DIABETES MELLITUS AND ATAXIA WITH ANTI-GAD65 ANTIBODIES

DIANA OLIVEIRA[1], RUI ARAÚJO[2], CAROLINA MORENO[1], DÍRCEA RODRIGUES[1], JOANA SARAIVA[1], NUNO VICENTE[1], LUÍS CARDOSO[1], DIANA MARTINS[1], ADRIANA LAGES[1], MARA VENTURA[1], SANDRA PAIVA[1], FRANCISCO CARRILHO[1]

[1] ENDOCRINOLOGY DEPARTMENT | COIMBRA HOSPITAL AND UNIVERSITY CENTER, COIMBRA, PORTUGAL
[2] NEUROLOGY DEPARTMENT | COIMBRA HOSPITAL AND UNIVERSITY CENTER, COIMBRA, PORTUGAL

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INTRODUCTION

- Glutamic acid decarboxylase (GAD65) is expressed by pancreatic beta cells and also by GABA (gamma-aminobutyric acid)-secreting neurons.
- Anti-GAD65 antibodies (antiGAD Ab) are found in most patients with autoimmune diabetes *Mellitus* (DM), as in rare neurological syndromes (the most common being *Stiff Person Syndrome*)
- Cerebellar ataxia is the second most common neurological syndrome associated with antiGAD Ab

CASE REPORT I.

- C.O., male, 69 years old
- Medical history:
  - obesity
  - atrial fibrilation
  - benign prostatic hypertrophy
- 2010 (64 years old): **dysarthria + ataxic gait**

Neurology department (jan/2011):

Neurological examination: marked cerebellar dysarthria; kinetic and static ataxia; evoked multidirectional nistagmus; altered vibration sensation and proprioception

Etiology study of ataxia (antineuronal antibodies, MRI, CSF study, tumor markers, thyroid hormones, vitamins): negative, except for antiGAD65 Ab

AntiGAD65 Ab 13,3 U/mL (<1,0)
ICA negative
Anti-insulin Ab negative
Anti-IA2 Ab 1,30 U/mL (<1)
C-peptide 6.7 ng/mL (1.0-7.6)

 # antiGAD65 Ab ataxia

Nov/2011 & jan/2012: **intravenous human immunoglobulin therapy** (30g id, 3 days + 35g id, 5 days) – improvement of neurological signs and symptoms

- DM: diagnosed 2010 (64 years old), initially medicated with oral antidiabetic agents and with premature need for insulin therapy, 4 years after diagnosis, for chronic inadequate metabolic control. Improved after intensification of insulin therapy.

HbA1c dec/2014: 6,8% → nov/2015: **10,1%** → feb/2016: **6,5%**

CASE REPORT II.

- M.S., female, 68 years old, normal weight
- Medical history:
  - paraplegic after vertebromedullary traumatism
  - arterial hypertension
  - DM since the age of 60 – difficult metabolic control with oral agents for 5 years, insulin added in 2012 – sustained significant glycemic lability
- 2015 (68 years old): **progressive positional vertigo, dysarthria and diplopia**

Neurology department (set/2015):

Neurological examination: flaccid paraplegia; kinetic ataxia of upper limbs; dysarthria; vertical nistagmus

Etiology study of ataxia: negative, except for antiGAD65 Ab

AntiGAD65 Ab 239,07 U/mL (<1,0)
ICA positive
Anti-insulin Ab 0.23 U/mL (< 0.4)
Anti-IA2 Ab 0,0 U/mL (<1)
C-peptide 0,4 ng/mL (1,0-7,6)
HbA1c 7,3%

 # antiGAD65 Ab ataxia

Dez/2015: **intravenous human immunoglobulin therapy** (30g id, 5 days) – improvement of neurological signs and symptoms

- DM: Considering the analytical results, oral antidiabetic agents were suspended and she initiated multiple daily injections of insulin with significant reduction of glycemic lability

CONCLUSION

- The autoimmune etiology of DM can be considered in any age group, especially when other autoimmune conditions are present. An accurate DM classification allows therapeutic adjustment and metabolic control optimization.
- In both the presented cases, age at diagnosis, positive autoimmunity for DM and absence of need for insulin therapy for more than 6 months after presentation, suggests the diagnosis of LADA (*Latent Autoimmune Diabetes in Adults*).
- In patients with DM and positive autoimmunity, with neurologic disorders not explained by diabetic neuropathy and after exclusion of other causes, ataxia associated with antiGAD Ab can be considered.

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