OPEN ACCESS

Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Evaluation of the Medical Treatment of Acromegaly (About 15 Cases)

Nawal Moussaid[1*], Kaoutar Rifai[1,2], Mohamedou Abdouly Abdellahi[1], Loubna Guissi[1], Khaoula Gorgi[1], Youssra Mesbah[2], Hinde Iraqi[1, 2]

[1]Department of Endocrinology and Metabolic Diseases, Ibn Sina Hospital of Rabat, Morocco
[2]Faculty of Medicine and Pharmacy of Rabat, Mohammed V University of Rabat, Morocco

DOI: 10.36348/sjm.2023.v08i06.001 | **Received:** 16.03.2023 | **Accepted:** 21.04.2023 | **Published:** 02.06.2023

***Corresponding Author:** Moussaid Nawal
Department of Endocrinology and Metabolic Diseases, Ibn Sina Hospital of Rabat, Morocco

Abstract

Acromegaly is a condition caused by an excessive secretion of growth hormone due to a somatotropic pituitary adenoma, leading to an acquired dysmorphic syndrome. The aim of this study is to evaluate the effectiveness and tolerance of medical treatment using Lanreotide LP 120 mg in 15 patients with acromegaly, who were followed up at the endocrinology department of Ibn Sina Hospital in Rabat between 2017 and 2018. The quality of life of the patients after Lanreotide treatment was evaluated using the AcroQol questionnaire. 80% of the patients were found to have acrofacial dysmorphic syndrome, with the diagnosis based on clinical, biological, and radiological data. Magnetic resonance imaging revealed a pituitary macroadenoma in 86.7% of the cases. All patients were treated with medical treatment using Lanreotide LP 120mg. Fourteen patients underwent adenomectomy, with 4 of them receiving GammaKnife radiotherapy. During treatment, complications were observed in 80% of patients, with half of them related to vesicular lithiasis. The AcroQol scores obtained in the study were less satisfactory than expected, indicating a lower quality of life compared to the general population.

Keywords: acromegaly, lanreotide, quality of life.

INTRODUCTION

Acromegaly, first described by Pierre Marie in 1886, results from excessive secretion of growth hormone. In over 99% of cases, it is caused by a somatotropic pituitary adenoma. It is a rare condition, with a prevalence estimated at 80-130 cases per million and an incidence of 3 to 4 cases per million per year. It is associated with multiple systemic complications and a high risk of mortality in the absence of treatment. Clinically, acromegaly manifests as an acrofacial dysmorphic syndrome associated with varying degrees of pituitary tumor syndrome. Diagnosis is based on the detection of a high plasma concentration of GH, especially non-suppressible by oral glucose tolerance test, with confirmation by elevation of insulin growth factor (IGF 1). The primary treatment for acromegaly is transphenoidal surgery, with medical treatment using somatostatin analogues (AS) often used as a second-line therapy after surgery. The objective of our work is to evaluate the efficacy and tolerance of medical treatment with Lanreotide LP 120mg in patients with acromegaly. The secondary outcome is to evaluate the quality of life of these patients.

PATIENTS AND METHODS

This is a retrospective descriptive study conducted over a period of 24 months, from January 2017 to December 2018, on 15 patients with acromegaly treated with somatostatin analogues (Lanreotide LP 120mg), followed at the Endocrinology Department of the Ibn Sina University Hospital in Rabat. Epidemiological, clinical, and paraclinical data, as well as therapeutic and evolutionary aspects, were collected for all patients. The quality of life of patients after treatment with Lanreotide was evaluated using a validated questionnaire: AcroQoL (Acromegaly Quality of Life). The data were analyzed and processed using the statistical software "Jamovi 1.6.14". Quantitative variables were expressed as mean values, and qualitative variables were expressed as frequency and percentage.

RESULTS

Epidemiological Aspects:

The study involved 15 patients with acromegaly. The mean age at the start of treatment was 49.1 ± 13.6 years, with a range from 23 to 70 years. There was a female predominance (66.6%) with a sex ratio (F/M) of 2.

