Tubular aggregate myopathy associated with retinal degeneration

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ABSTRACT • RÉSUMÉ

Case report: We report a case of congenital tubular aggregate myopathy associated with retinal degeneration.

Comments: Bilateral, asymmetric retinal degeneration developed in a 37-year-old woman with a history of congenital tubular aggregate myopathy. The major pathological feature was the presence of tubular aggregates, believed to arise from the sarcoplasmic reticulum, which are present in skeletal muscles only. The abnormal functioning of the smooth muscles of the pupillary dilator, together with retinal degeneration in our patient, suggests that tubular aggregates may represent a more generalized disequilibrium of intracellular calcium homeostasis that may not be confined to skeletal muscles.

Observations : Nous faisons état d'un cas de myopathie congénitale avec agrégats tubulaires associée avec une dégénérescence de la rétine.

Commentaires : Une dégénérescence bilatérale et asymétrique de la rétine s'est développée chez une femme de 37 ans qui avait une histoire de myopathie congénitale avec agrégats tubulaires. La principale caractéristique pathologique était la présence d'agrégats tubulaires qu'on estime provenir du réticulum sarcoplasmique, qui est présent seulement dans les muscles squelettiques. Le fonctionnement anormal des muscles lisses du dilatateur de la pupille, combiné avec la dégénérescence de la rétine de la patiente, laisse entendre que les agrégats tubulaires peuvent présenter un déséquilibre plus généralisé de l'homéostasie du calcium intracellulaire qui ne peut se confiner aux muscles squelettiques.

Tubular aggregate myopathy is a rare disease characterized by slowly progressive proximal muscle weakness or stiffness and the ultrastructural presence of tubular aggregates within skeletal muscle fibers.[1–4] Pupillary abnormalities[5] and gyrate atrophy of the choroid and retina[6] are rarely associated. We describe a case of retinal degeneration in a patient with tubular aggregate myopathy.

Case Report

The patient was a 37-year-old woman of Chinese descent whose condition was diagnosed as tubular aggregate myopathy 1 year before presentation. She had a history of progressive weakness of the arms and legs since childhood, as well as an elevated level of creatinine phosphatase. The diagnosis was confirmed by a biopsy of the quadriceps muscle, which showed multiple peripheral and central inclusions of granular material consisting of densely packed, parallel, double-walled tubules 50–70 nm in diameter on electronic microscopy.

The patient complained of gradual visual loss in the left eye and difficulty with night vision in both eyes for 2 years. On examination, visual acuity was 20/20 OD and 20/40 OS. Color vision (Ishihara) was 17/17 OD and 3/17 OS. Humphrey and Goldmann perimetry revealed a slightly enlarged blind spot OD, as well as a superior and inferior arcuate defect OS (Fig. 1). A mild left relative afferent pupillary reflex was present. Pupils were 1.5 mm in size and increased to only 2 mm on pharmacological dilation. There was no ptosis, strabismus, or cataract, and ductions were full. Funduscopy revealed a mildly abnormal foveal reflex OD (Fig. 2A), as well as attenuation of the retinal blood vessels and mild optic atrophy OS (Fig. 2B). There were no peripheral retinal changes, no signs of active inflammation or infection, and no sequelae of inflammation or infection.

Magnetic resonance imaging with gadolinium enhancement and fat suppression of the brain and orbits was normal. Fluorescein angiography showed peripapillary atrophy OD (Fig. 2C), as well as mottling of the retinal pigmentary epithelium, blocked hypofluorescein, and attenuation of the retinal vasculature OS (Fig. 2D). The electroretinogram and dark adaptometry showed wide-

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spread rod and cone dysfunction, with the left eye more severely affected (Fig. 3). The serum ornithine level was normal. The results of tests for syphilis, tuberculosis, and sarcoidosis were negative. Electrocardiogram and carotid Doppler ultrasound were normal. Western blot and immunohistochemistry for anti-retinal autoantibodies were negative for anti-recoverin (cancer-associated retinopathy antigen) and anti-alpha enolase antibodies but positive for autoantibodies against 65 kDa protein. Systemic workup for an occult carcinoma, including breast, chest, abdomen, and gynecological examinations, was negative.

