Pachydermoperiostosis mimicking acromegaly in an adult Filipino male: Case report

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Pachydermoperiostosis is a rare genetic disorder. The pathophysiology remains incompletely understood, and various patterns of inheritance have been proposed: autosomal dominant, autosomal recessive and x-linked. Variable penetrance has also been observed. Frequently manifesting with pachydermia, cutis verticis gyrata and enlarged limbs, pachydermoperiostosis may clinically resemble acromegaly. Features more frequently seen in pachydermoperiostosis rather than acromegaly include seborrhea, periorbital edema and clubbing. A 19-year-old Filipino male was referred to our clinic for further evaluation of coarsened skin on the scalp and face. Symptoms started at the age of 13 as insidious, progressive enlargement of bilateral lower extremities and hands, followed by thickening facial features and skin folds on the scalp. On work up, serum cortisol, FSH, LH, growth hormone levels and 75 gram oral glucose growth hormone suppression test were all normal. This led endocrinologists to consider this as a case of “burned out acromegaly,” a condition characterized by spontaneous involution of a pituitary adenoma. However, normal predicted height measurements and histopathologic findings did not support an endocrinological disorder. Furthermore, cranial imaging and ophthalmologic findings were not consistent with pituitary apoplexy. Periorbital edema, clubbing, and radiographic evidence of periosteal thickening pointed to pachydermoperiostosis. Similar physical findings in the patient’s siblings have prompted further investigation. This case highlights the importance of an exhaustive history and physical exam in any diagnostic dilemma, emphasizing that seemingly simple cases may not always be as straightforward. This report further underscores the importance of a multi-disciplinary approach to patient care, highlighting the role of dermatologists in systemic diseases.

Keywords: pachydermoperiostosis, cutis verticis gyrata, acromegaly

INTRODUCTION

Pachydermoperiostosis is a rare genetic disorder that presents with pachydermia (thickening of the skin), periostosis (formation of new bone), and clubbing. Some cases also present with periorbital edema, as well as cutis verticis gyrata, or irregular thickenings on the scalp so named for their resemblance to cerebriform folds. Worldwide, the incidence of pachydermoperiostosis is unknown. In the authors’ dermatology clinic at the Outpatient Department of a tertiary government hospital, only three such cases were reported from 2011 to 2015.

Certain endocrinologic disorders may present similarly. When excessive production of growth hormones occurs in childhood while epiphyseal plates are open, the result is gigantism. In adulthood, when epiphyseal plates have fused, this same disorder is referred to as acromegaly. Acromegaly is an endocrinologic disorder characterized by excess growth hormones in adults, most often due to a pituitary adenoma. Clinically, pachydermoperiostosis may resemble acromegaly, particularly when the skin of the face and extremities are involved.

Here the authors present the case of a patient with pachydermoperiostosis who was initially misdiagnosed as acromegaly.

CASE REPORT

A 19-year-old Filipino male without any co-morbidities consulted at the Outpatient Department of a tertiary government hospital for thickened skin folds on the scalp and face. In 2009, six years prior to consult, he first noticed gradual enlargement of both feet, manifesting as an increase in shoe size from a size 9 to a size 10 within one year. The patient was 13 years old at this time. He denied any trauma or associated pain, arthralgia, numbness or weakness. No medical attention was sought, and no medications were applied or ingested.

In 2013, he noted gradual enlargement of both hands, manifesting as the inability to fully close his hand and grasp objects properly. No other symptoms were noted, hence no consult or treatment was done.

In 2014, one year prior to consult, the patient then noticed coarsening of facial features, described as “worsening of eyebags.” While getting a haircut, he also noticed irregular, thickened folds on his scalp.

These symptoms led him to consult a private physician, who diagnosed and managed him as a case of elephantiasis. Over time, however, symptoms did not improve to the prescribed antibiotics, and the patient was lost to follow up.

In April 2015, he consulted at tertiary government hospital where he was eventually seen by Endocrinology and Dermatology for further evaluation and co-management. At this time, the patient also complained of blurring of vision, described as difficulty reading. However, he did not report any headache, vomiting, or any other symptoms.

Upon consulting at Dermatology, he was awake, ambulatory and coherent. He weighed 59 kg and stood 1.59 m tall, giving him a BMI of 24.5 kg/m² and categorizing...
him as overweight. Blood pressure and other vital signs were all normal. There was marked bilateral, periorbital edema. He also presented with bilateral, symmetric enlargement of the hands, and prominent clubbing (Figures 1-3). There was likewise bilateral, symmetric enlargement of the feet, accompanied by Grade II, non-pitting edema. The rest of the systemic physical examination was normal. Neurologic examination was also normal.

Dermatologic examination revealed irregularly shaped, soft, non-tender folds on the right temporal area of the scalp, as well as multiple erythematous papules and pustules on the forehead, both cheeks and upper third of the back. There were some visible open comedones on the nose. (Figures 4-5)

Work-up for this patient included measurement of follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone and insulin like growth factor-1 (IGF-1) levels. A skeletal survey and cranial MRI were also ordered, and a 4 mm punch biopsy of the indurated skin on the right leg was done. The patient was also referred to ophthalmology for evaluation.

Contrary to expected results, FSH, LH, testosterone and IGF-1 levels were all normal. Following this, a 75 gram oral glucose growth hormone suppression test was ordered. Cranial MRI results were normal. The pituitary and the sella appeared normal in size and homogenous, without any filling defects or intracranial masses. Skeletal survey showed a mesocephalic skull, and an intact sella and clinoids. There was no prognathism. Chest x-ray was normal. However, symmetric, periosteal thickening was seen in the shafts of both radii, ulnae, and tibiae. The cortices of the metatarsal shafts of both big toes were also thickened. These radiographic findings were compatible with mild, hypertrophic pachydermoperiostosis.

