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Speech, language, and hearing function in twins with Alport syndrome: A seven-year retrospective case report

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Abstract

Alport syndrome is an X-linked syndrome that results in nephritis, renal failure, sensorineural hearing loss, and eye deficits. As a result of sensorineural hearing loss, these individuals are likely to experience difficulties in the area of speech and language. While studies in the past have examined the speech and language characteristics of children with syndromic sensorineural hearing loss, to our knowledge there are no previous studies to have documented the speech and language characteristics of these children on a long-term basis. The current study addresses this limitation by reporting speech, language, hearing, and function of twin brothers with X-linked Alport syndrome across a seven-year period. Information was collected by examining the medical records of the participants as well as through a verbal interview with the participants' guardian. Results revealed that the participants' hearing abilities gradually deteriorated over the seven-year period which affected their speech and language development as well. The kidney function tests revealed significant presence of hematuria (blood in the urine) as well as proteinuria (protein in the urine) suggesting chronic kidney dysfunction. This longitudinal study demonstrates the functional relationship between the kidneys and the cochlea, although they appear to be independent of one another. As individuals with Alport syndrome exhibit systemic complications, interdisciplinary collaboration is essential among health care providers including audiologists, speech-language pathologists, nephrologists, and ophthalmologist to promote evidence-based practice.

Keywords: Alport syndrome; Hearing loss; Speech and language development; Kidney function

1. Introduction

Hearing loss is the most common birth defect in developed countries and affects about 6–8% of the population (Hilgert et al., 2009; Schrijver, 2004). Hearing loss is commonly categorized as either conductive, sensorineural, or mixed types (Schrijver, 2004). Sensorineural (SN) hearing loss is typically characterized by damage to the inner ear and is often irreversible. The incidence of SN hearing loss at birth is about 1–2 per 1000 births (Berlin and Keats, 2000). Approximately 50% of cases of SN hearing loss are caused by genetic factors (Schrijver, 2004). Out of this 50%, about 70% of the cases of SN hearing loss are associated with non-syndromic conditions and the remaining 30% are associated with syndromic conditions. Hearing loss that is associated with a syndromic condition is referred to as syndromic hearing loss (Berlin and Keats, 2000). A syndrome is defined as a disease or disorder that has significant and unique characteristics and symptoms. They can be either hereditary or appear with no family history. Many well-known syndromes present with hearing loss as one of the associated characteristics (Berlin and Keats, 2000). Syndromic hearing loss is typically categorized based on the mode of inheritance and includes autosomal dominant, autosomal recessive, and X-linked types. Autosomal dominant syndromes that present with hearing loss as a symptom include Waardenburg

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syndrome, branchiootorenal syndrome, stickler syndrome, and neurofibromatosis-2. Autosomal recessive syndromes that are associated with hearing loss include Usher syndrome, Jervell and Lange-Nielsen syndrome, Biotinidase deficiency, and Refsum disease. X-linked syndromes that present with hearing loss include Mohr–Tranebjaerg syndrome and Alport syndrome (Smith et al., 2014). Syndromic hearing loss is commonly accompanied by delays in speech and language development in addition to other problems such as cognitive impairment, learning disability and physical malformation. Although there is well-documented information on the phenotypic features of children with the above-mentioned syndromes, very little is known about speech and language development in children with syndromic hearing loss. The limited studies that have investigated speech and language in children with syndromic hearing loss have focused on how hearing and speech intelligibility improved post-amplification. For example, Daneshi, Hassanzadeh and Farhadi (2005) studied the effects of cochlear implantation in six children with Waardenburg syndrome. The post-implantation results revealed that speech intelligibility of these six children significantly improved and they were placed in regular education settings. Similar results were also seen in studies that investigated the effect of cochlear implantation in children with Usher syndrome and Mohr–Tranebjaerg syndrome (Loundon et al., 2003; Aguirre et al., 2006). Although these studies help us to understand the speech and language characteristics of children with different syndromic hearing loss, the long-term trajectory of speech and language development in children with syndromic hearing loss remains to be studied. It is essential to pursue this line of research not only to understand the impact of a syndrome on speech and language, but also to implement a successful treatment protocol for treating speech and language deficits in this population. To address this shortcoming, we present a retrospective case report of twins born with a rare syndrome called Alport syndrome (AS). Specifically, we provide background information on Alport syndrome and report developmental history, medical history, hearing function, and most importantly the development of speech and language of twins born with this syndrome.

1.1. Alport syndrome

AS is a heterogenous disease that is known primarily for progressive kidney dysfunction leading to end-stage renal disease (ESRD) and sensorineural deafness. It is the most common form of glomerulonephropathy, an umbrella term for kidney diseases (Mochizuki et al., 1994). Alport syndrome is associated with mutations in type IV collagen (COL_4) that is typically located in the glomerular (kidney-filtering) and cochlear basement membranes. There are six isoforms of COL_4 [α1(IV)–α6(IV)] encoded by six genes, COL4A1–COL4A6, that are variably expressed in basement membranes. Mutations in the α3, α4, or α5 COL_4 chains result in disruption of the α3–α4–α5(IV) network, which eventually leads to basement membrane dysfunction in kidneys as well as the cochlea (Mochizuki et al., 1994).

Prevalence for AS has been known to range from every 1 in 10,000 individuals to every 1 in 50,000 individuals (Mohammad et al., 2014). Individuals with AS are known to present with several systemic complications. The most frequent complications are nephritis and progressive renal failure (Wang et al., 2014). Progressive bilateral high-frequency SN hearing loss is also common among individuals with AS. This syndrome accounts for at least 1% of congenital hearing loss occurrences (Gorlin et al., 1995). Hearing loss typically presents itself during school age for those diagnosed with AS (Flinter et al., 1988). Other prominent features of AS include hematuria (presence of blood in the urine), proteinuria (excessive levels of protein in urine), and various eye complications (Jais et al., 2000). The eye complications that occur as a result of Alport syndrome are bilateral anterior lenticonus (a cone-shaped appearance on the anterior lens), perimacular flecks (yellow flecks that may or may not affect visual acuity), retinopathy, and retinal thinning (Gorlin et al., 1995; Kanski and Bowling, 2011). An individual with Alport syndrome may experience all, some, or none of the eye complications mentioned above.

1.2. Inheritance of Alport syndrome

AS can be inherited through three different genetic routes that include X-linked, autosomal recessive, and autosomal dominant types of inheritance. About 80% of AS is inherited through X-linked type (XLAS) due to mutations in COL4A5 located on the X chromosome (Miner, 2014). Almost all the males diagnosed with XLAS will develop ESRD. On the other hand affected heterozygous females exhibit a wide variability in disease severity ranging from living symptom-free to having significant kidney complications (Mochizuki et al., 1994). The autosomal recessive manner of inheritance accounts for about 15% of individuals with AS. In this case it is caused due to mutations in both the alleles of either COL4A3 or COL4A4. The autosomal dominant type of inheritance is the least common type and accounts for just 5% of individuals with AS and is caused by heterozygous mutations in either COL4A3 or COL4A4 (Mochizuki et al., 1994).

2. Method

2.1. Participants

Jacob and Tyler (names changed), are fraternal twins who were diagnosed with X-linked Alport syndrome in 2009. They served as participants for the current study and were recruited based on a convenience non-probability sampling. They were 15 years old at the time of recruitment. They have a female half-sister, aged 12 years, who was also diagnosed with Alport syndrome in 2009. She was not recruited as a participant due to her typical hearing abilities as well as typical speech and language development. The Institutional Review Board at the authors' University approved the current study (approval number: AS1595). The participants were living with their