Diagnostic Aspects:

The clinical presentation was dominated by the acrofacial dysmorphic syndrome found in 12 patients (80%). The tumoral pituitary syndrome was present in 6 patients (40%), secondary amenorrhea was observed in 5 female patients and galactorrhea in only one case. Two patients had developed secondary diabetes due to acromegaly (figure 1).

The IGF-1 level (in ng/ml) was high in all patients with an average of 735 ± 304.

On a morphological level, all patients underwent a hypothalamo-pituitary MRI (HP), a pituitary adenoma was found in 13 patients, i.e. 86.7%, one case had a cystic formation and another had an arachnoidocele.

Impact Assessment Data:

Uncontrolled diabetes was noted in 5 patients, 6 patients had dyslipidemia, and mild hypercalcemia was found in 4 cases. Regarding the pituitary hormone assessment, cortisol levels were low in 9 cases, hyperprolactinemia was found in 5 patients, three patients had low FT4, and gonadotropin deficiency was found in 7 patients.

Thirteen of our patients underwent ophthalmological evaluation, the results of which are detailed in Table 1.

Therapeutic Aspects:

All our patients received medical treatment with Lanreotide LP 120mg for an average treatment duration of 21.6 months ± 9.66. Fourteen patients underwent transphenoidal adenomectomy, and 4 patients received GammaKnife radiosurgery sessions postoperatively.

Evolutionary Aspects:

Improvement of acrofacial dysmorphic syndrome was observed in 10 patients (66.7%). The IGF1 level decreased with an average of 382 ± 371 ng/ml (p=0.015). Control HH MRI was normal in 4 patients (26.7%), and tumor residue was observed in 11 patients (73.3%). The average number of treatments that allowed clinical improvement was 23.2 ± 9.03, and radiological improvement was observed for an average number of treatments of 19.3 ± 9.22.

The adverse effects that occurred during treatment with Lanreotide 120mg were gallstone in 40% of cases, gastrointestinal disorders in 33% of cases, and appendicular peritonitis in 6% of cases (Figure 2).

Regarding the evaluation of the quality of life of our patients, twelve patients were interviewed (2 lost to follow-up and 1 deceased). The AcroQol scores' averages obtained are represented in table 2.

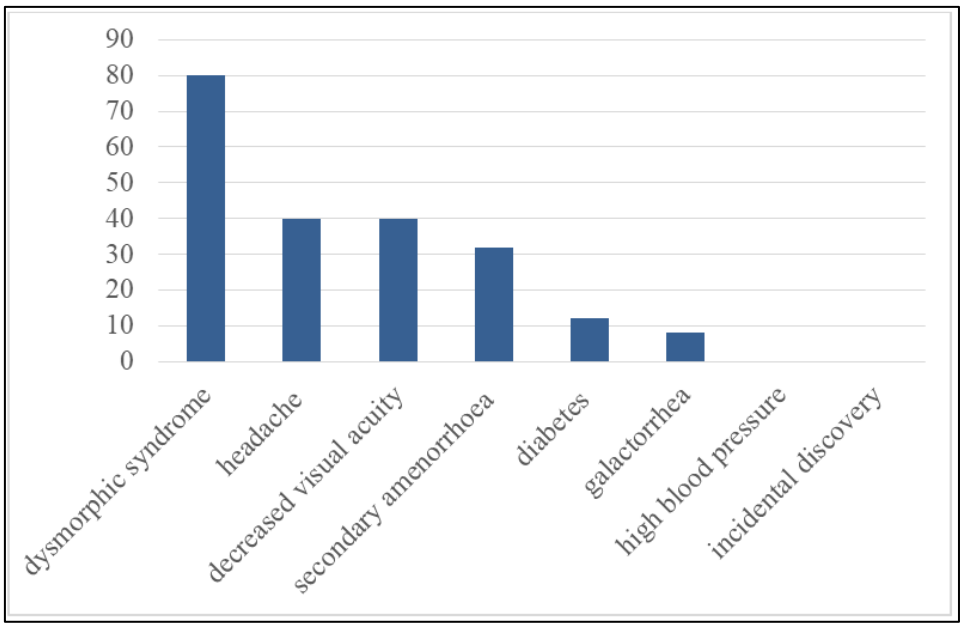

Figure 1: Reasons for consulting of our patients.

