms were first noted at 18 years of age. No other family members had a similar condition, and the patient had no history of trauma or fracture. He had been repeatedly operated on for facial purulent nodules at a local hospital, after which painful and pruritic skin tumors had formed. Informed consent for this evaluation was obtained from the patient.

On examination, the patient had different pronouncedly shaped keloids on his forehead and face, among the largest being 7 cm × 2 cm in size located on the forehead (Fig. 1a). In addition, the skin folds in the scalp were gyrus-like (Fig. 1b). The development of the patient's skin folds had been insidious and progressive. Clubbing of his fingers and toes (Fig. 1c–e) was observed. The patient had swollen ankles. Moreover, he had seborrhea and profuse sweating in his axillae, hands, and feet accompanied by muscle soreness.

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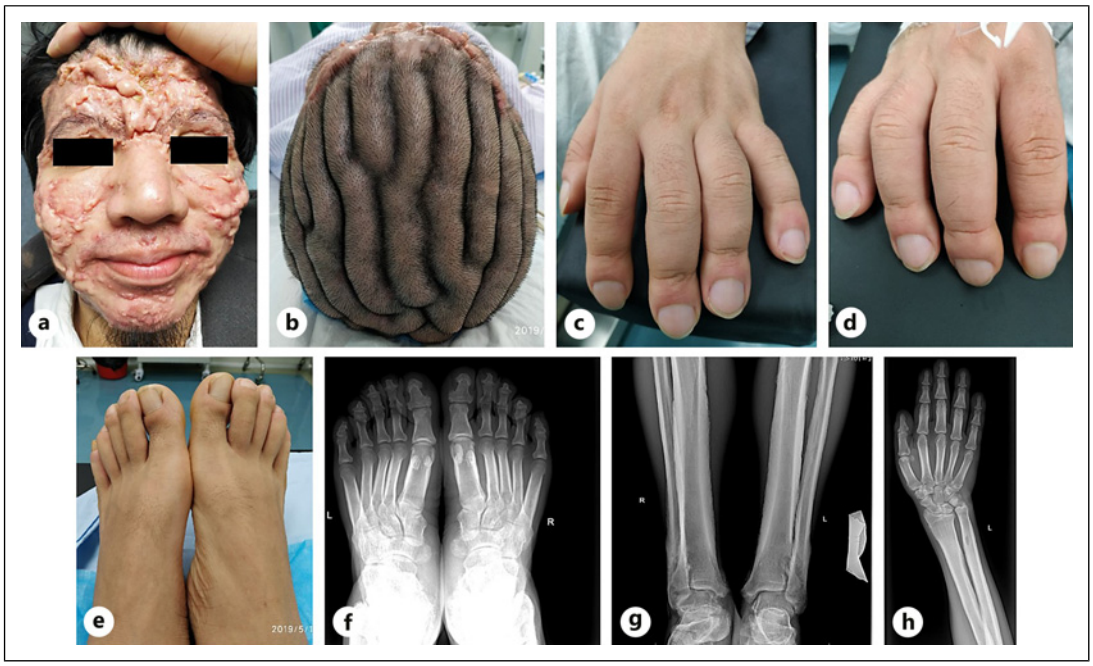

Fig. 1. a Facial appearance of the patient. **b** Marked thickening of the scalp (cutis verticis gyrata). **c–e** Clubbing of the fingers and toes. **f–h** Radiograph of the ankles, hands, and feet showing extensive periostosis.

Examination of the patient's cardiovascular, respiratory, urinary, and gastrointestinal systems revealed no significant abnormalities. Laboratory analyses of blood routine tests, electrolytes, thyroid function, liver function, renal function, blood sugar, parathyroid hormone, and adrenocorticotrophic hormone were normal. Radiographic investigations were performed to search for skeletal abnormalities. X-rays revealed thickening of the bone, indicating increased cortical bone formation in all four limbs. Moreover, there was a cystic region in the distal left ulna (Fig. 1f–h).

