Case Report

# Novel genetic syndrome manifesting with cerebral atrophy, cataract, hypoacusis, diabetes, and brachy-/syndactyly

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## Abstract

Genetic disorders manifest clinically in a variety of phenotypes. A patient with cataract, hypoacusis, hand and foot deformities, and diabetes was not reported. The patient is a 74-year-old male with a history of congenital foot and hand deformities manifesting as brachydactyly of fingers 4 and 5 on the right side and brachydactyly and syndactyly of the fingers 1-5 on the left side. Foot deformities required orthopedic surgery from an early age. He later developed cataract that required surgery, hypoacusis with tinnitus on the left side, and diabetes. Cerebral MRI revealed generalized atrophy. Since the family history was positive for deaf muteness in his father, a genetic defect was considered. In summary, a novel syndrome has been described that manifests itself in cerebral atrophy, cataract, hypoacusis, hand and foot deformities, and diabetes. Considering the father's deaf muteness, a genetic cause of the syndrome is likely.

**Keywords:** Brain atrophy, chromosomal aberration, deafness, hand deformity, mtDNA

## Introduction

Genetic defects can be due to either chromosomal defects or due to DNA mutations. Chromosomal defects include chromosomal aberrations and structural chromosomal defects.[1] Chromosome rearrangements usually occur during cell divisions. DNA mutations can affect either nuclear DNA or mitochondrial DNA.[2] The phenotypic manifestations of genetic disorders are diverse. A common manifestation of genetic defects is hand and foot deformities. They can manifest as polydactyly, macrodactyly, ectrodactyly, syndactyly, brachydactyly, finger aplasy or hypoplasy, cleft hand, split hand, club feet, Charcot feet, flat feet, high arched feet, or joint dislocations. Translocations, insertions, duplications, and deletions have been described as chromosomal causes of hand and foot malformations.[3-7] There are also a number of point mutations in nuclear genes associated with hand and foot malformations, such as *BOR2, PTHLH, P63, WNT10B, DLX5*, or *HOXA13*.[8,9] Hand and foot malformations can occur together with other phenotypic manifestations of a genetic defect. However, a genetic defect manifesting in cerebral atrophy, cataract, hypoacusis, diabetes, syndactyly, and brachydactyly, and foot deformities has not been reported. The following case is relevant for the general practitioner because he/she is the first to see patients with hand and foot deformities and must decide what further diagnostic steps need to be taken in order to make the correct diagnosis.

## Case Report

The patient is a 74-year-old male who was admitted for left-sided hypoacusis and tinnitus. He had a history of congenital foot and hand deformities manifesting with brachydactyly of the fingers 4 and 5 on the right side and brachy- and syndactyly of the fingers 1-5 on the left side [Figure 1]. Foot deformity required

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**Received:** 13-04-2023 **Revised:** 21-06-2023
**Accepted:** 30-08-2023 **Published:** 21-12-2023

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_642_23



**How to cite this article:** Finsterer J. Novel genetic syndrome manifesting with cerebral atrophy, cataract, hypoacusis, diabetes, and brachy-/syndactyly. J Family Med Prim Care 2023;12:3415-7.

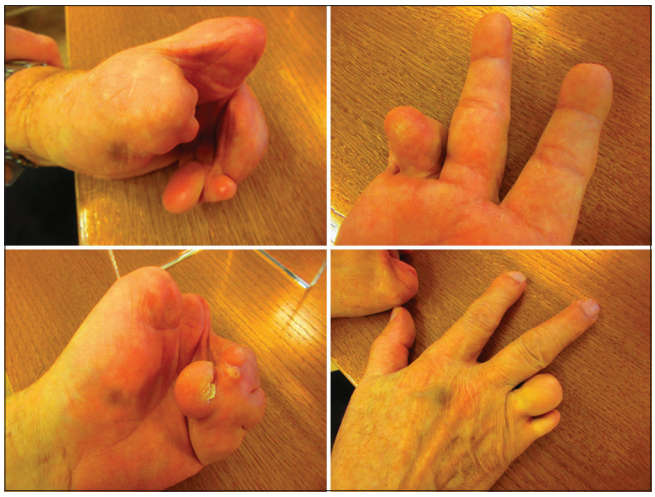

**Figure 1:** Hand deformities of the index patients showing brachydactyly of fingers 4 and 5 on the right hind (right panels) and brachydactyly of fingers 1-5 together with syndactyly of fingers 3-5 on the left hand (left panels)

