Long-term management of resistant acromegaly with pasireotide LAR in 2cases with a familial AIP mutation

Liliya Rostomyana, F. Daly Adriana, Natalia Pellegatab, Iulia Potoraca, Daniela Beteaa, Emilie Castermansc,

Emanuel Christd and Albert Beckersa

aDepartment of Endocrinology, Centre Hospitalier Universitaire de Liege, University of Liege, Domaine Universitaire du Sart-Tilman, 4000

Liege, Belgium; bInstitute for Diabetes and Cancer IDC, Helmholtz Center Munich and Joint Heidelberg-IDC Translational Diabetes Program,

Heidelberg University Hospital, Germany; cDepartment of Clinical Genetics, Centre Hospitalier Universitaire de Liege, University of Liege,

Domaine Universitaire du Sart-Tilman, 4000 Liege, Belgium; dInterdisciplinary Endocrinology, University Hospital Basel, Switzerland

**Introduction**: *AIP*-related somatotropinoma patients

tend to be resistant to medical therapy with somatostatin

receptor (SSTR) subtype 2 specific somatostatin analogues

(SSA). Pasireotide is a newer multiple SSTR

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binding SSA with activity primarily at SSTR5 and

SSTR2, which has not been widely studied in *AIP*mutated

patients.

**Results**: Case 1: A 29-year old male was diagnosed

with a GH-producing pituitary macroadenoma

(25x18x23 mm). He was from a FIPA kindred and his

sister had acromegaly due to a pituitary macroadenoma

(25mm) at age of 24 that was cured by neurosurgery. A

familial *AIP* mutation p.Gln217X was revealed in the

index patient, his sister and an unaffected nephew. The

patient underwent partial resection of a GH and prolactin

positive adenoma. He was treated for post-operative

corticotroph, thyrotroph and gonadotroph deficiencies

but GH hypersecretion by the residual tumor required

adjuvant medical treatment. He was treated with SSTR2

specific agents (lanreotide autogel and octreotide LAR),

but without hormonal control. Addition of cabergoline

did not improve hormonal suppression. An increase of

tumor residue size was observed on SSA treatment and

the residual tumor approximated the chiasma, which

precluded safe surgery and pegvisomant therapy, while

the patient declined radiotherapy.

Case 2: A female patient aged 19 years presented

with acromegaly due to an invasive pituitary macroadenoma

(37mm). A c.343delC *AIP* mutation in AIP was

detected in the patient, and in her father and sister neither

of whom had a pituitary tumor. She underwent

neurosurgical resection but GH/IGF-1 levels remained

elevated due to remnant tumor. An octreotide test

(100 μg sc) showed a paradoxal increase in GH levels.

Immunohistochemistry revealed a small amount of

SSTR2 and high expression of SSTR5 in the pituitary

tumor.

Both patients began pasireotide LAR and were uptitrated

to 60 mg/month. The clinical signs of acromegaly

improved, GH/IGF-1 was controlled and tumor size was

stable in the case 1 and significantly decreased within

12 months in the case 2. Pasireotide was associated with

worsening of existing impaired glucose control and

treatment with antidiabetic medication was required.

A switch to octreotide LAR in case 2 led to renewed

elevation in GH/IGF-1 and pasireotide was reinstated.

After 2 years of treatment the dose of pasiriotide was

decreased to 40 mg/4 weeks and further follow-up

showed tumor shrinkage and an empty sella. Glucose

metabolism worsened over time despite existing therapy

and exogenous insulin treatment was required in

the case 1.

**Conclusion**: In these two aggressive *AIP* mutation

positive acromegaly cases, resistance to surgery and

SSTR2-specific SSA was seen. Pasireotide permitted

clinical, hormonal and tumoral improvement, albeit

at the cost of long-term worsening of hyperglycemia

requiring antidiabetic therapy.