The Mask of Furrow: A Case of a 28-year-old Filipino Male with Pachydermoperiostosis*

Precious Imam, RN, MD[1]
Elizabeth P. Prieto MD, FPDS
Vilma Pelino MD, FPDS
Milali Torres MD, FPDS
Monique Lianne Lim Ang, MD, MBA, DPDS

ABSTRACT

Pachydermoperiostosis (PDP) or primary hypertrophic osteoarthropathy (PHO) is a rare genetic disorder that affects mainly skin and bones. Its main clinical features are pachyderma (thickening of the skin), periostosis (excessive bone formation) and clubbing of fingernails. The disease is more common among males with a 7:1 ratio, starts during adolescence and stabilize and cease progression after 5 – 20 years.

OBJECTIVE

To discuss the summary of the case, new management options, and outcomes of the management options.

CASE SUMMARY (Methods)

A 28-year-old male presents with a 9-year history of wrinkling of his facial skin. Other associated symptoms were seborrhea, acne, clubbed fingers, and occasional minimal knee joint pain. Histopathology results showed thickened dermis, fibrosis of the papillary dermis and around the folliculosebaceous units, hyalinized collagen bundles involving the fibrous trabeculae of the subcutis, and prominence of sebaceous and eccrine glands. The patient was given oral isotretinoin at 0.5 mg/kg/day, underwent fractional CO2 laser for rhytides and large pores, and given botulinum toxin A injection (total of 16 U) on 5 sites at the glabellar region. The patient was referred to plastic surgery for frontal rhytidectomy, and orthopedic surgery for management of joint pains.

RESULTS

The patient noted 80% improvement from baseline.

CONCLUSION

Treatment of pachydermoperiostosis is mainly symptomatic and requires a multi-specialty approach. Because of its rarity, treatment options for pachydermoperiostosis have yet to be standardized. In this particular case, all available options in the institution were utilized which led to satisfaction of the patient of the outcome.

Keywords: pachydermoperiostosis, primary hypertrophic osteoarthropathy

INTRODUCTION

Pachydermoperiostosis or primary hypertropic osteoarthropathy is a rare hereditary disorder that was first described in 1868. It is characterized by digital clubbing, pachydermia (thickening of the facial skin and/or scalp), and periostosis (swelling of periarticular tissue and subperiosteal new bone formation. It is associated with pain, polyarthritis, cutis verticis gyrata, seborrhea, eyelid ptosis, and hyperhidrosis. Touraine et al described 3 forms of pachydermoperiostosis or primary hypertropic osteoarthropathy: (1) a complete form with pachydermia and periostitis, (2) an incomplete form with evidence of bone abnormalities but lacking pachydermia, and (3) a forme fruste with prominent pachydermia and minimal-to-absent skeletal changes. [1,2]

*1st Place, 2021 Philippine Medical Association Case Report Presentation, June 21, 2021
[1]From Department of Dermatology, East Avenue Medical Center, Quezon City

The male to female ratio is 7:1, and the disease usually starts during adolescence, progressing up to 5-20 years and later on stabilizes. There is no known treatment for this disease, however, symptomatic therapies have been tried mostly with favorable results. The aim of this case report is to discuss the summary of the case, new management options, and outcomes of the management options. [1,2]

CASE REPORT

We are presented with 28-year-old male, Filipino, electrician helper, from Quezon City. His chief complaints were furrows on the face, plaques on the scalp and face, and digital clubbing. Nine years prior to consult when the patient noted few fine wrinkles on his forehead with a sudden increase in oiliness of his face. There were no other associated symptoms at that time. In the interim, the patient noted an asymptomatic clubbing of all his fingers as well as occasional minimal bilateral knee joints pain. The patient denies any dyspnea, cyanosis, or chest tightness. There was also no change in appetite or weight loss. Three years prior to consult the patient noted pruritic plaques with scales on both mandibular areas and frontal areas. The patient applied fruit peelings from "calamansi" and astringent which would cause an intense stinging sensation. This led the patient to discontinue using the fruit peelings and astringent. The patient also noticed increased wrinkling on his face, for which he was teased as "laging galit. He was advised 2D echo which was subsequently done and revealed normal results – hence he was referred to the dermatology department.

