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Research article

Acute Phase Reactants in Immune-Related Inner Ear Disease

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ABSTRACT: In this study, the clinical profile of patients with immune-related inner ear disease (IRIED) was correlated with the laboratory results of acute phase reactants and quantitative immunoglobulin as guide in the management of the disease. A 2-year prospective review of the patients with diagnosis of immune-related inner ear disease through the year 2004 to 2006 was carried out. IRIED accounted for 15 cases, 9 females and 6 males, the age ranging between 21 and 62, average of 45. Of this, autoimmune inner ear disease accounted for 8/15 (53%), Meniere's disease 4/15 (27%) and vestibular hydrops 3/15 (20%). The erythrocyte sedimentation rate(ESR), C-reactive protein(CRP) and Immunoglobulin E (Ig E) were elevated in 10/15 (67 %), 6/15 (40 %), and 6/15 (40 %) respectively; while rheumatoid factor was identified in 4/15(27%).The predisposing factor was presumed to be autoimmune in 7(48%), allergy in 6(40%) and one patient had trauma in addition. Following treatment, response to therapy was observed in 10/15(67%) patients; 6/8(75%) patients with AIED, 3/4 (75%) meniere's disease and 1/3(33%) vestibular hydrops. A high index of clinical suspicion and screening with ESR and CRP are useful guide in the management of patients, however, there is need for a simple and more specific immunodiagnostic assays.

Key Word: autoimmune inner ear disease, allergy, meniere's disease, laboratory results

INTRODUCTION

The immune system is complex and there are several ways that it can damage the inner ear; allergy, traditional autoimmune disease and autoimmune inner ear disease (AIED) have been documented.

AIED is uncommon, probably accounting for less than 1% of all cases of hearing impairment or dizziness and immune dysfunction has been reported in 6-16% of meniere's disease (Quick, 1975; Bernstein et al, 1996).

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In the cohort of patients with AIED reported by McCabe (1979), the patients' hearing improved after treatment with corticosteroids, thereby suggesting an autoimmune pathogenesis, this to therapy has also been reported by other workers (Harris et al, 1997; Hirose et al, 1999; Mosciki et al, 1999). The molecules considered as autoantigens in autoimmune sensorineural hearing loss and meniere's diseases include type II collagens, type IX collagens, 30 kD proteins of inner ear membranes, laminin, 68 kD proteins of inner ear, Raf I protein and beta-tubulin (Hughes et al, 1984; Dereby and Valenzuela, 1992; Suzuki et al, 1997; Boulassel et al, 2001)

However, considerable controversies still abound in the literature over the immunodiagnostic techniques concerning which antigens are recognized and by what fraction of patients. Hence diagnosis tends to be presumptive and outcome of treatment is dependent on proper selection of patient.

While the Western blot and serologic test have remained the confirmatory tests Suzuki et al, 1997; Boulassel et al, 2001, acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have also been reported useful as a

screening tool (Harris et al, 1997; Hirose et al, 1999; Mosciki et al, 1999).

This report is aimed at reviewing the profile of patients with immune related inner ear disorders and results of laboratory studies used in screening the patients.

MATERIALS AND METHODS

This is a prospective study of patients with presumed immune-related sensorineural hearing loss/vertigo attending the otorhinolaryngology outpatient Clinic of the University College Hospital, Ibadan. The study was carried out between February 2004 and June 2006. All the patients had complete blood count, estimation of serum with ESR and CRP, and Rheumatoid factor identification and pure tone audiometry. Immunoglobulin E was requested in cases with suspected allergy and computerized tomography scan of the temporal bone was requested in cases of unilateral vertigo/hearing loss to rule out a small acoustic neuroma. The criteria for autoimmune inner ear disease was based on the report in the literature which included bilateral and asymmetric sensori-neural loss and/or vertigo progressing over weeks to month in the absence of other known aetiological factors, meniere's disease was based on the presence of vertigo, hearing loss, tinnitus and vomiting and vestibular hydrops was based on a history of recurrent/fluctuating vertigo in the absence of other aetiological factor, allergy was determined by history of hypersensitivity reactions with elevated serum IgE. The immunochemical studies were reviewed and the results were presented in table.

The pure tone average was assessed using pure tone audiometry carried out in an acoustic booth by a speech pathologist who also had audiology as part of the training.The pre- and post –treatment hearing threshold was assessed for positive response which was defined as an improvement in hearing threshold by average of 15 dB in 2 frequencies and/or decrease in vertigo. The data, presented in table, were analysed using simple statistics.

