J Am Acad Audiol 4: 116–121 (1993)

Audiologic and Otolaryngologic Findings in Progeria: Case Report

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Abstract

Progeria is a rare syndrome, with an estimated incidence of 1 per 250,000 births. Although children with progeria have the appearance of premature aging or senility, the term is misleading because reported cases of progeria have not manifested most physical or biochemical aspects of old age. Many children with progeria appear normal at birth and then progressively, and rather rapidly, develop the characteristic features during early childhood. Although first described in the 1880s, only approximately 100 cases of progeria are reported in the international literature. The single case study of hearing in progeria, which appeared in 1965, is limited to pure-tone and speech audiometry findings. We report the results of otolaryngologic examination and pure-tone, speech, immittance, and auditory brainstem response (ABR) audiometry for a 5-year-old female with progeria. The patient had a mild-to-moderate, bilateral, conductive hearing loss. Immittance measurements were consistent with fixation of the ossicular chain and this was confirmed surgically. Mildly prolonged ABR wave I–V latencies suggest possible auditory central nervous system involvement.

Key Words: Auditory brainstem response (ABR) audiometry, conductive hearing loss, pure-tone audiometry, progeria, speech audiometry, syndrome

The term "progeria," coined by Gilford in 1904, is used to describe children with the appearance of premature aging or senility. Progeria is a rare syndrome. The reported incidence is 1 per 250,000 live births (Bergsma, 1979), although an earlier estimate based on published reports between 1915 and 1967 was as low as 1 per 8,000,000 births (DeBusk, 1972). A patient with characteristics of progeria was first described in print in 1752, and a second patient, with more detail, in 1886 (Hutchinson, 1886; Jones, 1988). However, less than 100 cases of progeria are reported in the international literature.

The term progeria is misleading because reported cases of progeria have not manifested most physical or biochemical aspects of old age. Infants and young children afflicted by several conditions, such as Cockayne syndrome and Werner syndrome, may appear prematurely aged and may manifest selected features summarized in Table 1, but these physical findings are most closely associated with Hutchinson-Gilford progeria. Many of these children appear normal at birth and then progressively, and rather rapidly, develop the characteristic features during early childhood. This is in distinct contrast to Wiedemann-Rautenstrauch neonatal pseudohydrocephalic progeroid syndrome (Martin et al, 1984), a degenerative central nervous system disorder, which is typically apparent from birth. With Hutchinson-Gilford progeria, death is most often due to arterial atheromatosis and coronary occlusion and generally occurs between 7 and 27 years, with a mean age of 13.5 years (DeBusk, 1972). Recently, longevity up to 45 years has been reported for three patients (Ogihara et al, 1986; Parkash et al, 1990).

A prominent physical feature of progeria is marked outward protrusion of the ears (pinna) and absence of ear lobes, yet there is a general consensus in the literature that hearing in children with progeria is not impaired, at least by clinical examination (DeBusk, 1972). Nelson (1962, 1965), however, documented a flat con-

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Table 1 Summary of Prominent Characteristics of the Progeria Syndrome

General
Short stature
Decreased weight for height
Incomplete sexual maturation
Skin
Diminished subcutaneous fat
Thin, dry, wrinkled skin
Prominent superficial veins
Head
Craniofacial disproportionate size
Anterior fontanelle patent
Beaked nose
Micrognathia
Thin lips
Prominent eyes
Protruding ears
Absent earlobes
"Plucked bird" appearance
Hair
Alopecia (hair loss)
Absent eyebrows and eyelashes
Teeth
Dentition delayed and abnormal (crowding)
Trunk and Limbs
Pear-shaped thorax
Short clavicles
Wide-based, shuffling gate
Thin limbs
Dystrophic finger nails (brittle, yellowish, curved)
Radioluscent terminal phalanges
Prominent and stiff joints

Not all characteristics are consistently present (Adapted in part from DeBusk, 1972 and Jones, 1988).

figuration, moderate-to-severe, bilateral mixed hearing loss in a girl with progeria. Audiometric assessments were made when the patient was 11 and 12 years old and attending public school. The patient's air conduction thresholds were in the 50 to 75 dB HL range at both ages, whereas bone-conduction thresholds progressed from the 20 to 35 dB range to the 45 to 55 dB range. Word recognition scores were consistently 96 percent to 100 percent. The patient was fitted with a hearing aid. She died of cardiac disease at the age of 13.