His review of systems was generally unremarkable except for bilateral knee joint pains. He was not known to have any co-morbidities. His family history revealed allergies to chicken meat, hypertension, and diabetes mellitus. The family genogram is demonstrated in the figure below. He is a non-smoker and an occasional alcoholic beverage drinker.

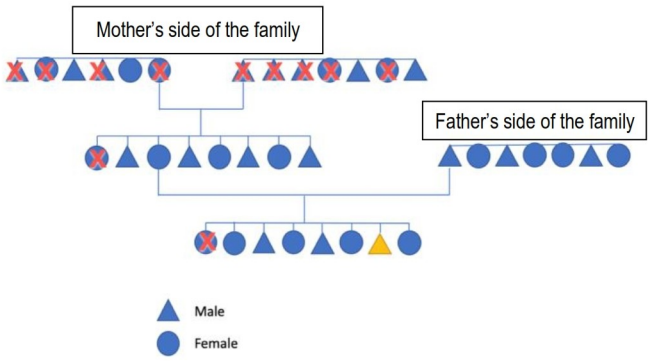

Figure 1. Family Genogram of the Patient

Physical examination was generally unremarkable except for bilateral swelling of knee joints. His cutaneous examination revealed thickened and greasy facial skin with deep frontal, glabellar, and perioral rhytides, erythematous plaques with greasy scales on bilateral mandibular areas, frontal scalp, and bilateral eyebrows, skin colored to yellowish papule on the nose and mentum, erythematous papules on the face, large pores and digital clubbing.

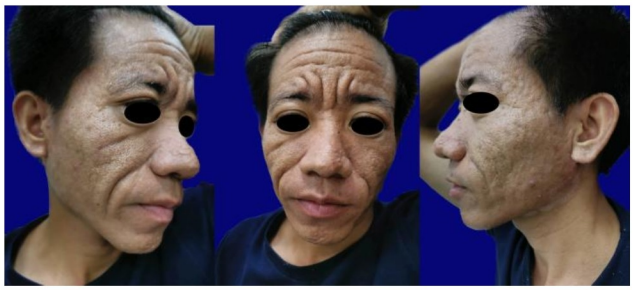

Figure 2. Picture of the patient's face showing deep wrinkles, seborrhea, acne, and seborrheic dermatitis

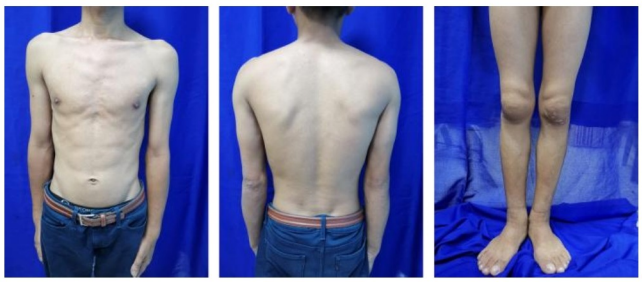

Figure 3. Picture of the patient's trunk and extremities with noted swelling of both knees

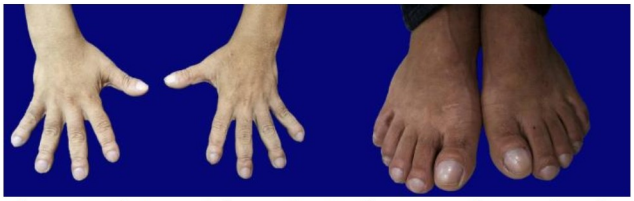

Figure 4. Picture of the patient's fingers and toes showing digital clubbing

Skin punch biopsy was done which showed somewhat thickened dermis, fibrosis of the papillary dermis and around the folliculosebaceous units, slightly thickened collagen bundles in the reticular dermis, focal area of mild edema and mucin deposition in the mid-reticular dermis, focal area of markedly thickened, hyalinized collagen bundles involving the fibrous trabeculae of the subcutis, prominence of sebaceous and eccrine glands and a mild lymphocytic infiltrate around the superficial plexus and folliculosebaceous units. The epidermis shows slight acanthosis. The findings were compatible with Pachydermoperiostosis.