Table 1: Results of the fundus oculi and visual fields performed

	Number	Results
Visual field (VF)	13	Normal in 7 patients 2 cases of temporal quadrianopsia 2 cases of scotomas 1 case of bilateral blindness 1 case of decreased visual acuity with glaucoma sequels
Fundus oculi	13	Normal in 8 patients 3 cases of cataract 2 cases of macula of bad reflection

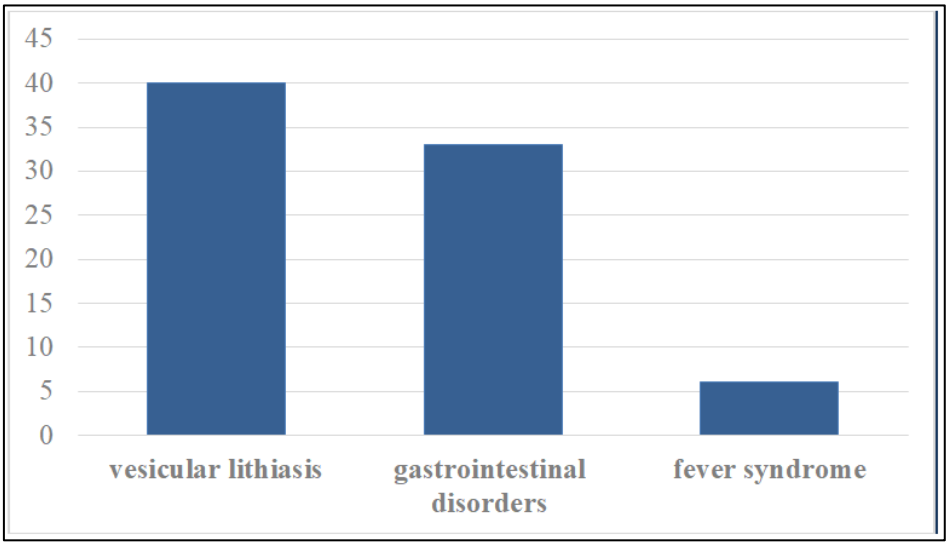

Figure 2: Side effects of Lanreotide LP 120mg treatment in our patients.

Table 2: Averages of AcroQol scores in our series

	Number of patients	Score of responses in %	Average in %
Global	12	9.1 to 54.5	33.8
Physics	12	15.6 to 84.4	41.1
Psychological / Global	12	17.9 to 89.3	56.9
Psychological / Aspect	12	14.3 to 82.1	48.2
Psychological / Personal relationships	12	21.4 to 100	65.5

DISCUSSION

In our study, the mean age of our patients (49 years) was comparable to international reviews [5, 6]. There is no gender predominance according to the literature [7], but a female predominance was observed in our series (66.7%), which can be explained by the sample size and selection bias (our study only included patients who received medical treatment). In our series, the main reason for consultation was acrofacial dysmorphic syndrome found in 80% of our patients, similar results were found by Anajjar et al. and Beckers et al. [8, 9].

The biological diagnosis of acromegaly is primarily based on the measurement of IGF-1 which is a representative marker of pulsatile GH secretion. According to the latest consensus of the Endocrine Society on acromegaly, IGF-1 measurement is recommended in patients presenting with acrofacial dysmorphic syndrome [4]. In our series, all our patients had a manifest dysmorphic syndrome, and a simple IGF-1 measurement was sufficient to make the diagnosis. After biological confirmation of acromegaly, an MRI of the pituitary gland is the reference examination to confirm the diagnosis of somatotroph pituitary adenoma, evaluate its extension, and assess its operability. In our series, a pituitary macroadenoma was found in 86.7% of cases, which is consistent with the literature [10]. Visual impairment is common in acromegaly [11], and temporal hemianopsia was noted in 15.38% of our patients. Metabolically, diabetes was found in 33% of cases, which seems to be supported by the literature [12].