We report in this paper behavioral and electrophysiologic auditory findings for a young girl with progeria.

CASE REPORT

The patient was a 5-year-old girl with progeria who manifested typical characteristics of the disease, including short stature, alopecia, a small beak-like nose, micrognathia, and protruding ears. Diagnosis was made by a dysmorphologist in the department of pediatrics. Computerized tomography showed a poorly pneumatized mastoid system. Otolaryngologic examination of the tympanic membrane and middle ear was unremarkable. A thorough otologic history, including information on possible middle ear disease, was not available.

Pure-tone and speech audiometry, and aural immittance measurements, were carried out with commercially available equipment in a sound-treated chamber. Pure-tone audiogram showed a mild-to-moderate conductive hearing impairment (Fig. 1). Bone-conduction audiometry was initially conducted with a portable audiometer without masking. Unmasked bone-conduction audiometry yielded thresholds that were well within normal limits for octave frequencies up to 2000 Hz and at 25 dB HL at 4000 Hz. Without masking, however, these pure-tone bone-conduction thresholds are not ear-specific. Masked word recognition scores at a high intensity level were 88 percent for the right ear and 92 percent for the left ear. Immittance measurement for each ear yielded a normally shaped tympanogram, but no observable acoustic reflex activity in the uncrossed condition (crossed acoustic reflexes were not measured). This audiometric pattern was consistent with fixation of the ossicular chain bilaterally.

Exploratory tympanotomy of the right ear, 6 months after the initial audiologic assessment, revealed an extremely large external auditory meatus with the middle ear cavity rotated 20 degress in a clockwise direction. Fibrous adhesions were noted on the stapes footplate and between the incudostapedial joint and the tympanic membrane. The fallopian canal was dehiscent. After lysis of the adhesion, the ossicular chain was mobile.

Auditory brainstem response (ABR) recordings were made in the operating room with the patient under general anesthesia, immediately after ossicular chain mobilization. She was normothermic at the time of ABR measurement. The ABR was elicited with 0.1 msec click stimuli presented monaurally at a rate of 21.1/sec. Air-conduction stimuli were presented with TDH-49 earphones enclosed within MX-AR/41 cushions at intensity levels of 85 dB nHL down to 20 dB on the right ear and 35 dB on the left ear. Bone-conduction stimulation at the mastoid was presented with a Maico B70 bone-oscillator at intensity levels of 40 dB nHL down to 0 dB nHL. Contralateral masking was not used for air- or bone-conduction ABR record-