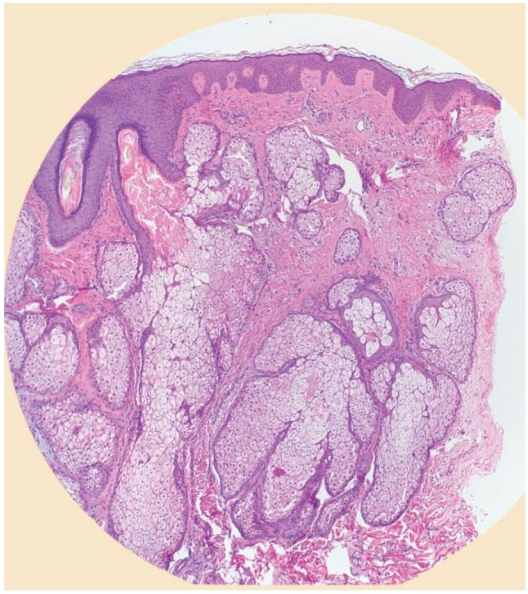

Figure 5. Histopathology (H & E stain) of the patient's skin showing prominence of sebaceous and eccrine glands.

Other ancillary tests such as CBC, Thyroid Panel, Serum growth hormone, Lipid profile, Liver and Kidney function tests were normal. Bones series showed periosteal reaction, no fractures, and infiltrates on the chest were seen.

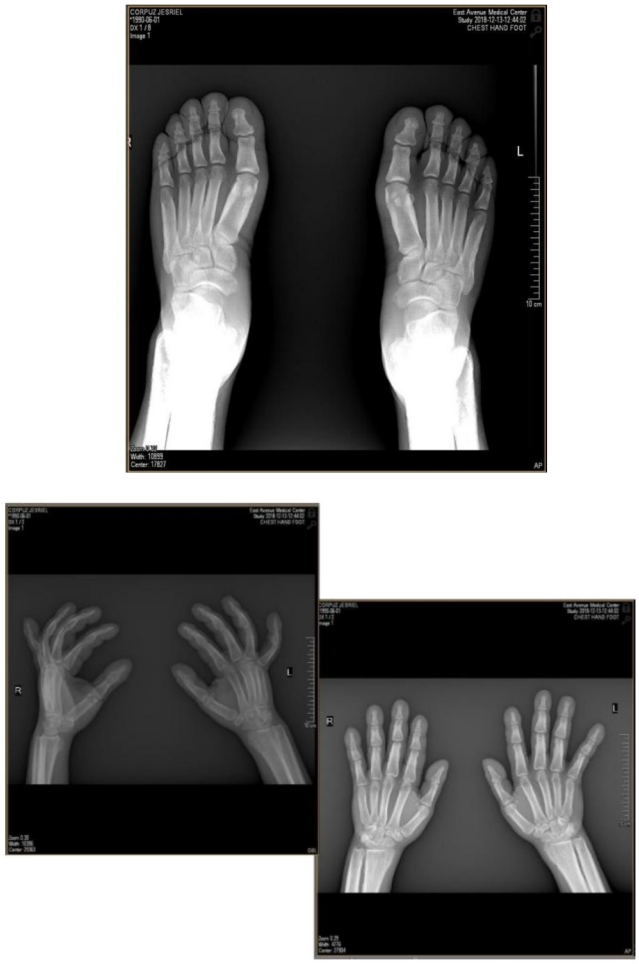

Figure 6. Roentgenogram of patient's extremities showing periosteal reaction.