RESULTS

Immune – related inner ear disease accounted for 15 out of 37 (41 %) cases of idiopathic inner ear disease seen during the period of the study. AIED accounted for 8/15(53%), meniere's disease 4/15 (27%) and vestibular hydrops disease 3/15 (20%) There were 9 females and 6 males, the age ranging between 21 and 62, average of 45.

Asymmetric bilateral hearing loss and tinnitus were seen in 6/8 AIED, the remaining 2 had vertigo in addition, full symptoms of bilateral hearing loss, vertigo and vomiting was seen in 4 patients with meniere's disease while the 3 patients presented with unilateral vertigo.

The erythrocyte sedimentation rate (ESR) was elevated in 10/15 (67 %), Immunoglobulin E (Ig E) was elevated in 6/15 (40 %), C-reactive protein (CRP) was elevated in 6/15 (40 %), rheumatoid factor was identified in 4/15(27%), while 2 (13%) patients had normal results. The predisposing factor was presumed to be autoimmune in 7(48%), allergy in 6(40%), one patient had trauma in addition while no predisposition was found in 2 cases.

The patients with suspected AIED were treated with dexamethasone tablet for 2 – 3 months, allergy was treated with anthistamine and cromolyn sodium for 2-3 months and the meniere's disease was treated with diuretics, antihistamine and vestibular suppressant for 1 month.

There was response to therapy, shown by resolution of the vertigo and/or an average of 15 dB improvement in the hearing threshold was observed in 10/15(67%) patients; 6/8(75%) patients with AIED, 3/4 (75%) meniere's disease and 1/3(33%) case of vestibular hydrops, overall, there was no improvement in 4/15(27 %) cases.

DISCUSSION

Immune related inner ear disease is not a common pathology, probably accounting for less than 1% of all cases of hearing impairment or dizziness although the precise incidence is not known. This is also reflected in this report of 15 cases in 2years, less than I case per month. However, the response to medical treatment has made it interesting. The classical bilateral asymmetric bilateral hearing loss seen in 6/8 AIED and full symptoms of meniere's disease were pointers to diagnosis in this series. Bilateral hearing loss and vertigo has been reported in 79% and 50% of immune related inner ear disorders (Harris et al, 1997; Dereby and Valenzuela, 1996). The mean age of our patients is 45 with female preponderance of 60%. This is similar to the report of Harris[4] and Hughes[7] who reported 65% and 63% in favour of females and age range between 30 and 61.Our series showed resolution of symptoms in 6/8 AIED. The overall steroid response rates reported is approximately 60% (Hirose et al, 1999; Mosciki *et al*, 1999; Harris and Sharp, 1990).

Table 1:
Showing the biodata and clinical profile of the patients

Subject	AGE/SEX	Clinical Presentation	ESR(0-75)	CRP (0-10 mg/L)	Ig E (0-30 KU/L)	Rheumatoid factor	Aetiology	Presumptive Diagnosis	Response to therapy
1	F/46 years	Asymmetric SHL	127	4	NR	positive	Autoimmune	AIED	Positive
2	M/34	Asymmetric SHL	172	10	NR	Negative	Autoimmune	AIED	Positive
3	F/5years	SHL and vertigo	15	5. 00	41.20	NR	Trauma and allergy	Delayed Vestibular hydrops	Positive
*4	F/61	Asymmetric SHL	57	1.5	NR	Negatiove	Unknown	AIED	Positive
5	M/56	Unilateral Vertigo	93	7	49.3	Negative	Allergy	Vestibular Hydrops	Nil
*6	F/41	Asymmetric SHL	70	2.5	NR	Negative	Unknown	AIED	Positive
7	F/49	Asymmetric SHL	152	0.1	NR	positive	Autoimmune	AIED	Nil
8	M/53	Asymmetric BV	95	1.0	35.7	Neagative	Allergy	Vestibular Hydrops	Positive
9	M/31	Asymmetric SHL and unilateral vertigo	54	19.2	46.2	NR	Allergy	Menieres disease	Nil
10	F/37	Asymmetric SHL	116	12.0	NR	Negative	Autoimmune	AIED	Positive
11	F/39	Asymmetric SHL and vertigo	160	32	NR	positive	Autoimmune	AIED	Positive
12	m/52	Asymmetric SHL &vertigo	204	21.3	38.6	NR	Allergy	menieres disease	Positive
13	F/68	Asymmetric SHL and vertigo	195	3.7	NR	Positive	Autoimmune	AIED	Nil
14	M/47	Asymmetric SHL and vertigo	42	27.0	41.0	NR	Allergy	menieres disease	Positive
15	F/49	SHL and vertigo	182	19.1	5.0	NR	Unknown	Menieres disease	Nil

They used improvement in threshold of 15 dB at 1 frequency, 10 dB at 2 consecutive frequencies, or a significant improvement in discrimination score as measure of response, while we used an improvement in threshold by average of 15dB in 2 frequencies.