Based on the existing data from history, examination, and investigation, the patient was diagnosed with complete primary PDP and facial keloid scars. After diagnoses and exclusion of relevant surgical contraindications, the patient underwent skin dermabrasion on his face and forehead. After satisfactory general anesthesia, iodine was applied to disinfect the patient's forehead and face, and sterile drapes were placed. The forehead and the sides of the face were anesthetized via tumescent anesthesia with lidocaine solution containing 1:100,000 epinephrine.

A 1 cm × 0.5 cm–long fusiform incision was made at the skin junction between the forehead and scalp with a No. 10 circular blade up to the subcutaneous fat layer. Then, we sent the tissue for pathological biopsy, and the wound was closed with intermittent suture using a No. 1 silk tread. A No. 10 bard-parker scalpel blade was used to cut the raised skin lesions on the forehead and on both sides of the face until the wound was covered with normal skin. Subsequently, the bleeding was stopped with electrocoagulation hemostasis.

The patient's face was disinfected with povidone iodine a second time and treated with a carbon dioxide lattice laser with a minimum energy of 100 mJ, a coverage rate of 2.89%, and a spot size of 15 mm × 15 mm; this process was repeated 4 times and followed by multipoint injections of a mixture composed of 3 mL 2% lidocaine, 1 mL Diprosan and 1 mL fluorouracil and a mixture containing 10 mL normal saline and 100 units botulinum toxin type A, administered separately with a 1 mL syringe.

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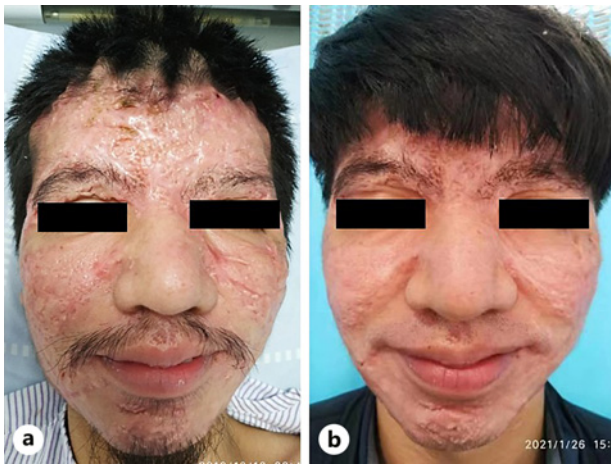

Fig. 2. Patient after 5 months (**a**) and more than 1 year (**b**) of treatment.

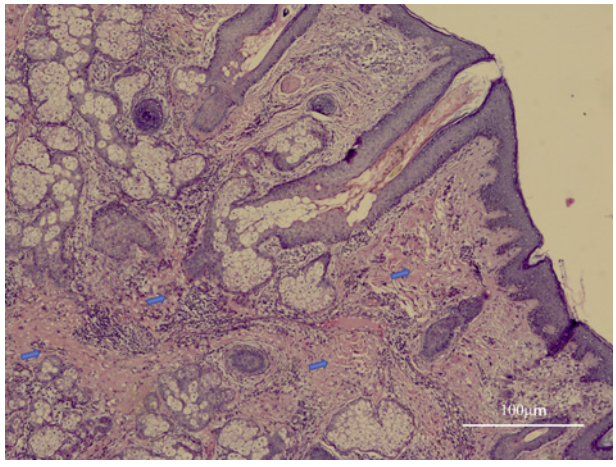

Fig. 3. Microscopic evaluation of the excised skin of a PDP patient (hematoxylin-eosin, original magnification: ×100). Arrows indicate dermal vasculature, lymphoid tissue cells, plasma cells, neutrophilic leukocytes, and fibrous tissue hyperplasia.

Tranilast was taken orally three times a day at a dose of 0.1 g, isotretinoin capsules were taken orally once a day at a dose of 30 mg, and spirolactone was taken two times a day at a dose of 20 mg postoperatively. The patient was satisfied with the postoperative outcome. Subsequently, he was injected with botulinum toxin type A once every 6 months (Fig. 2).

