Clinical Vignette

Taking Another Look

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Case Report

A 64-year-old Hispanic female presented to her primary care clinic for a follow-up visit. She had type 2 diabetes and complained of bilateral hand pain for six months. The pain was dull, constant, and at a level 4/10. Patient denied any fever, chills, weight loss or rash. She was treated with a number of non-steroidal anti-inflammatory medications without improvement. Past medical history includes diabetes, osteoporosis and osteoarthritis with right knee arthroplasty.

She was an obese Hispanic female with coarse facial features, prominent chin, thickened dull skin, and large thick lips. She was 5'2" and 173 pounds with BMI of 31. Exam was remarkable for a large tongue and abundant soft tissue on her large hands and feet. Light was not seen between digits. Phalen's and Tinel's signs were negative and she had normal grip strength bilateral without thenar atrophy.

Initial labs included a normal comprehensive metabolic panel and complete blood count (CBC), negative rheumatoid factor and normal thyroid stimulating hormone (TSH). The hemoglobin (HgB) A1C was slightly elevated at 6.3% (4.0-6.0%).

Due to her unusual features and the changes in her facial features compared to an older photo ID, the physician obtained an insulin-like growth factor level that was elevated at 345 nanograms per milliliter (ng/mL) (87-178 ng/mL). MRI of her brain was remarkable for a 6 millimeter (mm) lesion in the right aspect of the pituitary gland suggestive of a pituitary microadenoma. There is minimal extension into the suprasellar cistern, but no evidence of impingement of the optic chiasm. Bilateral hand x-rays showed generalized osteoporosis and minimal degenerative changes of bilateral metacarpophalangeal joints.

Discussion

Acromegaly is a disorder due to excessive production of the growth hormone, most commonly due to a benign growth hormone secreting pituitary tumor. Diagnosis is often delayed up to 10 years or more due to indolent growth of the somatotroph adenoma and often subtle clinical findings in early stages[1]. The usual age of diagnosis is middle aged. Men and women are affected equally with prevalence estimated at 60 per million and incidence of about 3 cases per 1 million persons/year[2].

Clinical features of acromegalic patients are enlarged forehead and mandible (frontal bossing, and prognathism, respectively.) Other facial findings include large noses, thick lips and prominent facial lines/folds as is seen in our patient[3]. (Figure 1) Distal extremities are broad with dough-like hands and feet, with hypertrophy of soft tissue causing total occlusion of inter-digital spaces. (Figures 2-5) Patients tend to have low deep voices[1].

Acromegalic patients often complain of musculoskeletal symptoms such as arthralgias/arthritis, myalgias, paresthesias[4]. Back pain is common due to dorsal kyphosis, and scoliosis[5]. Incidence of carpal tunnel syndrome is increased due to growth hormone mediated median nerve edema that resolves with treatment of the disease[5]. Headaches are common in acromegalics. Interestingly, they are independent of pituitary tumor size and appear to be multifactorial. Hypertension, arrhythmias, valvular disease, and congestive heart failure are associated with acromegaly[1]. These conditions do not resolve after treatment to decrease growth hormone or insulin-like growth factor- I[2]. More

than half of acromegalics have obstructive sleep apnea and may complain of snoring, morning fatigue, daytime sleepiness, headaches, and frequently have poorly controlled hypertension.

Patients with acromegaly have an increased risk for colon cancer double of that of the general population[2]. Growth hormone's metabolic effects on these patients include insulin resistance, with difficult to control diabetes, impaired glucose tolerance, and hypertriglyceridemia[1,2]. Suspicion of acromegaly starts with clinical findings and is confirmed with biochemical tests. Usually insulin-like growth factor [IGF-I] level is ordered. If IGF-I level is elevated, then an oral glucose suppression test with growth hormonal [GH] is recommended. For the most part, suppression of GH after an oral glucose challenge rules out the diagnosis of acromegaly. If the oral glucose suppression test is positive, i.e., no suppression of GH, then an MRI of the pituitary is done to localize the source of GH secretion.

There are several methods to treat acromegaly. In general, transphennoidal surgery is used to treat microadenomas and to decompress mass effects of an adenoma on adjacent tissues. Surgery is an effective way to reduce GH and IGF-I levels[5]. Patients who fail surgical treatment are offered radiation and medical therapy.

Radiation therapy involves highly focused beam to minimize damage to adjacent organs[1,5]. Half of the patients treated with radiation therapy end up with hypopituitarism[2]. Treatment with somatostatin receptor ligands is also a highly effective way to normalize both GH and IGF-I levels. Somatostatin receptor ligands used in the United States are octreotide and lanreotide; both are injectable and costly. These drugs are used as first line therapy for poor surgical candidates, unresectable tumors, and are used as second line treatment for patients who failed surgical and radiation therapy. Treatment with somatostatin receptor ligands is chronic and required to be continued long term. Side effects of this medication include nausea, diarrhea, and abdominal pain. Gallbladder stones or sludge can occur up to 20% of patients using these medications[5].

Pegvisomant is a novel agent used to treat acromegaly. It is an injectable growth hormone like protein and works by blocking at the growth hormone receptor and inhibits endogenous GH activities, such as the production of IGF-I . It is used on patients who failed somatostatin analogue therapy. It is very effective in decreasing IGF-I production in up to 90% of those treated[5]. Because it has been associated with a small increase in tumor size it is contraindicated in patients with compressive symptoms. If this medication is used, then close monitoring of tumor size is recommended. The most common side effects of the medication are diarrhea, nausea, and hepatotoxicity, and liver enzymes should be monitored routinely[2,5].