In managing the patients, we rely on elevated ESR and CRP as our guide in patients with suggestive symptomatology. The elevated ESR and CRP seen in 60% of the patients and detection of rheumatoid factor; in our impression this is suggestive of an inflammatory process which is presumed to be immunologic in these cases; hence our rationale for commencing steroid. This is similar to the report of McCabe (1979) who also proposed the use of ESR, antinuclear factor, rheumatoid factor, complement levels, and quantitative immunoglobulin levels as a screening panel for autoimmune inner ear disease in high risk patients. In the review of 82 patients, Hirose et al (1999) made a similar remark. However, autoimmune testing has been reported by several authors as the most reliable diagnostic method. Harris and Sharp (1992) reported the detection of a specific auto-antibody with a molecular weight of 68 kilodaltons (kDa) using Western blot analysis in 32% of their 279 patients which was found to be heat shock protein. Mosicki (1994) also found this in 89% of patients with active progressive bilateral sensorineural hearing loss suggestive of AIED, out of which 75% responded to

steroid therapy. Similarly, Hirose et al (1999) reported that 50-60% of steroid-responsive patients are western blot-positive thus suggesting the usefulness of western blot for steroid response predictability. Others have reported antibodies to inner ear proteins of various molecular weight in 28 - 44% of AIED and meniere's disease (Hughes et al, 1984; Dereby and Valenzuela, 1992; Suzuki et al, 1997; Boulassel et al, 2001).

Despite all of this, most of the antigens that have been biochemically characterized are also common to non–inner ear specifictissues making interpretation difficult and at times the result has been found to be inconsistent (Billings et al, 1998; Cao et al, 1996). It is also not readily available yet in most centres, hence a high index of suspicion becomes important.

However, in managing the patients other conditions that can present similarly were also considered; this include small acoustic neuroma, which was suspected in the three patients with unilateral vertigo, the computerized axial tomography scanning of the petrous bone showed a normal internal auditory canal. The other is otosyphillis, the absence of sexually transmitted disease in the history and examination of the patient was relied on to rule this out. Systemic autoimmune disease has been reported in 29% of patients (Kempf, 1989) although this was not found in any of our patients, further follow-up may be needed to confirm this. In the series of 52 patients, Hughe found cogan's syndrome in 7, rheumatoid arthritis in 4 and systemic lupus erythematosus in 1 while the rest was suspected of having inner ear disease, although the etiology was uncertain but evidence suggested immunologic basis (Hughes et al, 1988).

Allergy was seen in 6 cases although 4 cases presented with symptoms of definitive meniere's, while the others had vestibular hydrops disease. All the cases of allergy were confirmed with an elevated serum Ig E. One case of meniere's disease was seen in a 5 year old following a head injury sustained three years before presentation, she showed dramatic improvement with diuretic and antihistamine treatment. Delayed endolymphatichydrops following head trauma has been explained by a break in the endolymphatic sac with release of inner ear antigen provoking an autoimmune process (Harris et al, 1997; Dereby and Valenzuela, 1992). However, confirmation of an anticochlear antibody with a western blot is also needed. Antibodies has been demonstrated in 58.8% of bilateral meniere's disease, 37.5% of contralateral delayed endolymphatichydrops, and 33.3% of unilateral meniere's disease (Rauch et al, 1995) and specific anticochlear antibody has been reported positive in 30% of patients with meniere's disease (Gottschilch et al, 1997). Dereberryet al (1992) also reported elevated immune complexes in 96% suggesting an immunologic basis. Derebery & Belliner (2000) reported airborne and food allergies in 59.2% and 40.3% respectively of 734 cases of meniere's disease, these prevalence rates were significantly higher than those found in the control group with 42.7% and 25% of airborne and food allergies. Thus they concluded that the prevalence of allergy appears to be much higher in patients with meniere's disease than in the general population or the population of patients visiting an otologic clinic for other symptoms (Derebery & Belliner, 2000).

In conclusion, a high index of suspicion is important in management of immune – related inner ear disease, although search for a simple immunodiagnostic assays which will be readily available, easy to perform and sensitive should continue. This will aid in resolving the dilemma of commencing steroid therapy in the absence of laboratory confirmation of disease. The risk of complication of steroid therapy in a patient is weighed against leaving the patient with persistent hearing loss, at present; this may be resolved by counseling the patient and getting the consent.

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