The treatment of acromegaly is primarily based on transphenoidal surgery, with medical treatment often used as a second option after surgery [4]. Somatostatin analogues can be prescribed as a first-line treatment in cases of non-resectable invasive

adenoma or if the patient refuses surgery [13]. First-generation somatostatin analogues, such as Lanreotide, act by binding to subtypes 2 and 5 of somatostatin receptors expressed by adenomatous cells. In our series, selective adenomectomy was performed in 93.3% of cases. The persistence of GH hypersecretion ± residual tumor on imaging led to the prescription of complementary medical treatment with Lanreotide LP 120mg in all operated patients, with Gamma Knife treatment performed in 26.6% of cases. The anti-secretory efficacy of somatostatin analogues varies according to studies, ranging from 40 to 75% [14, 15]. We found a similar result among our patients, with a 73% decrease in IGF-1 levels. In our patients, clinical improvement was observed in 66.6% of cases and radiological improvement in only 26.6% of cases, with a reduction in tumor volume of over 20% found in nearly half of the patients in the study by Caron et al [16].

Lanreotide-based medical treatment can cause mainly digestive side effects. In our series, the most frequent adverse effect was gallstone disease found in 40% of our patients, a lower rate (24%) was reported by other authors [17]. This could be explained by the small size of our sample and the patients' lifestyle (high-fat diet).

In our study, we also evaluated the quality of life of our patients with a validated questionnaire (AcroQol), and the scores we obtained were similar to those of Webb et al and Caron et al [18, 19]. Although treatment improves the quality of life of acromegalic patients, it remains less satisfactory compared to that of the general population. Quality of life remains impaired and only partially improves after effective treatment of acromegaly [20]. In our series, 93% of patients received surgical treatment before starting somatostatin analogue treatment, with lower scores than the average. This low score may be explained by delayed diagnosis and management.

CONCLUSION

Medical treatment of acromegaly is often indicated as a second-line therapy after surgery to restore a normal somatotropic axis function due to its effectiveness and rapid action. Through our work, we have demonstrated that Lanreotide represents an interesting option in the medical management of acromegaly, due to its efficacy and ease of administration. Furthermore, this treatment is associated with adverse effects, particularly gallstones, and further prospective studies are needed within our institution to shed the light on the efficacy and tolerability of this treatment.

Conflicts of Interest

The authors declare no conflict of interest.

REFERENCES

1. Carroll, P. V., & Joshi, M. N. (2022). Acromegaly. *Endotext [Internet]*.
2. Daly, A. F., Tichomirowa, M. A., & Beckers, A. (2009). The epidemiology and genetics of pituitary adenomas. *Best practice & research Clinical endocrinology & metabolism*, *23*(5), 543-554.
3. Day, P. F., Loto, M. G., Glerean, M., Picasso, M. F. R., Lovazzano, S., & Giunta, D. H. (2016). Incidence and prevalence of clinically relevant pituitary adenomas: retrospective cohort study in a Health Management Organization in Buenos Aires, Argentina. *Archives of endocrinology and metabolism*, *60*, 554-561.
4. Katznelson, L., Laws Jr, E. R., Melmed, S., Molitch, M. E., Murad, M. H., Utz, A., & Wass, J. A. (2014). Acromegaly: an endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, *99*(11), 3933-3951.
5. BENGTSSON, B. Å., EDÉN, S., ERNEST, I., ODÉN, A., & SJÖGREN, B. (1988). Epidemiology and long-term survival in acromegaly: a study of 166 cases diagnosed between 1955 and 1984. *Acta Medica Scandinavica*, *223*(4), 327-335.
6. Vroonen, L., Daly, A. F., & Beckers, A. (2019). Epidemiology and management challenges in prolactinomas. *Neuroendocrinology*, *109*(1), 20-27.
7. Chanson, P., & Salenave, S. (2008). Acromegaly. *Orphanet journal of rare diseases*, *3*(1), 1-17.
8. Anajjar, I., Meillet, L., Mohn, A., Tschudnowsky, M., Bourgon, C., Bruckert, I., ... & Borot, S. (2015, September). Prise en charge de l'acromégalie en Franche-Comté: à propos de 72 cas. In *Annales d'Endocrinologie* (Vol. 76, No. 4, p. 407). Elsevier Masson.
9. Beckers, A., Lodish, M. B., Trivellin, G., Rostomyan, L., Lee, M., Faucz, F. R., ... & Stratakis, C. A. (2015). X-linked acrogigantism syndrome: clinical profile and therapeutic responses. *Endocrine-related cancer*, *22*(3), 353-367.
10. Potorac, I., Petrossians, P., Daly, A. F., Schillo, F., Ben Slama, C., Nagi, S., ... & Bonneville, J. F. (2015). Pituitary MRI characteristics in 297 acromegaly patients based on T2-weighted sequences. *Endocr Relat Cancer*, *22*(2), 169-177.
11. Raverot, G., Vasiljevic, A., Raverot, V., Lapras, V., Favrel, V., & Trouillas, J. (2014). Adénomes hypophysaires gonadotropes. EMC-Endocrinol. *Nutr*, *11*, 1-11.
12. Fieffe, S., Morange, I., Petrossians, P., Chanson, P., Rohmer, V., Cortet, C., ... & Delemer, B. (2011). Diabetes in acromegaly, prevalence, risk factors, and evolution: data from the French Acromegaly Registry. *European journal of endocrinology*, *164*(6), 877-884.
13. Puig-Domingo, M., Gil, J., Sampedro-Nuñez, M., Jordà, M., Webb, S. M., Serra, G., ... & Marazuela, M. (2020). Molecular profiling for acromegaly