The patient was started on oral isotretinoin at 20 mg/ day, topical antifungals and hydrocortisone for the Seborrheic dermatitis, and Celecoxib 100 mg/ day as needed for joint pains. The patient was referred to Orthopedics and Plastics Surgery. Frontal rhytidectomy was done improving the patient's deep wrinkles on the forehead. Fractional CO2 laser for deep rhytides setting and Botulinum toxin injection (total of 16 Units on 4 sites on the forehead) were performed.

The patient noted an 80% improvement overall with noted decrease in oiliness, acne eruption, and seborrheic dermatitis flares. The deep wrinkles on his face have also become more superficial. The patient was scheduled to have monthly sessions of fractional CO2 laser and every

3 to 6 months repeat injections of Botolinum toxin however he was lost to follow-up. The patient was last seen on his 8th consult (7 weeks post-frontal rhytidectomy, 2 weeks post-fractional CO2 laser, and 4 days post-Botulinum toxin type A injection).

DISCUSSION

Pachydermoperisotosis (PDP, Touraine–Solente– Gole syndrome or Primary Hypertrophic Osteoarthropathy) is a rare disorder characterized by digital clubbing, pachydermia (thickening of the facial skin and/or scalp), and periostosis (swelling of periarticular tissue and subperiosteal new bone formation. It is associated with pain, polyarthritis, cutis verticis gyrata, seborrhea, eyelid ptosis, and hyperhidrosis. Touraine et al described 3 forms of pachydermoperiostosis or primary hypertropic osteoarthropathy: (1) a complete form with pachydermia and periostitis, (2) an incomplete form with evidence of bone abnormalities but lacking pachydermia, and (3) a forme fruste with prominent pachydermia and minimal-to-absent skeletal changes. The male to female ratio is 7:1, and the disease usually starts during adolescence, progressing up to 5-20 years and later on stabilizes. (Joshi, et al). According to the Philippine Dermatological Society, there were only 8 cases reported from 2011 to 2018. Worldwide prevalence rate was reported to be at an estimated 0.16% [1,2,3]

The diagnosis of PDP can be made clinically and radiologically, however, due to rarity of this disorder it is often overlooked.[1] Dermatologists help establish the diagnosis by doing clinical and histopathological correlation.

The diagnostic criteria for PDP include major criteria consisting of pachyderma, periostosis, and finger clubbing, as well as minor criteria including hyperhidrosis, arthralgia, gastric ulcer, cutis verticis gyrate, blepharoptosis, joint effusion, column-like legs, edema, seborrhea, acne, and flushing. On the basis of the physical examination, radiologic, and histopathologic findings, the final diagnosis is that of a complete form of PDP. [1,2]

The differentials for PDP include the following:

Leprosy (Hansen's Disease) is a chronic infectious disease which is acquired through the droplet route from chronic exposure to affected individuals. It primarily involves the cutaneous system and peripheral nerves. The etiologic agent is an acid-fast bacilli Mycobacterium leprae. Hansen's disease is classified according to clinical manifestations and number of bacilli, from the tuberculoid type (TT) to the lepromatous type (LL). Lepromatous leprosy, the form with the least cellular immunity and most number of bacilli, initially manifests as erythematous macules, papules, nodules, and plaques. Some patients also manifest with ocular problems, widening of the nasal root, enlargement of ear lobes, thickening of the forehead skin and folding hence the "leonine facies". Other signs and symptoms include hypoesthesia or anesthesia in a stocking or glove pattern, enlarged peripheral nerves, madarosis, saddle nose deformity. The most commonly involved areas are the face and buttocks, mostly on cool areas. [4] The patient presented with **thickened forehead skin** and **furrows resembling the leonine facies,** however he does not have exposure to patients with Leprosy, he denies hypoesthesia or anesthesia, he does not have enlarged peripheral nerves, other cutaneous findings such as macules, papules, nodules, or plaques, nor madarosis. Hence, Hansen's disease is not a likely diagnosis.