orthopedic surgery already in early infancy. He later developed arterial hyperetension, bilateral cataract, requiring surgery and diabetes. Despite his hand deformities, the patient had worked as a tinner during 13 years. The family history was positive for deaf muteness in his father but negative for genetic defects in the family of the mother's side and was negative for consanguinity and any complications during pregnancy. The sister and the children of the index patient were healthy.

Clinical neurologic exam revealed unrounded pupils, hypoacusis on the left side, brachydactyly on the right hand and brachy- and syndactyly of the fingers 1-5 on the left hand [Figure 1], absent tendon reflexes on the lower limbs, and a foot deformity bilaterally after reconstruction surgery.

Blood tests revealed a HbA1c of 7.6, and nerve conduction studies (NCSs) were indicative of demyelinating polyneuropathy. Cerebral MRI revealed generalised cerebral atrophy including the cerebellum and leucoaraiosis without cognitive impairment [Figure 2]. His current medication included metformin and candesartan. Unfortunately, the patient refused to undergo chromosomal investigations or genetic tests to unravel the presumed genetic background of the described phenotypic abnormalities.

## Discussion

The index patient is interesting because of the combination of cerebral atrophy, cataract, hypoacusis, tinnitus, diabetes, and bilateral complex deformities of the hands and feet. Since the family history was positive for deaf muteness in the index patient's father, a genetic cause for the described anomalies in the index patient was suspected. Genetic work-up was suggested but the patient did not agree. Assuming that the anomalies described were due to one common genetic defect, searches of various literature databases yielded a negative result for a syndrome encompassing all features of the index patient. There was also

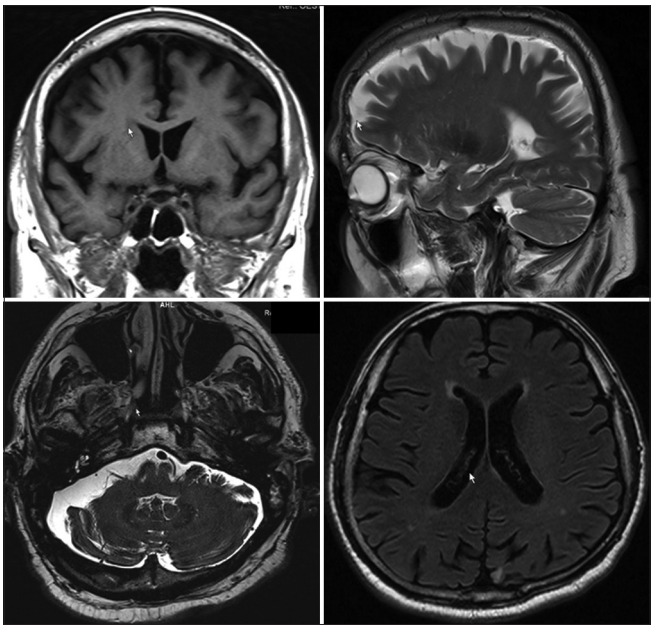

**Figure 2:** MRI of the brain showing leucocariosis and cerebral atrophy including the atrophy of the cerebellum

no hit for deaf muteness in combination with brachydactyly or syndactyly. However, cataract, hearing loss, and diabetes have been reported in Wolfram syndrome.[10] The combination of cataract, hearing loss, diabetes, and dysmorphism has been reported in various syndromic and non-syndromic mitochondrial disorders (MIDs).[11] Congenital rubella syndrome (CRS) was ruled out because the index patient had no microophthalmia, patent ductus arteriosus, or pulmonary stenosis.[12]

In summary, the case describes a novel syndrome that manifests itself in cerebral atrophy, cataract, hypoacusis, hand and foot deformities, and diabetes. Considering the father's deaf muteness, a genetic cause of the syndrome is plausible.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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