Challenge of Dealing with Acromegalic Patient with Non-Culprit Lesion

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Abstract

Acromegaly is commonly caused by GH secreting pituitary adenoma, which are nearly always identifiable in conventional magnetic resonance (MRI). Rarely encountered, a patient with normal pituitary MRI, pose a diagnostic and therapeutic challenge. In this case a work up for ectopic acromegalic source of GH/GHRH should be considered. We herein report the case of a 60-year-old woman in whom we confirmed the GH excess. However, the imaging studies failed to identify the source of this pathology. Pituitary MRI failed to find an identifiable adenoma in MRI. The work up of ectopic GH/GHRH tumor was negative. In the lack of standard guidelines, our case is added to those reported in the literature to review the diagnostic challenge and management in such acromegalic patients.

Keywords: Acromegaly; MRI negative; Pituitary; Somatostatin analogs

Introduction

Acromegaly is a rare and slowly progressive disease caused by chronic hypersecretion of growth hormone (GH) and excess circulating insulin-like growth factor-1 (IGF-1). The subtle of the symptom induce a delay in the diagnosis. Its prevalence is estimated to 36-60 cases per million with an annual incidence of 3-4 per million [1]. This hormonal disorder is characterized typically skeletal changes with coarsened facial features, acral and soft tissue overgrowth, and a large variety of systemic manifestations, including cardiovascular, respiratory, gastrointestinal and metabolic systems. In the vast majority of cases, acromegalic patients harbor a growth hormone (GH) secreting pituitary adenoma, usually more than 1 cm, involving somatotroph cells [2]. For this reason, pituitary MRI is recommended as the first line imaging test to ascertain tumor size, location, and invasiveness [3].

Rarely, in less than 5% of cases, it is due to an excess of GHRH from a hypothalamic tumor or a neuroendocrine tumor (usually from lung or pancreas origin). More rarely an ectopic source of GH related to abdominal or hematopoietic tumor may be the etiology of acromegaly [4,5]. In some cases, the source of excess of GH became a challenge when the investigations failed to identify the etiology of acromegaly. There is a lack of a standard guidelines in management of such form of acromegaly with unidentifiable source of GH.

Case Report

A 60-year-old woman was referred to our hospital on clinical suspicion of acromegaly. She had a history of progressive change in facial appearance, with coarse facial features, and progressive enlargement of hands and feet. Acromegaly was confirmed by a lack of growth hormone level after 75 g glucose challenge test. by oral glucose tolerance test (OGTT) showing and elevated level of Insulin-like growth factor-1 (IGF-1). Other pituitary hormones are summarized in Table 1.

Pituitary MRI with was normal (Figures 1 and 2). Search for an ectopic tumor included chest, abdomen computed tomography didn't reveal any abnormality. Octreoscan did not show any ectopic uptake. Measurement of serum GHRH was normal: 0.78 ng/ml (0-10 ng/ml).

In the absence of standard practice guidelines for the management of acromegaly with unidentifiable source of GH excess, we give the patient the option to undergo a surgical exploration of the pituitary gland, but she refused it. Our patient accepted medical treatment with Somatostatin receptor ligands (SRLs), as an alternative approach. Therefore, she was treated with somatostatin analogue. After one year of the treatment we achieve a biochemical remission with normal (IGF-1).

Table 1: Hormonal analysis of patient.

| Test               | Results   |
|--------------------|-----------|
| Basal serum GH μg/L| 4.74      |
| GH nadir during OGGT μg/L | 3.45     |
| IGF-1: (117-329 μg/L) | 548.6    |
| TSH: (0.3-5.5 mIU/L)  | 0.72      |
| FT4: (5.1-19.5 ng/l) | 12.28     |
| FSH: (1.5-12.4 mIU/L) | 46.71     |
| LH: (1.6-8.5 mIU/L)  | 15.86     |

References

1. [1]
2. [2]
3. [3]
4. [4]
5. [5]

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Discussion

In view of the laboratory investigations that included measurement of serum insulin-like growth factor 1 (IGF1) and lack of suppression of GH to <1 µg/l during OGTT test.

