2020 PNS Virtual Event

27 JUNE - 30 JUNE, 2020

PNS
PERIPHERAL NERVE SOCIETY

1113.**Rare mutational variant (Ile93Val) of heredity amyloidosis with severe dysautonomia treated with inotersen (ASO).**

A. Rodríguez, P. Landriscina, R. Pedelhez, L. Mosqueras
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Introduction

- Hereditary transthyretin amyloidosis (h-ATTR) is a disease caused by the mutation of the TTR gene, generating deposits of the mutated protein in different organs, the systems affected are related to the type of mutation found.
- The Val50met variant (VAL30met) is the most frequent mutation and The early onset presentation is characterized by peripheral neuropathy. It is a rare, progressive and fatal disease, with treatment options today.

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Objetives

- To present a case report with a rare mutation in treatment with antisense-Oligonucleotide(ASO), inotersen.

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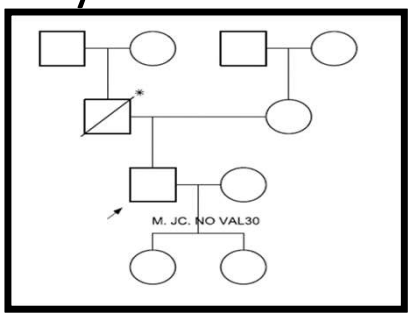
Methods and Materials

- 50-year-old male, with a history of gastrointestinal disorders (GI), weight loss, erectile dysfunction, syncopes and paraesthesia in the territory of both medium nerves and lower limbs of 5 years of evolution.
- Family history: father and paternal uncle with GI disorders.
- On neurological examination as positive signs: distal lower limb hypoaesthesia, bilateral positive Tinel sign.



- Conduction velocity electromyogram (EMG), Quantitative sensory testing (QST), evaluation of the autonomic nervous system (SNA), skin and salivary gland biopsy and next generation sequencing for TTR gene are requested.

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Results

- **EMG**: bilateral carpal tunnel syndrome, **QST**: dysfunction of type C unmyelinated fibers, alteration in the evaluation of ANS. **Echocardiography studies (strain)** showed pattern compatible with amyloid deposits. **Genetic analysis** demonstrated the presence of **Ile93val mutation**, a rare genetic variant in the TTR gene.Due to the severe autonomic involvement and infrequent mutation of the patient, it was decided to start treatment with **inotersen 284 mg.** weekly subcutaneous, in current follow-up with good tolerance to it.

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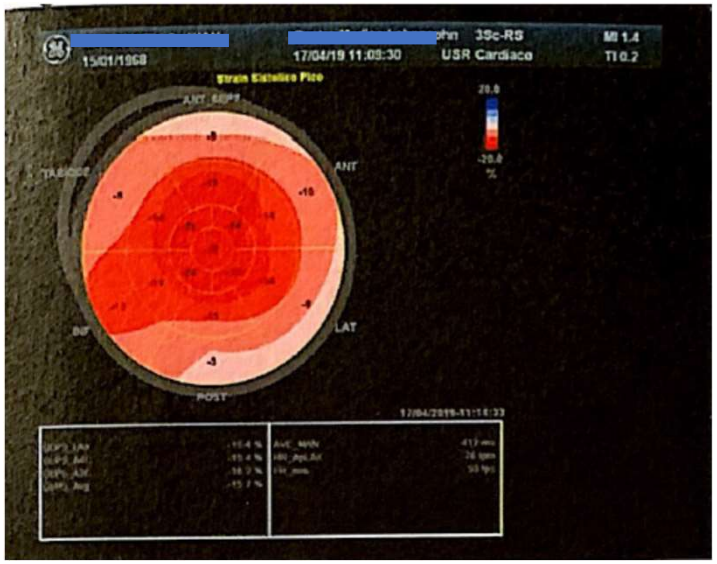


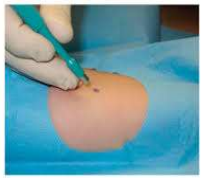
Echocardiography studies (strain) showed pattern compatible with amyloid deposits

Resultado

Diagnóstico: Amiloidosis asociada al gen TTR

Gen	Posición	Variante	Consecuencia	Copias
TTR	chr18:29.175.159	A > G	p.Ile93Val ENST00000237014	Heterocigosis (1 copia)

Genetic analysis demonstrated the presence of Ile93val mutation



Biopsy of salivary glands with Congo red was negative.

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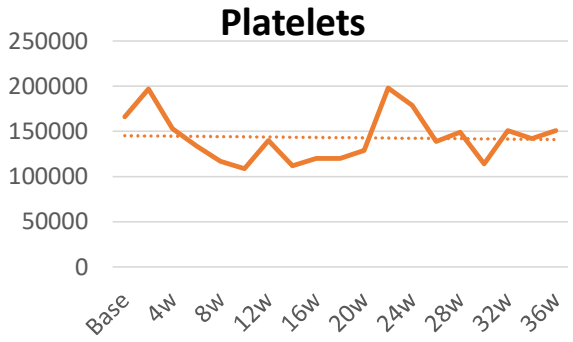
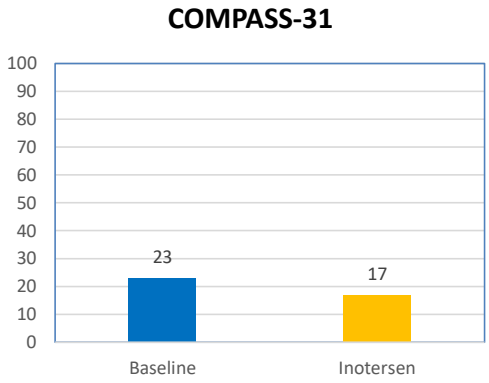
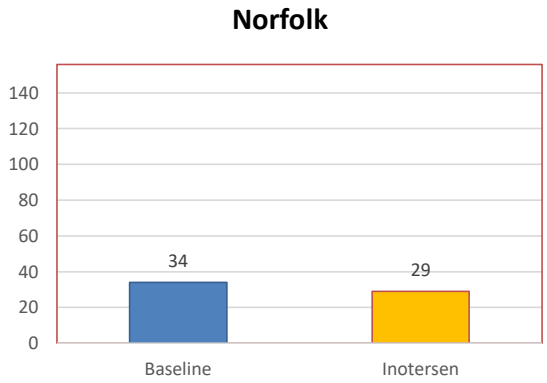


Biweekly platelet count throughout inotersen treatment.





Compas-31 and Norfolk scale, before and 10 months after starting treatment.

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Conclusions

- This rare mutation, **Ile93Val**, is reported for the **first time in Argentina**, existing only reports of it in Taiwan and Bangladesh. **Early onset with dysautonomia** that **precedes peripheral neurological involvement** seems to be characteristic of this variant. Subsequent studies in **patient follow-up** may determine the **impact of inotersen** treatment on this form of presentation.

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Many Thanks.

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