

## Video Abstracts

**Progressive Ataxia and Palatal Tremor: Think about *POLG* Mutations**Marie Mongin<sup>1,2</sup>, Cécile Delorme<sup>3,4</sup>, Timothée Lenglet<sup>5</sup>, Claude Jardel<sup>6,7</sup>, Catherine Vignal<sup>8</sup> & Emmanuel Roze<sup>3,4\*</sup>

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**Abstract**

**Background:** Progressive ataxia and palatal tremor (PAPT) can be observed in both acquired brainstem or cerebellar lesions and genetic disorders.

**Phenomenology shown:** PAPT due to mutation in *POLG*, the gene encoding the mitochondrial DNA polymerase.

**Educational value:** *POLG* mutation should be considered in patients with PAPT, particularly when additional clues such as a sensory neuropathy or an ophthalmoplegia are present.

**Keywords:** Polymerase gamma mutation, progressive ataxia and palatal tremor, ganglionopathy, ophthalmoplegia

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**Ethics Statements:** All patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

We show a 43-year-old Finnish patient with a 2-year history of progressive ataxia and palatal tremor (PAPT). In addition to the palatal tremor, examination found a cerebellar syndrome with mild gait ataxia, ataxic dysarthria and limb dysmetria (Video 1). The patient had no nystagmus. She had a slight limitation of movements of both eyes in all directions. Ankle jerks were absent and vibration sense was reduced in the lower limbs. Electrophysiological assessment was consistent with a sensory neuropathy. Brain magnetic resonance imaging showed mild cerebellar atrophy and bilateral hypertrophy of the inferior olivary nuclei with hyperintensity on T2-weighted images. There was no signal change in the cerebellum or the basal ganglia.

Molecular analysis found a homozygous W748S mutation in *POLG*, the gene encoding the mitochondrial DNA polymerase. This

pathogenic mutation has a high carrier frequency in Finland, and all chromosomes with this mutation are likely to originate from a single common ancient founder in populations of European descent.<sup>1</sup>

PAPT is a rare syndrome characterized by the combination of a low-frequency palatal tremor and a cerebellar disorder that gradually worsens. Although its cause remains undetermined in most patients, PAPT has been linked to both acquired brainstem or cerebellar lesions and genetic disorders, including Alexander's disease and mitochondrial disorders.<sup>2</sup> In our patient, PAPT was the initial manifestation of the disorder, as recently reported in another patient with *POLG* mutation.<sup>3</sup>

*POLG* mutation is a highly pleomorphic disease. The most frequent manifestations are ptosis, ophthalmoplegia, limb muscle weakness, features of sensory neuropathy, cerebellar syndrome, hyperkinetic



**Video 1. Ataxic Dysarthria.** Rhythmic, permanent and involuntary tremor of the soft palate at a frequency of 2.5 Hz. Broad-based ataxic gait and difficulties with tandem gait. Dysmetria of the upper limbs.

movement disorders (dystonia, myoclonus, tremor, or chorea), epilepsy, cognitive and psychiatric disturbances, and hypoacusia. The combination of muscle involvement and multiple neurological disorders is a good clue to the diagnosis.<sup>4</sup> When present, sensory neuropathy is strongly suggestive of *POLG* mutation in this setting.

Our observation further illustrates that a wide range of phenotypes can reveal *POLG* mutations and provides a demonstrative video of this

rare clinical picture. *POLG* mutation should be considered in patients with PAPT, particularly when additional clues such as a sensory neuropathy or an ophthalmoplegia are present.

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