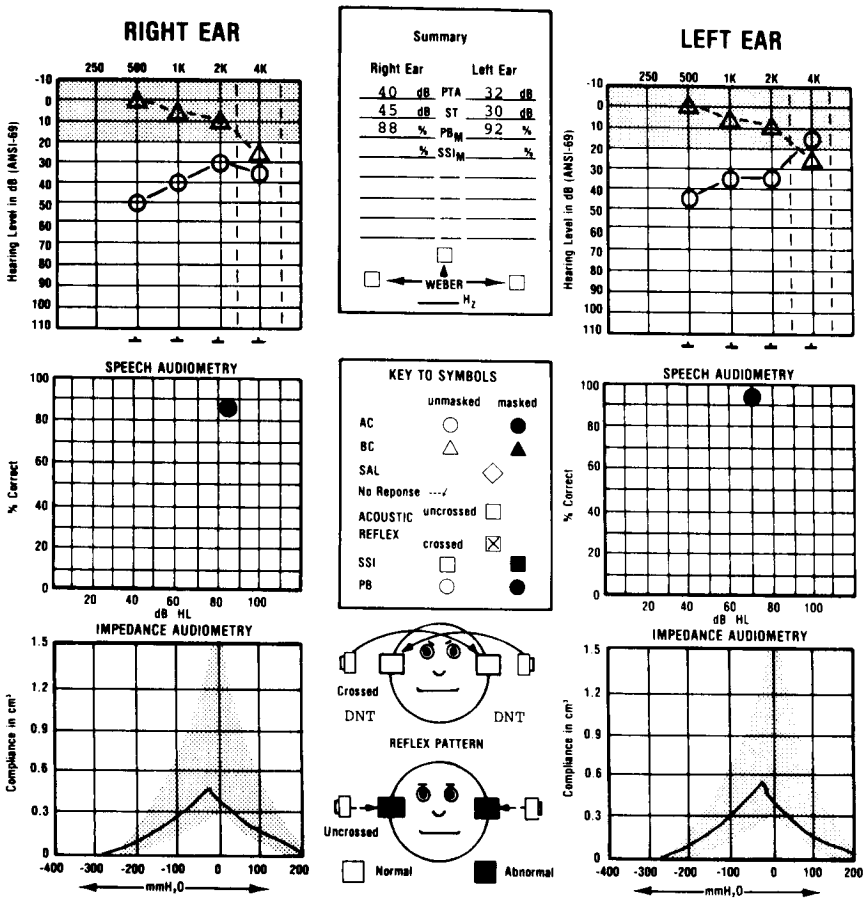

Figure 1 Pure-tone audiogram showing mild-to-moderate primarily conductive hearing impairment in a 5-year-old girl with progeria.

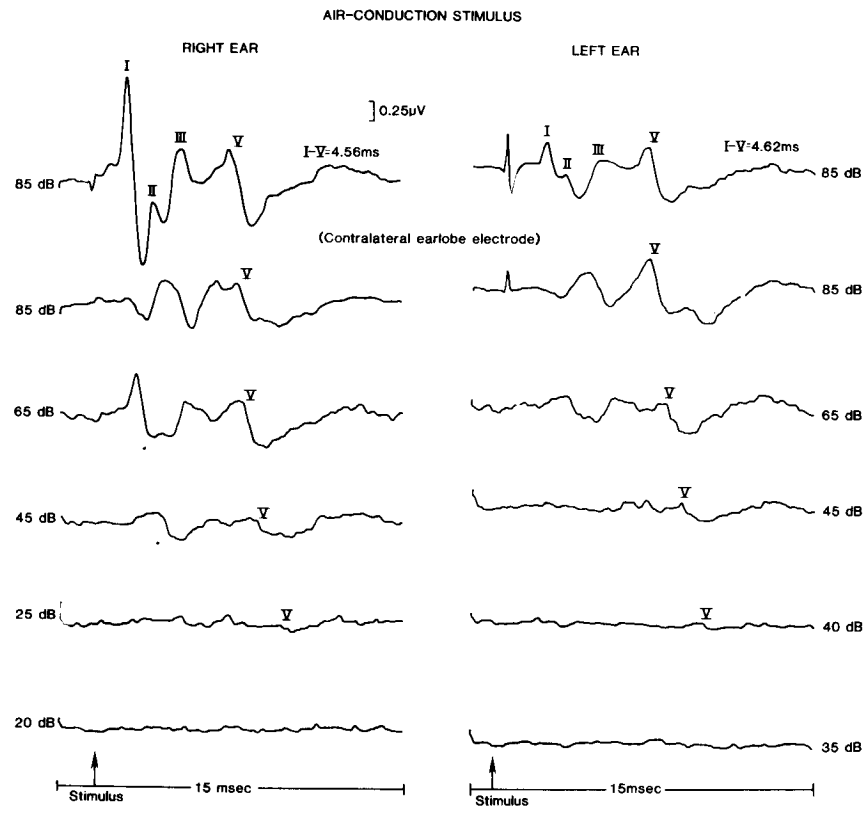

Figure 2 Auditory brainstem responses for air-conduction stimulation in a 5-year-old girl with progeria.