Thyroid acropachy is rare manifestation of an autoimmune thyroid disorder and usually presents first with **ophthalmopathy** (ptosis, exophthalmos, upper eye lid retraction, and conjunctivitis), followed by **dermopathy** (erythematous and edematous lower extremities especially the tibial regions), and finally **acropachy** (soft-tissue swelling of the hands and feet and digital clubbing). [1] The patient denies any history suggestive of thyroid problems such as palpitations, heat or cold intolerance, appetite changes, weight changes. The patient does not have ophthalmopathy and dermopathy, although he has acropachy. The thyroid function tests of the patient also turned out normal.

Acromegaly. Gigantism refers to abnormally high linear growth due to excessive action of insulinlike growth factor I (IGF-I) while the epiphyseal growth plates are open during childhood. Acromegaly is the same disorder of IGF-I excess but occurs after the growth plate cartilage fuses in adulthood. The average time of diagnosis of acromegaly is between 40-45 years old. Acromegaly can be an insidious disease. The symptoms are either due to the excessive Growth Hormone/IGF-1 or intracranial tumor. Patients with acromegaly may present with soft tissue swelling and enlargement of extremities, increase in ring or shoe size, hyperhidrosis, coarsening of facial features, large pores, wide spacing of teeth, deepening of the creases on the forehead and nasolabial folds, cutis verticis gyrate, skin tags, oily skin, acanthosis nigricans,hypertrichosis, prognathism, macroglossia, arthritis, and increased incidences of DM, electrolyte disturbances, and CHF. [1,2] Although the patient has **coarse facial features**, **arthritis, oily skin, and large pores**, he does not have other acromegalic features as mentioned. The patient's GH is normal, hence we can rule this out.

Phymatous rosacea is a subtype of rosacea characterized by centrofacial flushing, centrofacial erythema and telangiectasia seen in other forms of rosacea. This disease shows marked skin thickening and irregular surface nodularities of the nose, chin, forehead, one or both ears and/or the eyelids and patulous follicular orifices. [5] However, in our patient while there is thickening over the facial area, the other characteristics of rosacea are absent. Furthermore, there are no joint or bone abnormalities seen in rosacea.

Treatment options vary for PDP, in general. One case report noted that colchicine improved the articular symptoms, folliculitis, and pachyderma. Another report showed joint symptoms were responsive to IV pamidronate. Oral isotretinoin helped with skin manifestations (pachyderma and cutis verticis gyrate). Variants of PDP include RosenfeldKloepfer syndrome (characterized by enlargement of the jaws, especially mandible, and of the hands and feet, nose, lips, tongue, and forehead, along with cutis vertices gyrata and corneal leukoma); Currarino idiopathic osteoarthropathy (an incomplete form of PDP seen in children and adolescents and characterized by the presence of eczema and sutural diastases); and a localized form with only radiographic features of PDP in the lower extremities. [2]

This patient was given oral isotretinoin to help with increased sebum production which predisposes him to acne and recurrent seborrheic dermatitis. Isotretinoin is usually given at 0.5 mg/kg/day with a maximum of 2.0 mg/kg/day. Park et al reported giving oral isotretinoin to a patient with PDP with a favorable result and patient satisfaction in terms of facial seborrhea. [6]

He was then referred to orthopedics and plastic surgery for evaluation. Orthopedics disposition included close observation and agreed with giving of pain medication for the knee joint pains. Plastics surgery performed frontal rhytidectomy.

