Audiologic and Otolologic Manifestations of Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes

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ABSTRACT

Objectives: To characterize the audiologic and otologic manifestations of inherited bone marrow failure syndromes.

Study Design: Prospective case series

Methods: From 2002 to early 2012, patients with Fanconi Anemia (FA), Dykeresasteros Congenita, Diamond-Blackfan Anemia, Shwachman-Diamond Syndrome, and Thrombocytopenia Absent Radii were enrolled along with their unaffected relatives. Each underwent otolaryngologic and audiologic evaluation as well as temporal bone computerized tomography (CT) in patients with FA.

Results: Two-hundred eighty-one patients and relatives (562 ears) had sufficient data for audiologic analysis. Patients with FA had a significantly higher proportion of conductive and subclinical conductive hearing loss (HL) compared with the unaffected relatives. Of the 562 ears (562 patients) with FA, 4 ears were excluded from audiologic analysis because of prior surgery. Twenty-eight (48%) ears showed hearing within normal limits, 11 (19%) conductive HL, 8 (14%) subclinical conductive involvement, 2 (3.5%) mixed HL, and 3 (5%) sensorineural HL. Of the 54 ears undergoing microscopic exam, abnormal ear findings (small tympanic membrane, anteriorly displaced malleus, and/or a bony plate arising from the annulus) were noted in 31 (57%). Temporal bone CTs from 52 ears when compared with normal age matched controls showed significantly smaller measurements for the height and width of the tympanic bony annulus (p<0.001). There was one case each of aural atresia and cochlear nerve hypoplasia.

Conclusions: Conductive HL is associated with FA. Syndromic specific congenital ear malformations are noted in FA patients; recognition of these abnormalities should prompt further investigation and lead to earlier FA diagnosis and management of HL.

METHODS

From 2002 until 2012, patients with FA, DC, SDS, DBA, and TAR and their unaffected relatives were enrolled in an IRB approved prospective IBMFS study. Each underwent a complete history and physical examination as well as comprehensive audiologic and otologic evaluation exam. High resolution computerized tomography (CT) as well as microscopic otoscopy was performed in patients with FA because of the association with middle ear abnormalities noted anecdotally and in previous reports.4-6 Middle ear abnormalities were noted and the height and width of the bony annulus on CT scan was compared to age matched controls. Ear-specific audiologic data was gathered and reported. Type and degree of hearing loss (HL) are defined because of the association with middle ear abnormalities.

RESULTS

A total of 281 patients and family members were enrolled. Patients with FA had a significantly higher proportion of conductive and subclinical conductive HL when compared with their unaffected family members (Figure 1). No characteristic type of hearing loss was seen with the other syndromes.

Thirty-one FA patients were evaluated and were included in a subgroup analysis. Of those 31 patients (62 ears) with FA, 4 ears were excluded from audiologic analysis because of prior surgery. Twenty-eight (48%) ears showed hearing within normal limits, 11 (19%) conductive HL, 8 (14%) subclinical conductive involvement, 2 (3.5%) mixed HL, and 3 (5%) sensorineural HL. The average air-bone threshold gap (ABG) was 14dB; an ABG of less than 10dB is considered normal. Charts 1 and 2 are examples of subclinical conductive and conductive HL.

Tympanic membrane and middle ear abnormalities were noted in 31 of the 51 FA ears (57%) that underwent microscopic exam; the most common were small tympanic membrane, anteriorly displaced malleus, abnormal course of the chorda tympani, and a bony plate arising from the annulus (Figures 2 and 3). A number of middle ear abnormalities were noted on the temporal bone CT scans of FA patients including malformed ossicles and a bony plate within the TM (Figures 4a,b,c). Temporal bone CTs from 52 FA ears were compared with normal age matched controls. FA patients showed significantly smaller measurements for the height and width of the tympanic bony annulus (p<0.001) based on two-tailed t-test (Figures 5a,b,c). The temporal bone CT also revealed aural atresia and cochlear nerve hypoplasia in two separate FA patients.

DISCUSSION

Audiologic and otologic manifestations have not been fully described in the IBMFS as they are rare disorders. This is the first comprehensive study to show that no characteristic auditory and otologic features are found in IBMFS except in FA. In our series, 33% of FA patients had a conductive or subclinical conductive hearing loss which we attribute to the middle ear abnormalities. Furthermore, middle ear abnormalities can be present even when hearing loss is subtle. On CT, measurements of annulus height and width were smaller in the FA patients, indicating smaller tympanic membranes and underdevelopment of the outer and middle ear. The bony plates seen on otoscopic exam affect the movement of the TM and/or ossicles and also contribute to the conductive component of the HL. McDonough reported a case of a 21 year old woman with deformed thumbs who underwent multiple surgeries during her childhood and teenage years for congenital conductive HL due to middle ear abnormalities.3 She was later diagnosed with FA after biopsy of an oral lesion revealed squamous cell carcinoma and subsequent laboratory evaluation revealed anemia. This case and our study illustrate that FA-related genes may play a significant role in the embryogenesis of the ear and how earlier diagnosis of FA can be made if certain features are recognized by the otolaryngologist.

CONCLUSIONS

FA is associated with conductive hearing loss and congenital middle ear malformations. When these findings are seen in a patient with other manifestations such as absent thumbs or cytopenia, work-up for bone marrow failure should be initiated. Recognition of these ear abnormalities in conjunction with other findings in FA may lead to improved prognosis due to earlier diagnosis and management.

REFERENCES