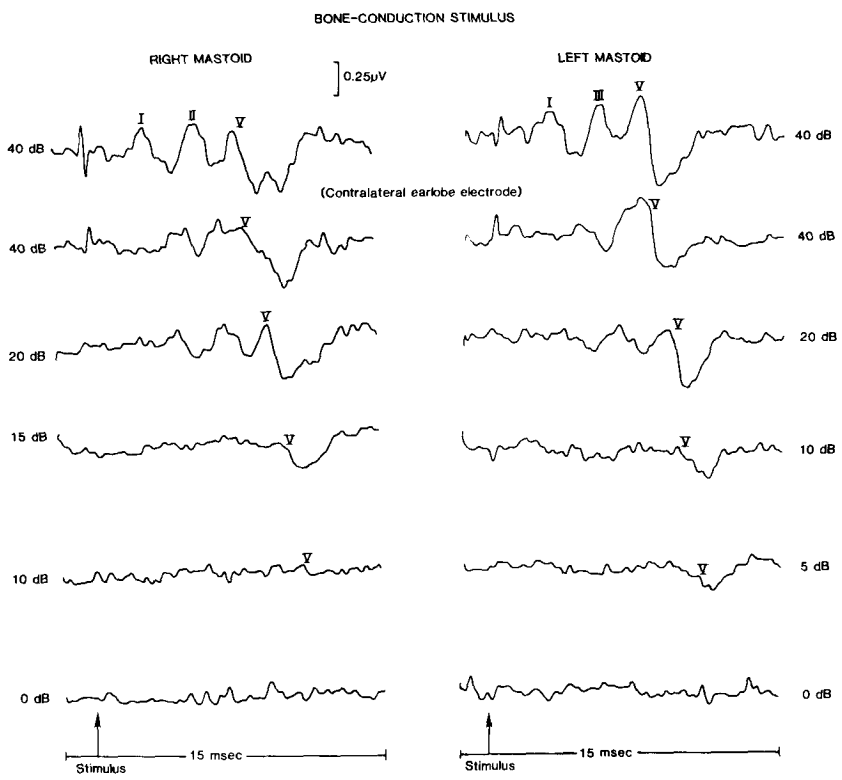

Figure 3 Auditory brainstem responses for bone-conduction stimulation in a 5-year-old girl with progeria.

ings. The ABR was detected simultaneously with a two-channel electrode array (Hall, 1992). The noninverting electrode for both channels was located at the Fz site according to the International 10–20 electrode system (Jasper, 1958). The inverting electrode was located on the earlobe ipsilateral to the stimulus for the channel one (ipsilateral channel) and the contralateral earlobe for the second channel (contralateral channel). Bandpass filter settings were 150 Hz (high pass) and 3000 Hz (low pass). No notch filter was used. Two replicated ABR waveforms were averaged from 2000 stimuli and then summed.

ABR waveforms for air- and bone-conduction stimulation are illustrated in Figures 2 and 3, respectively. There was a reliable response for air-conduction stimulation at intensity levels down to 25 dB nHL on the right and 45 dB nHL on the left. At high intensity levels, a clear wave I component was detected only with the ipsilateral electrode array, confirming that the response was due to activation of the test ear, rather than acoustic crossover to the nontest ear (Hall, 1992). Absolute latency values for all waves, including wave I, were abnormally delayed, consistent with conductive hearing impairment. The wave I–V latency interval, at a stimulus intensity level of 85 dB nHL, was 4.56 msec for the right ear and 4.62 msec for the left ear. These latency values are abnormally prolonged (exceeding 2.5 standard deviations of normal mean values) in comparison to age-matched normative data (Eggermont and Salamy, 1988).

