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More than autophony: a case of Kennedy's disease presenting with autophony as an early clinical manifestation

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Abstract

Background. As autophony can be accompanied by several conditions, it is important to find co-morbidities. This paper reports a patient with Kennedy's disease (spinobulbar muscular atrophy, an X-linked, hereditary, lower motor neuron disease) having autophony as the first symptom.

Case report. A 62-year-old male presented to the otorhinolaryngology department with autophony that began 2 years previously and worsened after losing weight 3 months prior to presentation. Otoscopic examination demonstrated inward and outward movement of the tympanic membrane, synchronised with respiration. Although he had no other symptoms, facial twitching was found on physical examination. In the neurology department, lower motor neuron disease, with subtle weakness of the tongue, face and upper limbs, and gynaecomastia, were confirmed. He was diagnosed with Kennedy's disease based on genetic analysis.

Conclusion. Autophonia was presumed to be attributed to bulbofacial muscle weakness due to Kennedy's disease, and worsened by recent weight loss. Patients with autophony require a thorough history-taking and complete physical examination to assess the nasopharynx and the integrity of lower cranial function.

Introduction

Autophony is the hyperperception of one's own voice and breathing. Autophony is thought to be caused by an abnormally patent Eustachian tube, and prolonged communication between the middle ear and the nasopharynx.[1] Autophony can be accompanied by a variety of systemic and medical conditions. The severity of autophony varies from being asymptomatic to causing severe discomfort to resulting in an exceedingly reduced quality of life. There is no known consistently reliable treatment.[2] For these reasons, it is very important to identify the aetiology of autophony and detect treatable causes.

Kennedy's disease, also known as spinal and bulbar muscular atrophy, is a rare, X-linked, hereditary, lower motor neuron disease caused by an expansion in CAG (cytosine-adenine-guanine) triplet repeats of the androgen receptor (AR) gene in Xq11-12.[3] Abnormal androgen receptors are expressed at several central nervous system loci. They regulate the hypothalamic–pituitary–gonadal axis pathways. They are also expressed in the peripheral nervous system, including anterior horn cells and dorsal root ganglia. These wide distributions are responsible for characteristic features that distinguish Kennedy's disease from other motor neuron diseases.[4,5] Slowly progressive lower motor neuron features such as muscle weakness, atrophy, cramp, fasciculation and tremor – especially in the bulbar, facial and upper limb muscles – over years and decades, are typical symptoms; these are the first manifestations and are associated with the most severe discomfort for most patients.[6] Additional presentations include sensory neuropathy and neuronopathy, mild central nervous system dysfunction such as sleep and cognitive impairment, and mild androgen insensitivity such as gynaecomastia, infertility and testis atrophy. These features can lead the patient to see a physician, but they can also be easily underestimated. Patients often are misdiagnosed with other diseases. Sometimes, they are not even diagnosed, as it is a heterogeneous presentation.[6]

Herein, we report a diagnosis of Kennedy's disease in a patient with autophony as the first clinical manifestation. This case is the first report in the English literature to the best of our knowledge.

Case report

A 62-year-old male presented to the otorhinolaryngology department complaining of autophony and nasal speech. He had noticed these symptoms about two years previously. These symptoms became aggravated two months prior to presentation. His body weight was 72 kg. He reported a weight loss of 3 kg due to a loss of appetite three months earlier.

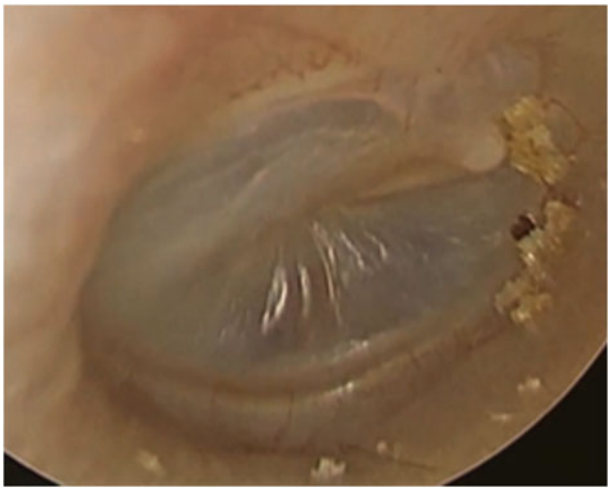

Figure 1. Still image from Supplementary Video 1 (available on *The Journal of Laryngology & Otology* website), showing a wrinkled right tympanic membrane in a resting state.

He also complained of aural fullness and a flapping noise in his right ear for several months. He had no other medical or family history. He denied other systemic symptoms.

The patient's aural symptoms were temporally relieved by placing his head down in a dependent position between his legs. Otoscopic examination demonstrated a wrinkled tympanic membrane in a resting state. In addition, inward and outward movements of his tympanic membrane, synchronised with his respiration, only on the right side, were observed (Figure 1, taken from Supplementary Video 1 (available on *The Journal of Laryngology & Otology* website)). Examination of the nasopharynx with a flexible fibre-optic endoscope revealed a widened Eustachian tube orifice on the right side. Tongue fasciculation and right facial muscle twitching were observed on physical examination, for which he was referred to the neurology department.

