

Double trouble progressive external ophthalmoplegia and Huntington's disease.

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With interest we read the article by Filosto et al. about a 70 yo female with the double trouble chronic progressive external ophthalmoplegia (CPEO) due to the point mutation m.5613T>C in the tRNA(Ala) gene and Huntington's disease (HD) due to a CAG-repeat expansion of 38 in the huntingtin gene [1]. We have the following comments and concerns.

We do not agree with the description of the presented phenotype as CPEO. The patient obviously had multisystem disease manifesting as cognitive impairment, chorea, cerebellar atrophy resulting in dysarthria, dysphagia, and gait disturbance, hypoacusis, neuropathy, and myopathy [1]. Which of these manifestations are attributable to CPEO and which to HD is difficult to decide since the tRNA mutation was described as novel and since all typical clinical manifestations of HD have been also described in MIDs. Chorea for example has been described in MELAS [2], cerebellar atrophy in ponto-cerebellar hypoplasia [3], and cortical atrophy in Leigh-syndrome [4]. Additionally, CPEO due to mtDNA point mutations has been previously reported to manifest as multisystem disease affecting the cerebrum (callosal agenesis, neuropsychological deficits, head tremor, myoclonus) [5,6,7], ears (hypoacusis) [8], eyes (retinopathy) [9], endocrine system (hypogonadism) [10], and the skeletal muscle (myopathy).

Arguments against a manifesting HD are that CAG-repeat expansions of 38 may or may not manifest with prominent HD features, that onset of HD is usually before age 64 y in the thirties or forties, and that MIDs have been reported which mimic HD.

Overall, this interesting case should be re-classified as either CPEO plus or as non-syndromic multisystem MID (mitochondrial multiorgan disorder syndrome (MIMODS)). We also should be informed about investigations of endocrine organs, the gastrointestinal tract, the kidneys, the peripheral nerves, the bones, and the skin to see if there is more extensive subclinical multiorgan involvement. This includes long-term ECG recordings since ventricular arrhythmias may go undetected but nonetheless require appropriate drug or device therapy.

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