treatment: a validation study. *Endocrine-Related Cancer*, *27*(6), 375-389.

14. Colao, A., Auriemma, R. S., Galdiero, M., Lombardi, G., & Pivonello, R. (2009). Effects of initial therapy for five years with somatostatin analogs for acromegaly on growth hormone and insulin-like growth factor-I levels, tumor shrinkage, and cardiovascular disease: a prospective study. *The Journal of Clinical Endocrinology & Metabolism*, *94*(10), 3746-3756.
15. Caron, P. H., Beckers, A., Cullen, D. R., Goth, M. I., Gutt, B., Laurberg, P., ... & Zgliczynski, W. (2002). Efficacy of the new long-acting formulation of lanreotide (lanreotide Autogel) in the management of acromegaly. *The Journal of Clinical Endocrinology & Metabolism*, *87*(1), 99-104.
16. Caron, P. J., Bevan, J. S., Petersenn, S., Flanagan, D., Tabarin, A., Prévost, G., ... & PRIMARYS Investigators. (2014). Tumor shrinkage with lanreotide Autogel 120 mg as primary therapy in acromegaly: results of a prospective multicenter clinical trial. *The Journal of Clinical Endocrinology & Metabolism*, *99*(4), 1282-1290.
17. Ipsen Biopharm, Royaume uni. MONOGRAPHIE DE PRODUIT : SOMATULINE AUTOGEL lanreotide injectable 60, 90, 120mg de lanreotide, Anti-Hormone de croissance ;code ATC : H01CB03 225592 (2019).
18. Webb, S. M., Badia, X., & Nuria Lara Surinach for the Spanish AcroQoL Study Group. (2006). Validity and clinical applicability of the acromegaly quality of life questionnaire, AcroQoL: a 6-month prospective study. *European journal of endocrinology*, *155*(2), 269-277.
19. Caron, P., Petersenn, S., Flanagan, D., Tabarin, A., Prevost, G., Maisonobe, P., ... & Bevan, J. (2014, October). Amélioration de la qualité de vie des patients acromégales au cours du traitement primaire par lanréotide Autogel 120 mg: résultats de l'étude PRIMARYS.(NCT00690898). In *Annales d'Endocrinologie* (Vol. 75, No. 5-6, p. 290). Elsevier Masson.
20. Biermasz, N. R., van Thiel, S. W., Pereira, A. M., Hoftijzer, H. C., van Hemert, A. M., Smit, J. W., ... & Roelfsema, F. (2004). Decreased quality of life in patients with acromegaly despite long-term cure of growth hormone excess. *The Journal of Clinical Endocrinology & Metabolism*, *89*(11), 5369-5376.