Comments

We have described a young woman with a history of tubular aggregate myopathy, insidious onset of decreased vision, and nyctalopia. The funduscopic findings (without any signs of active or previous inflammation) as well as the abnormal electroretinogram and visual evoked potentials were consistent with bilateral retinal degeneration. In addition, the presence of a mild relative afferent pupillary reflex, an enlarged blind spot OD, and arcuate defects OS, as well as mild optic disc pallor in the left eye, suggested secondary involvement of the optic nerve(s). Extensive investigations for any underlying etiologies, including infection, inflammation, and unilateral carotid diseases, that may cause asymmetric retinopathy were noncontributory, but infection such as diffuse unilateral subacute neuroretinitis could not be completely ruled out. Although the presence of autoantigens against both recoverin and 65 kDa has been reported in patients with cancer-associated retinopathy,[7] the presence of autoantibodies against 65 kDa protein alone is nonspecific—it is not a definitive paraneoplastic marker nor has it alone been associated with any type of retinopathy. Systemic workup for an occult carcinoma was also negative.

Tubular aggregates are traditionally thought to arise from sarcoplasmic reticulum and are found only in skeletal muscles; they represent a response to injuries that affect

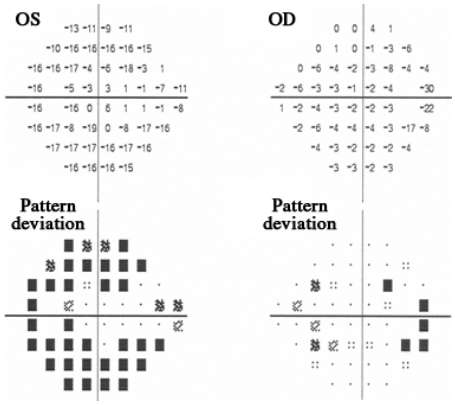

Fig. 1—Humphrey visual fields showing a superior and inferior arcuate defect OS as well as a slightly enlarged blind spot OD.

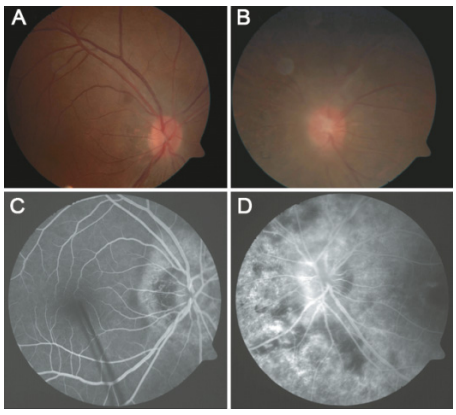

Fig. 2—Fundus photographs showing (A) a mildly abnormal foveal reflex, normal optic disc and retinal vasculature OD, and (B) attenuation of the retinal blood vessels and a mild optic atrophy OS. Fluorescein angiography showing (C) peripapillary atrophy OD, and (D) mottling of the retinal pigmentary epithelium, blocked hypofluorescein, and attenuation of the retinal vasculature OS.

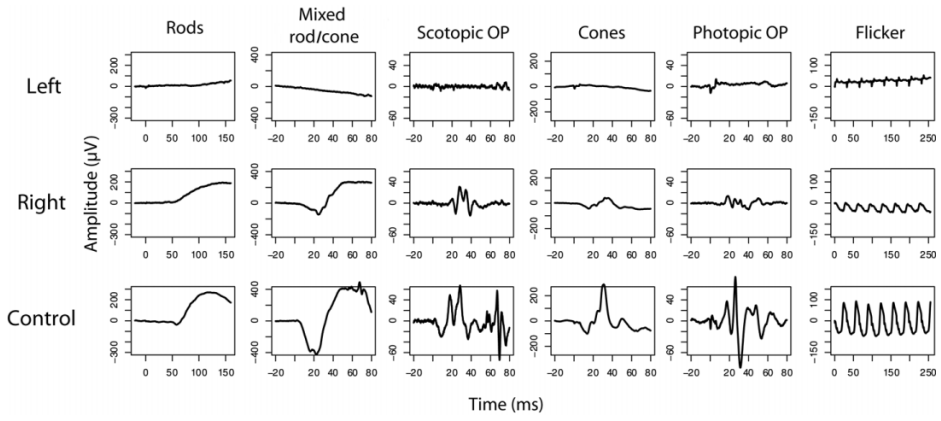

Fig. 3—Electroretinogram showing widespread rod and cone dysfunction, with the left eye more severely affected.

calcium homeostasis.[8] Recent evidence, however, suggests that tubular aggregates can also be found in the smooth muscles of the pupillary dilator in patients with gyrate atrophy of the choroid and retina with hyperornithinemia,[6] and they could also arise from endoplasmic reticulum, which is ubiquitous in all mammalian cells.[4] The presence of abnormal pupil dilation and retinal degeneration in our patient provides further support that tubular aggregates may represent a more generalized abnormal alteration of calcium homeostasis that may not be confined to skeletal muscles.

To the best of our knowledge, this is the first report of retinal degeneration associated with tubular aggregate myopathy. Whether there is a true association between these 2 diseases or whether they are coincidental findings in our patient remains to be elucidated.

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