Dopamine receptor agonists have also been used to treat acromegaly. In general, they are not as effective treatment, however, cabergoline when used in combination with somatostatin receptor ligands has a synergistic effect to decrease growth hormones levels.

This patient had complained of headaches and hand/wrist pain for more than 15 years. Her hands/wrist pains were diagnosed as carpal tunnel syndrome, a common condition in diabetes but also found in acromegaly.

Other symptoms documented in her chart include headaches with occasional blurry vision. However, no neurologic exam was recorded or plans for further investigation documented in the following visits.

Many patients with carpal tunnel syndrome have negative Phalen's and Tinel's signs, as these signs are not sensitive. However, if a patient fails treatment, further investigation may be warranted. Hand and wrist pain was most likely due to the expansion of bones and connective tissues from acromegaly[1,4]. Earlier diagnosis of acromegaly may have prevented damaging consequences of a chronic progressive disease.

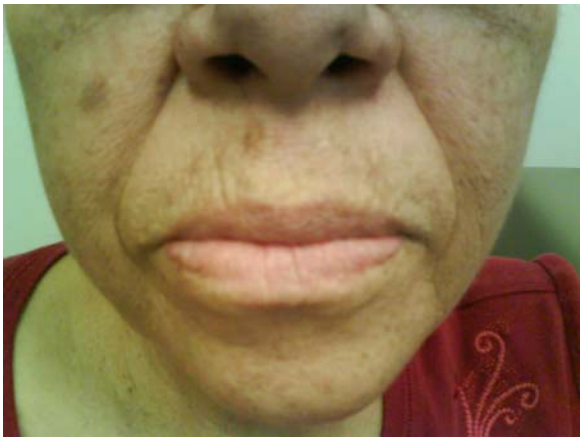
Once the diagnosis was made, patient was referred to get appropriate therapy. She underwent transsphenoidal resection of her pituitary tumor. Her headaches, hand and wrist pain had resolved after surgery.

Conclusion

In conclusion, in this case the general appearance of a patient can help guide the physician to the diagnosis as long as the physician keeps an open mind and is not biased by prior working diagnoses. Physicians should consider alternative explanation for conditions that do not resolve.

FIGURE LEGENDS:

Figure 1. Notice patient coarse facial features, android like with prominent chin, thick dull skin, large thick lips and large nose.



Figures 2-4. Different views of patient's hands. Hands are soft and doughy and spade-like with excess soft tissue.

Figure 2.

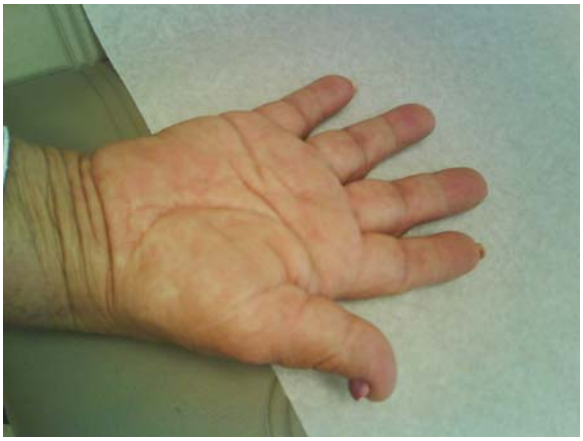


Figure 3.

Figure 4.

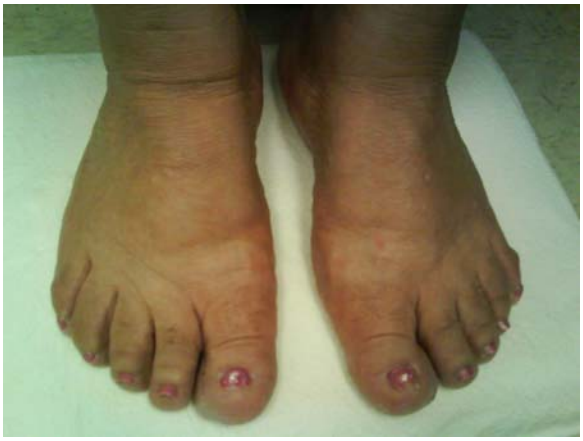


Figure 5. Feet are thick with doughy toes. Inter-digital space would be lost when toes are adducted.

REFERENCES:

1. **Ben-Shlomo A, Melmed S**. Acromegaly. *Endocrinol Metab Clin North Am*. 2001 Sep;30(3):565-83, vi. Review. PubMed PMID: 11571931.
2. **Melmed S**. *Medical Progress*: Acromegaly. N Engl J Med. 2006 Dec 14;355(24):2558-73. Review. Erratum in: N Engl J Med. 2007 Feb 22;356(8):879. PubMed PMID: 17167139.
3. **Chan MR, Ziebert M, Maas DL, Chan PS**. "My rings won't fit anymore". Ectopic growth hormone-secreting tumor. *Am Fam Physician*. 2005 May 1;71(9):1766-7. PubMed PMID: 15887456.
4. **Jacobs-Kosmin D, DeHoratius RJ**. Musculoskeletal manifestations of endocrine disorders. *Curr Opin Rheumatol*. 2005 Jan;17(1):64-9. Review. PubMed PMID: 15604907.
5. **Chanson P, Salenave S**. Acromegaly. *Orphanet J Rare Dis*. 2008 Jun 25;3:17. Review. PubMed PMID: 18578866; PubMed Central PMCID: PMC2459162.

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