Microscopic evaluation of the excised skin revealed hyperkeratosis of the epidermis and neutrophilic abscess. Dermal vasculature, lymphoid tissue cells, plasma cells, neutrophilic leukocytes, and fibrous tissue hyperplasia were observed. Scars had formed. Some blood vessels were perpendicular to the epidermis (Fig. 3).

Discussion

PDP is a rare genetic disease characterized by digital clubbing, periostosis, pachydermia, and acro-osteolysis [13]. Most affected male patients are older than 40 years. However, the etiology of this disease is unknown, and it is generally believed that it may be related to the biological activity of fibroblasts [2]. No specific treatment exists for PDH. However, in most

cases, the PDP tends to stabilize over time [14]. Plastic surgery can be recommended for patients with complete primary PDH to improve their quality of life. The best treatment for patients with keloids is a combination of multiple approaches.

Similarly, keloids are a kind of dermatosis characterized by connective tissue hyperplasia. Several etiological factors for keloids, including genetic predisposition, tension present in the local skin environment, and immunoendocrine factors, have been proposed. However, the pathogenesis of keloid formation has not been elucidated, and there is no appropriate treatment that can yield a satisfactory therapeutic effect. At present, comprehensive treatment based on clinical manifestations is mainly applied to obtain the best therapeutic effect [15].

Intralesional injection of steroids, which inhibits and breaks down lesions by inhibiting fibroblast growth and accelerating collagen degradation, is one of the gold standards for keloid therapy [16, 17]. Current evidence has confirmed that 5-fluorouracil, a pyrimidine analog that inhibits the synthesis of deoxyribonucleic acids, is a safe and practical alternative for the treatment of keloids by inhibiting fibroblast proliferation [18]. Botulinum toxin, a powerful neurotoxin, inhibits neuromuscular transmission. Type A botulinum toxin can reduce scar formation by decreasing muscle tension during wound healing [19, 20], which may contribute to a pause in the fibroblast cycle, maintaining a nonproliferative state (G0 or G1) and affecting the expression of TGF-β [21, 22]. Carbon dioxide lasers are effective and safe treatments for hypertrophic scars and keloids [23]. Laser treatments vaporize blood vessels, restricting the access of inflammatory cytokines to hypertrophic scars and keloids and effectively suppressing abnormal scar formation [16]. Tranilast, an antifibrotic drug, is also combined with other agents for treating fibrotic conditions such as keloids and scleroderma [24, 25].

In this case, in consideration of the patient's physiological derangement of fibroblasts, after skin dermabrasion, we combined intralesional botulinum toxin type A, diprospan (a novel drug formulation of steroids), and 5-fluorouracil injections with a carbon dioxide lattice laser. We also used isotretinoin and spirolactone to inhibit oil secretion, while tranilast was used for the prevention of allergic reactions. The dose of isotretinoin depended on the patient's weight and severity of illness. The patient was pleased with the postoperative outcome.

The present case is unique because of the rarity of this disease, which was characterized by the presence of PDP with large facial keloids, and because of its comprehensive treatment. Consistent with the findings of previous reports, treatment by dermabrasion combined with intralesional botulinum toxin type A, diprospan and 5-fluorouracil injections and a carbon dioxide lattice laser yielded excellent therapeutic outcomes. This report provides additional evidence that laser therapy and local injection therapy are safe and effective treatment options for keloids in patients with complete primary PDP.

Statement of Ethics

Ethical approval is not required for this case report in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of his medical case and any accompanying images. Written informed consent was obtained from the patient for publication of the details of his medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. Haibo Zhao and Dr. Jianglin Zhang collected the information and wrote the manuscript. Dr. Renliang He and Dr. Linlin Bao revised the manuscript.

Data Availability Statement

All the data generated or analyzed during this case report are included in this article. Further inquiries can be directed to the corresponding author.

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