A reliable ABR was observed for bone-conduction stimulation of the right mastoid at intensity levels down to 15 dB on the right and down to 5 dB with stimulation at the left mastoid. As with air-conduction stimulation, the bone-conducted stimuli produced a response with a clear wave I component in the ipsilateral recording channel, but not in the contralateral channel. This observation confirmed that the bone-conduction ABR findings were ear-specific, even though masking of the nontest ear was not employed. ABR latency-intensity functions for air- and bone-conduction stimulation (Fig. 4) illustrate the delay in absolute wave V latency values, the presence of an air-bone gap, relatively better postoperative hearing sensitivity for the right ear, and a delay in the wave I–V latency value bilaterally.

Audiometric assessment 3 months post surgery (Fig. 5) showed improvement in pure tone and speech thresholds for the right ear. There were no consistent audiometric changes for the left ear, although the 2000 Hz threshold was

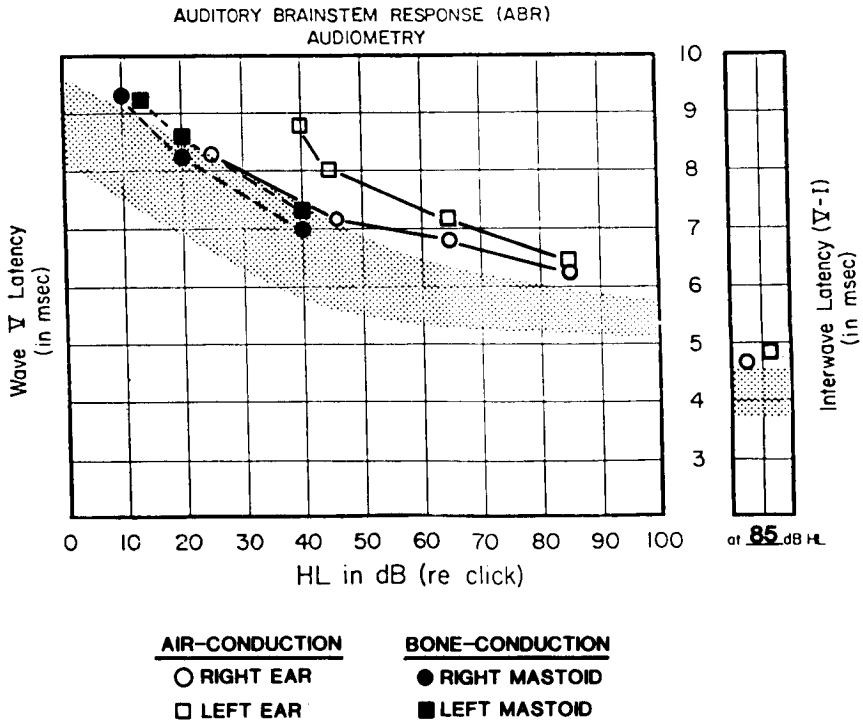

Figure 4 Auditory brainstem latency-intensity functions for air- and bone-conduction stimulation in a 5-year-old girl with progeria.

improved. We have no ready explanation for this apparent change. The patient was lost to further follow up when the authors relocated.

COMMENTS

Consistent with the only published audiometric study of a child with progeria (Nelson, 1962, 1965), we found a bilateral hearing impairment with a conductive component. There are at least two differences in findings for our case versus the previously reported patient. For our 5-year-old patient, the degree of hearing impairment was in the range of 30 to 50 dB HL and sensorineural status appeared normal, whereas Nelson's (1962, 1965) 11- to 12-year-old patient had hearing threshold levels that were 20 to 40 dB poorer and also abnormal bone conduction thresholds. If the auditory deficits in progeria are progressive, this might account for