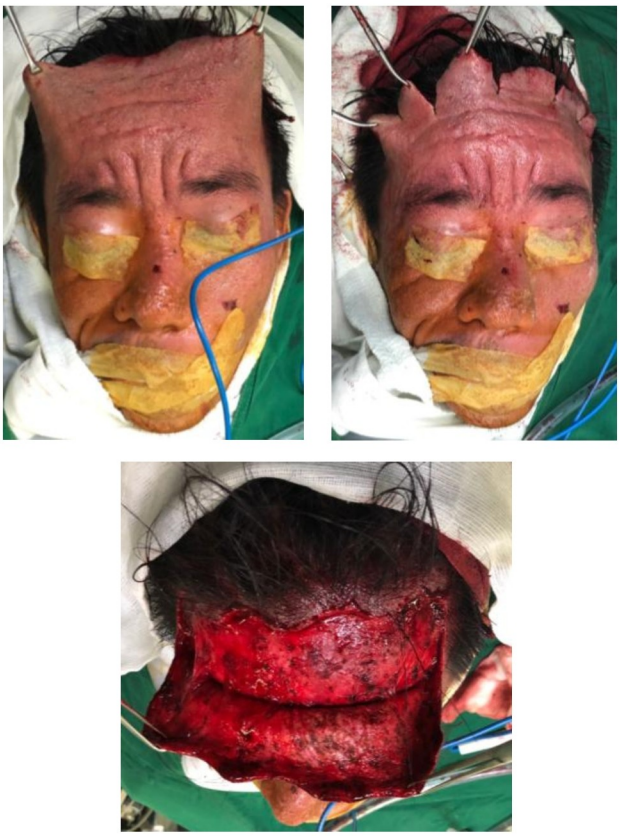

Figure 7. Frontal rhytidectomy done on the patient.

In 2019, Salah et al reported a case of a 19-year-old male with PDP who underwent frontal rhytidecotomy which significantly improved the deep wrinkles on the patient's face. This was the basis in doing the same procedure to our patient. Similar results were also achieved with the said procedure. [7]

In two separate journals, Salah et al and Chen et al reported the use of Botulinum toxin type A for deep rhytides and seborrhea. The doses given were between 1 to 4 Units per site in 4 to 5 sites of the face. The patients were followed-up every 6 months and re-injection of Botulinum toxin type A were done on follow-up with noted treatment satisfaction from the patients. Botulinum toxin type A temporarily helps in pachyderma and seborrhea by blocking the release of acetylcholine which is the principal neurotransmitter of the neuromuscular junction. [7,8] In our patient, a total of 16 Units was given (4 units per site for 4 sites) on the frontal areas. The patient was lost to follow-up hence the effect of Botulinum toxin type A could not be assessed.

In published journals, the use of Fractional CO2 laser for the treatment of deep wrinkles seen in PDP has not been documented yet. To the author's knowledge, this is the first case in the Philippines that the said laser technique was used for this specific case. This modality was chosen due to its safety profile, efficiency, and precision. [9] The wavelength of CO2 is 10,600 nm which targets water (dermis contains a very high water percentage). This makes the CO2 fractional laser ideal for deep wrinkle whose main pathology lies on the dermis. [9]

The pathophysiology of PDP has been linked to a range of processes which include malignancy, autoimmune diseases such as Crohn disease, and myelofibrosis. (2) Patients with PDP harbor defects in either the HPGD (15-hydroxyprostaglandin dehydrogenase) gene or the SLCO2A1 (solute carrier organic anion transporter family member 2A1) gene, resulting in elevated prostaglandin E2 levels. Thus, it is postulated to play roles in pleiotropic actions in different tissues. [7]

As a consequence of increased soft tissue bulk and hyperostosis, complications of PDP to watch out for include ptosis, compression of the nerve endings, hearing problems, kyphosis, arthrosis, osteonecrosis of the femoral head, and carpal tunnel syndrome. [2]

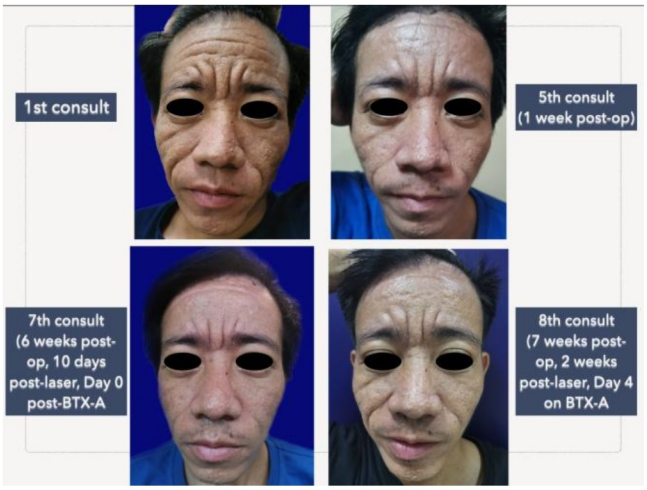

Figure 8. Comparison photos of the patient from baseline to his eighth consult.