Once the biochemical diagnosis of acromegaly is made, current guidelines recommend contrast-enhanced pituitary MRI as the first line imaging modality [6].

Pituitary computed tomography should be performed if MRI is contraindicated or unavailable. At diagnosis, macroadenomas are detected in 73% of patients sometimes with extracapsular extension [1].

In rare case, acromegaly can be caused by GH secreting pituitary adenoma that are not evident on conventional MRI but discovered at transsphenoidal pituitary exploration.

One of the previous reports discuss the value of selective samples from the inferior petrosal sinuses in acromegalic patients in whom imaging studies of the pituitary gland failed to indicate the presence of an adenoma. The study showed that samples from the inferior petrosal sinuses had more elevated levels of growth hormone than samples from a peripheral vein. It ranged from fivefold to 36-fold at the basic and 53-fold to 74-fold in response to GHRH stimulation. In all patients surgical pituitary exploration concluded to GH microadenoma. However, the cut-off of criteria for central to peripheral ratios are not well established [7].

With the advances in imaging exploration of the pituitary, Daud et al. report the case of an acromegalic patient in whom the MRI with and without contrast, including thin-cut spoiled-gradient recalled (SPGR) imaging failed to show any pituitary adenoma. Surgical pituitary adenoma discovered a 9-mm adenoma which was resected. The biochemical remission was obtained in the follow up [8].

In a retrospective review at two tertiary care centers, the frequency of tumors in 190 acromegalic patients with negative MRI imaging was 3.2% (3 male patients and 3 female patients).

For tumor localization, similar to the SPGR technique, the contrast-enhanced volumetric interpolated breath-hold examination MRI sequence (1.2 mm of thickness) VIBE MRI imaging, can provide superior soft tissue sensitivity. This later was used in three patients in whom the conventional T1-weighted imaging didn't provide evidence of an adenoma. As a result, in one of these three patients VIBE MRI imaging detected a 4 mm microadenoma that was confirmed to be GH-secreting one at surgery and histological analysis. In the other five cases in this study a pituitary adenoma was identified and removed at transsphenoidal pituitary surgery (mean diameter: 5.6 mm; range 5-6.7 mm). The biochemical remission was achieved in all patients after surgical resection [9]. In our case, the conventional MRI did not show any pituitary mass. In the lack of VIBE MRI in our country, the work up for ectopic source of excess of GH didn’t conclude to any tumor. Currently there is no consensus for the management of a patient with unidentified source of acromegaly. In most of the previous reports, the surgical exploration of the pituitary identified a microadenoma. The subsequent resection of the lesion and histopathologic examination confirmed the somatotrope nature biochemical remission was excellent in all the cases. The surgical treatment of GH adenoma is considered the first line therapy in almost all patients with GH adenoma. The success and long-term remission depend on surgeon experience and can reached the rate of more than 85% in microadenoma and 40% to 50% for macroadenoma [10,11].

Radiation therapy (either fractionated or stereotactic radiosurgery) for GH-secreting pituitary adenomas is mainly used for: after non-curative surgery and poor response or inaccessibility to medical treatment. Furthermore, the effectiveness of radiation therapy in normalizing GH levels occurs over years, and adjuvant medical therapy is necessary to maintain biochemical control during that period of time [12].

For these reasons, surgery is considered the initial therapy of choice in almost all patients.

In our case our patient refuse the surgery therefore medical was an alternative option treatment so we prescribed a somatostatin analogues. After one year of follow-up we reached a biochemical remission. However she should be contrained to a long term medical therapy.

Conclusion

We have added our case report to expose the challenge in the management of acromegaly in rare cases when no remarkable pituitary imaging and no evidence of ectopic GH/GHRH production. The transsphenoidal pituitary surgery is considered effective in most patients to identify and subsequently resect microadenoma with successful remission. Long term treatment with Somatostatin receptor ligands (SRLs) can be an alternative approach if the reimbursement for specific drugs is possible.

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