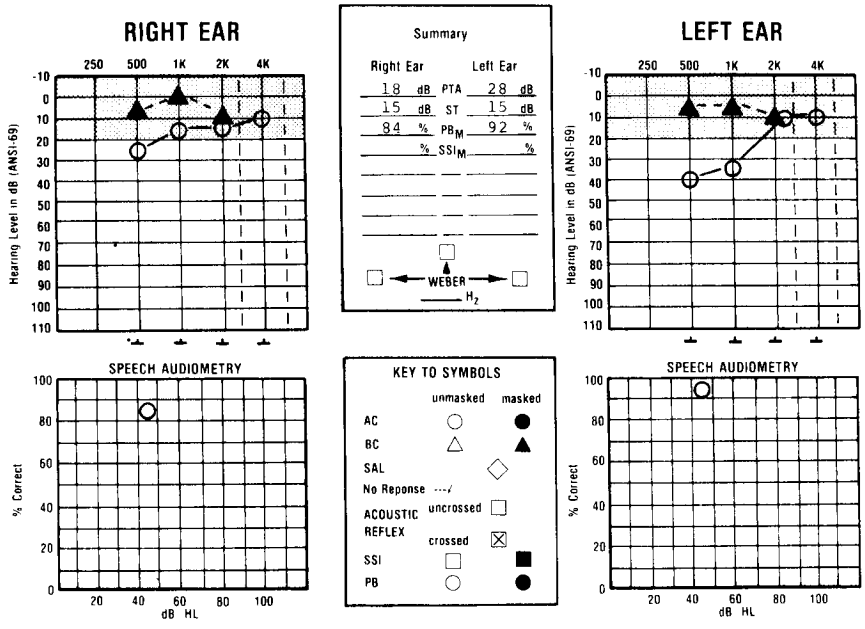

Figure 5 Audiometric assessment 3 months after surgery in a 5-year-old girl with progeria.

the differences between the two studies and for the general impression, in the literature, that hearing is not affected in young children with the disease. Our findings are not compatible with the hearing sensitivity deficits commonly associated with aging. That is, we found no evidence to support premature peripheral presbyacusis in progeria. The audiometric pattern of the conductive hearing loss for our patient was consistent with fixation of the ossicular chain. Middle ear exploration confirmed ossicular adhesions. It was not possible to determine whether the middle ear pathology for our patient was related to general physical characteristics of progeria, such as craniofacial anomalies and joint stiffness. The previously reported study (Nelson, 1965) was conducted before immittance measures were commonly made, and the author reported no otologic findings.

In addition to these middle ear abnormalities, and conductive hearing impairment, we recorded an ABR with wave I–V latency values that exceeded age-matched normal limits bilaterally. This finding was not specific to either the wave I–III or III–V latency interval but, rather, distributed evenly from wave I to wave V. CNS pathology is not a reported feature of Hutchinson-Gilford progeria. Nervous system development and intelligence in this syndrome are normal. In contrast, neuropathology is the salient characteristic of Wiedemann-Rautenstrauch or neonatal progeroid syndrome (Martin et al, 1984; Rudin et al, 1988). However, cerebral vascular disease and generalized atherosclerosis does occur in Hutchinson-Gilford progeria. It is possible that the ABR alterations for our patient are an early reflection of CNS effects of cerebral vascular disease, although she did not have any other clinical neurologic findings.

Peripheral and, possibly, central auditory dysfunction appears to be a feature of progeria. Although children with progeria will very rarely be encountered by audiologists and otolaryngologists in most clinical settings, aggressive management of otologic pathology and resulting hearing deficits is warranted to optimize educational development, social interaction, and quality of life in general. Audiologists involved in newborn hearing screening should also be aware of the neonatal progeroid syndrome. This degenerative development disorder would probably be encompassed within the 1990 Joint Committee risk criteria for infant from 29 days to 2 years, specifically criterion #7 which includes "children with neurodegenerative disorders such as .... any metachromatic leukodystrophy or any infantile demyelinating neuropathy" (Joint Committee, 1991, p 15).

Acknowledgment. The patient reported in this paper was evaluated while the authors were affiliated with the Department of Otolaryngology at the University of Texas Medical School in Houston. Susan Tompkins and Wende Yellin assisted with data collection while they were on staff at the University of Texas. Jane Baer, Division of Hearing and Speech Sciences, Vanderbilt University School of Medicine, contributed to the literature review.

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