CONCLUSION

The diagnosis of PDP can be done clinically however the help of histopathology increases the accuracy of the diagnosis given that this condition is rare and requires expertise and experience from clinicians to be able to diagnose the disease. It is also useful to differentiate primary from the more insidious secondary type of hypertrophic osteoarthropathies.

Treatment of pachydermoperiostosis is mainly symptomatic and requires a multi-specialty approach. Because of its rarity, treatment options for pachydermoperiostosis have yet to be standardized. In this patient, we note that he benefited significantly through a holistic approach such as plastic surgery, laser surgery, and botulinum toxin injection as well as oral and topical therapies for his secondary problems such as acne and seborrheic dermatitis. In this particular case, all available options in the institution were utilized which led to patient satisfaction of the outcome.

REFERENCES

1. Joshi A, Nepal G, Shing YK, Panthi HP, Baral S. Pachydermoperiostosis (Touraine-Solente-Gole syndrome): a case report. J Med Case Rep. 2019 Feb 21;13 (1):39. doi: 10.1186/s13256-018-1961-z.PMID: 30786934; PMCID: PMC6383214.

2. Supradeeptha C, Shandilya SM, Vikram Reddy K, Satyaprasad J.Pachydermoperiostosis - a case report of complete form and literature review. J Clin Orthop Trauma. 2014 Mar;5 (1):27-32. doi: 10.1016/j.jcot.2014.02.003. Epub 2014 Mar 20. PMID: 25983465; PMCID: PMC4009462.

3. Jajic I., Jajic Z. Prevalence of primary hypertrophic osteoarthropathy in selected population. *Clin Ex Rheum.* 1992;10:73.

4. Salgado CG, Brito AC, Salgado UI, Spencer, JS. Fitzpatrick's Dermatology. 9th edition. United States of America: Palatino LT Std by Cenveo® Publisher Services; c2019. Chapter 159, Hansen's Disease; p. 2892-2911.

5. Steinhoff M, Buddenkotte J. Fitzpatrick's Dermatology. 9th edition. United States of America:Palatino LT Std by Cenveo® Publisher Services; c2019. Chapter 79, Rosacea; p. 1419-1433.

6. K Park, Y & Joo Kim, Hyung & Yang Chung, Kee. (1988). Pachydermoperiostosis: Trial with Isotretinoin. Yonsei medical journal. 29. 204-7. 10.3349/ymj.1988.29.2.204.

7. Salah BI, Husari KI, Hassouneh A, Al-Ali Z, Rawashdeh B. Complete primary pachydermoperiostosis: A case report from Jordan and review of literature. Clin Case Rep. 2019 Jan 9;7(2):346-352. doi: 10.1002/ccr3. 1971. PMID: 30847204; PMCID: PMC6389490.

8. Chen, Wen-Shan & Lai, Chih-Sheng & Juan, Chao-Kuei & Yang, Chi-Shun & Chiu, You-Hsin & Tseng, Chih-wei & Chen, Yi-Ju. (2018). Pachydermoperiostosis in a 19-year-old Taiwanese man. Dermatologica Sinica. 36. 10.1016/j.dsi.2018.05.002.

9. Omi T, Numano K. The Role of the CO2 Laser and Fractional CO2 Laser in Dermatology. Laser Ther. 2014 Mar 27;23(1):49-60. doi: 10.5978/islsm.14-RE-01. PMID: 24771971; PMCID: PMC3999431.