Histologic findings of the skin segment obtained from the right leg showed a mild, superficial, perivascular lymphocytic infiltrate and slight widening of the collagen bundles in the dermis, consistent with papillomatous epidermal hyperplasia. Sebaceous glands were not noted to be prominent, nor were the collagen bundles or fibroblasts increased.

Formal evaluation by an ophthalmologist confirmed the presence of bilateral periorbital edema. He was diagnosed with bilateral error of refraction, but all other findings were normal.

At this time, endocrinologists proposed that the patient might be in a state of burned out acromegaly, a condition
characterized by spontaneous apoplexy of the pituitary gland.

**DISCUSSION**

Coarsened facial features, cutis verticis gyrata and enlarged hands and feet may present in both pachydermoperiostosis and acromegaly. For this reason, an exhaustive and analytic review of the history, physical exam and laboratory findings are necessary to differentiate the two.

The consistently normal hormone levels in this patient was very remarkable. In acromegaly patients, growth hormone measurement may prove challenging because of its pulsatile nature and short half-life. However, insulin-like growth factor-1 has excellent correlation with growth hormone, and is the most reliable biochemical indicator of acromegaly. Therefore, the normal IGF-1 level found in this patient was a reliable indicator of normal growth hormone levels.

As a confirmatory test, the 75 or 100 gram oral glucose tolerance test can be done. This entails measuring growth hormone levels 1-2 hours after administering oral glucose. Normally, growth hormones are suppressed, and failure to do so is diagnostic of acromegaly. Two hours after glucose ingestion, the patient’s growth hormone levels were markedly below normal, ruling out acromegaly.
Nonetheless, because the patient complained of blurring of vision and because most cases of acromegaly are caused by a pituitary adenoma, the authors thought it prudent to evaluate for an intracranial mass. However, neurologic exam was normal, and cranial MRI did not detect any intracranial mass. Furthermore, ophthalmologic examination was normal except for bilateral error of refraction and bilateral periorbital edema. A patient with a pituitary mass would be expected to have visual field cuts, which this patient did not have. Finally, patients with acromegaly present with tortuous retinal vessels, and these were not seen in the patient.

Gingival hyperplasia, macroglossia and prognathism are also consistent with acromegaly. These findings were not present, and radiographic imaging of the skull confirmed the absence of prognathism. (Figure 6)

Studies have described cases of acromegaly where the pituitary tumor undergoes infarction and necrosis, and resolves spontaneously without intervention. This pituitary apoplexy may manifest as a normally appearing sella on imaging. However, following this necrosis, the space previously occupied by the pituitary would persist as a filling defect containing cerebrospinal fluid. On sagittal views of cranial MRI images, this was not seen. Furthermore, pituitary apoplexy is rarely associated with complete normalization of growth hormone levels.

On histopathology, prominent sebaceous glands and increased fibroblasts are expected in patients with acromegaly. These characteristics were notably absent in the patient’s skin biopsy.

Pachydermoperiostosis, on the other hand, roughly translates to “thickening of the skin and bones.” It is a rare genetic disorder that may clinically mimic acromegaly.

While the patient’s initial appearance may suggest acromegaly, an analytic review of the history suggests otherwise. The patient’s symptoms began at 13-years-old, when the epiphyseal plates are still expected to be open. If this were truly a condition marked by excess growth hormone, more appropriately called gigantism in a pediatric patient rather than acromegaly, the manifestation would be an increase in height. Unfortunately, the patient’s anthropometric records were neither complete nor available for review. Only his foot size had been reliably documented, however this is not a routinely measured parameter in growing children, and normograms for them are non-existent. In an effort to compensate for this, the authors computed his expected height based on both his parents’ height. The investigators saw that, at a current height of 158.5 cm, he did not even meet his expected height of 169 cm. This made growth hormone excess unlikely.

Furthermore, studies have described a greater incidence of periorbital edema, clubbing and seborrhea among pachydermoperiostosis patients compared to acromegaly patients. All these were present in this patient.

Radiographically, symmetric periosteal thickening was seen in the cortices of both radii, ulnae, tibiae, and metatarsal shafts. This is also consistent with pachydermoperiostosis.

The Borochowitz criteria has been proposed to establish the diagnosis of pachydermoperiostosis. This is comprised of family history of the same condition, clubbing, hypertrophic skin changes, and bone pain or radiographic changes. This patient presented with coarsened facial and scalp skin, clubbing, and had radiographic evidence of periostosis, satisfying three out of the four requirements. The absence of any ophthalmologic or neurologic symptoms, hormonal level abnormalities, histopathologic changes suggestive of an endocrinopathy, prognathism and intracranial mass further underscores that this is a case of pachydermoperiostosis rather than acromegaly.

CONCLUSION

Pachydermoperiostosis and acromegaly have remarkable clinical overlap. However, clubbing and periostosis without prognathism, an enlarged sella turcica or abnormal levels of growth hormone point more towards pachydermoperiostosis.

Both primary and secondary forms of pachydermoperiostosis may exist. Currently, the patient is undergoing further tests geared towards identifying a possible malignancy to rule out a cause of secondary pachydermoperiostosis. Appropriate management of acne vulgaris has likewise been started, and the possibility of plastic surgery to correct coarsened facial folds has been discussed with the patient. The patient’s brothers, who present with similar but milder clinical features, have been advised and encouraged to undergo work up.

This case highlights the complex nature of dealing with diseases that span both the pediatric and adult ages. History and examination findings must always be taken with the appropriate context. This case likewise demonstrates how a multi-disciplinary approach is most beneficial for patients, and emphasizes the role dermatologists play in diagnosing and managing systemic diseases.