Ancillary physical and neurological examinations were performed in the neurology department. On the ancillary physical examination, tongue atrophy, twitching, asymmetric right-sided facial muscle fasciculation and mild gynaecomastia were observed (Figure 2). Neurological examination revealed asymmetrically right-dominant facial diplegia. Mild weakness was noted in the proximal muscle of the upper limbs bilaterally. Deep tendon reflexes were decreased at both knees and ankles. Quantitative sensory examination findings were normal in all modalities, including pain, temperature, position and vibration. No abnormalities in the legs were found. Pathological reflexes including jaw jerk, Hoffman's sign, Babinski sign and ankle clonus were not found.

Results of a serum study demonstrated elevated muscle enzyme levels (lactate dehydrogenase = 255 U/l, reference range = 135–225 U/l; creatine phosphokinase = 896 U/l, reference range = 39–308 U/l). Other laboratory findings were within their normal ranges, including inflammatory, autoimmune and paraneoplastic markers.

Brain magnetic resonance imaging (MRI) showed normal parenchyma and cranial nerves. However, both tensor veli palatini and levator veli palatini muscles showed fatty infiltration and atrophic changes. In addition, the sizes of the right tensor veli palatini and levator veli palatini muscles were relatively smaller than those of the asymptomatic left ones on the patient's brain MRI scan (Figure 3). Nerve conduction studies were performed bilaterally on the upper and lower limbs. All parameters were within their normal limits. Electromyography revealed wide-spreading denervation changes and reinnervation processes on several facial, limb, paravertebral and tongue muscles. These findings were consistent with lower motor neuron diseases.

A genetic test was performed based on suspicion of Kennedy's disease, a lower motor neuron disease with characteristic patterns involving the bulbofacial region. Genetic analysis confirmed that the number of CAG repeats was 38, which is higher than that of normal people (reference range, 10–36 repeats).

Discussion

The decrease in the size of the surrounding tissue, including Ostmann's fatty bodies, might affect the occurrence of patulous Eustachian tube.[7–9] In addition, some neuromuscular diseases involving the oromandibular muscle, such as Kennedy's disease, have been reported to be accompanied by autophonia.[2,10–12] These diseases can cause atrophy of the tensor veli palatini and levator veli palatini muscles that surround the Eustachian tube, which is presumed to be the cause of patulous Eustachian tube.[12] Careful examination of the lower cranial nerves can provide important diagnostic clues for these diseases. Furthermore, a flexible fibre-optic endoscope can be helpful in detecting any abnormalities in the Eustachian tube and surrounding structures.

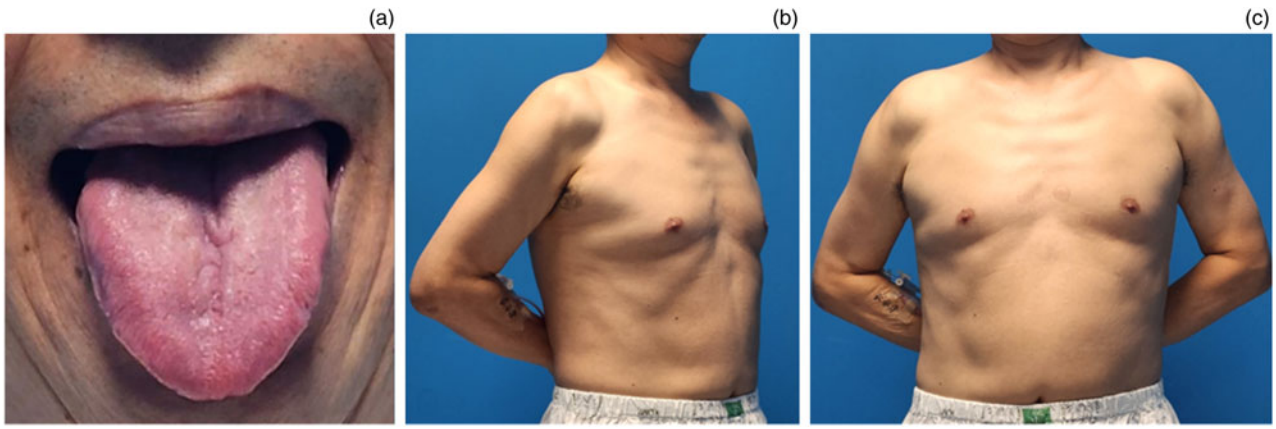

Figure 2. Mild tongue atrophy (a) and gynaecomastia (b & c).

