Response to Pasireotide in an acromegaly patient with resistance to conventional medical treatment

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<u>Success rates (normalization of IGF-1 levels)*:</u>

Transsphenoidal surgery 40-50% Octreotide 17-35% Pegvisomant 63% Cabergoline 21-30%

*Katznelson L. et al. Acromegaly: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2014/10/30

"Pasireotide exerts its activity via binding to four of the five known somatostatin receptors (SSTR), specifically: SSTR1, SSTR2, SSTR3, and SSTR5. Pasireotide is different from the currently marketed somatostatin receptor analogs in the pattern of SST receptor binding and in the affinity that it has for individual SST receptors."

*FDA briefing document NDA 200677.

Pasireotide was approved by the EMA and the FDA for its use in acromegaly on 2014. In Spain, it can be prescribed for compassionate use only.

CLINICAL CASE

Female with a diagnosis of acromegaly at 24 years. She had a 3 cm macroadenoma.

Undergone treatments:

- -Transsphenoidal surgery and transfrontal surgery, both in 1993.
- -Radiotherapy in 1993
- -On medical treatment since 1993 without success. On Octreotide LAR 30 mg monthly + Cabergoline 2 mg/week:

03/2008: IGF-1 589 ng/ml, GH 12.1 ng/ml

-Change to **Pegvisomant 15 mg/day**: achieved normal IGF-1 levels but caused **severe lipohypertrophy**.

An International Novartis Committee approved treatment on Pasireotide 40 mg monthly starting on June 2012. Dose was increased to 60 mg monthly on March 2013:

	06/2012	09/2012	08/2014
GH (ng/mL)	33,9	8	2,3
IGF-1 (ng/mL)	661	709 261	
	(101-267)	(101-267)	(94-252)

No joint pain after improvement of IGF-1 levels, but diabetes mellitus

	06/2012	11/2013	12/2014
FPG (mg/dl)	91	145	_
HbA1c (%)	5.8	6.7	6.6
Treatment	None	Metformin	Metformin/Vildagliptin
		(up to 2550 mg/day)	(2000 mg/100 mg)

CONCLUSION

In this clinical case, Pasireotide LAR has achieved clinical improvement, IGF1 control, GH safety values, and diabetes mellitus as a side effect