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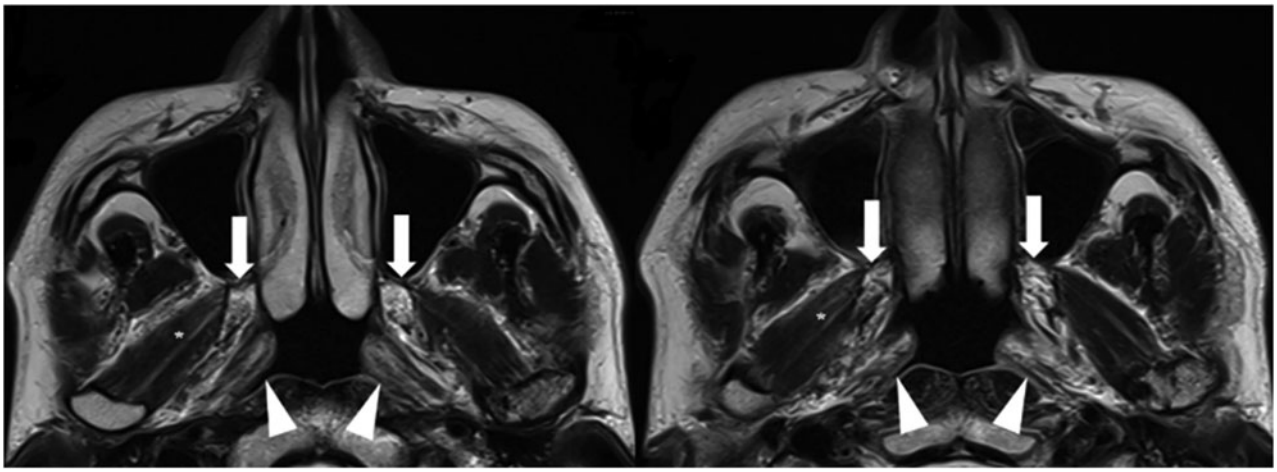

Figure 3. Axial, T2-weighted magnetic resonance images of the patient. Tensor veli palatini (arrows) and levator veli palatini (arrowheads) muscles appear whitish compared to the lateral pterygoid muscle (asterisks) due to fatty infiltration. The right tensor veli palatini and levator veli palatini muscles are relatively small compared to the left ones.

Kennedy's disease is one of the nine polyglutamine-expansion disease families. It is caused by an expansion of the polyglutamine region of the N-terminal domain of the AR protein-encoding exon located on the X-chromosome.[13] This region is polymorphic within the normal population, having 10–36 repeats. When the number of repeats exceeds 38, it causes pathological changes, which can be diagnosed as Kennedy's disease. Most patients have more than 40 repeats.[14] Individuals with higher numbers of repeats generally tend to develop more severe and earlier symptoms, as for other trinucleotide repeat expansion diseases.[3,14,15]

Patients with Kennedy's disease often do not realise that it is a hereditary disease if they do not have a male sibling because of X-linked recessive inheritance, and they may not even recognise their own symptoms because of the mild and slow course of the disease, likewise with physicians.[16] In the present case, the patient's symptoms were very mild. They progressed slowly because of a mild CAG expansion of 38 repeats. Thus, he was not aware of the symptoms at all. Weakness and atrophy of the palatal muscles due to Kennedy's disease in this patient were presumed to have caused patulous Eustachian tube. It was aggravated because of weight loss two months earlier, followed by aggravated autophony, which was the only symptom he recognised.

- Autophony can be accompanied by several systemic and medical conditions; it is important to identify the aetiology of autophony and detect treatable causes
- Neuromuscular diseases involving the oromandibular muscle can cause atrophy of tensor veli palatini and levator veli palatini muscles surrounding the Eustachian tube, a presumed cause of patulous Eustachian tube
- When patients are affected by a slowly progressive, mildly discomforting disease, they sometimes do not recognise their symptoms
- It is helpful for patients with autophony to have a thorough neurological examination, to confirm cranial nerve function
- Examination should include flexible endoscopy, to assess palatal symmetry and evidence of visible atrophy at Eustachian tube openings in the nasopharynx

Most patients with Kennedy's disease eventually depend on a wheelchair later in life, but can have a normal life span. However, recurrent aspiration due to bulbar and respiratory muscle weakness is a major complication in patients with Kennedy's disease, leading to debilitation, frequent hospitalisation and even unexpected early death.[14] Appropriate patient education and rehabilitation should be provided to Kennedy's disease patients, to optimise function and improve quality of life, even in the absence of proven disease-modifying treatments. Thus, early recognition and diagnosis of Kennedy's disease are crucial. Hence, it is very helpful for patients with autophony to have a thorough neurological examination, to confirm cranial nerve function. This should include flexible endoscopy to assess palatal symmetry and establish evidence of visible atrophy at the Eustachian tube openings in the nasopharynx, even if the patient does not complain of other symptoms.

Competing interests. None declared

Supplementary material. The supplementary video for this article can be found at https://doi.org/10.1017/S002221512300172X.

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