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Past, present and future of a research line: A case report

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ABSTRACT

This is a synthesis of a Research Line we started back in 1982 and have pursued up to now and we think it should continue to develop. It started with one patient who came to us with a classic Menière's disease clinical presentation and also had severe headaches and drop attacks that many times resulted in traumatic lesions to his body. The daughter who brought him had exactly the same clinical picture except for the absence of drop attacks. We soon found three brothers with the same syndrome. All of them had severe headaches and low tones sensorineural hearing losses. We studied carefully this family and published our results. From then on, we asked two questions: what kind of headache was present in this family according to the International Headache Society (IHS) classification? How often this familial syndrome could be found among our patients? A few years later we found another big family whose index patient had a typical Menière's disease syndrome with severe headache and low tones sensorineural hearing loss.

Keywords: Syndrome, traumatic**,** clinical, sensorineural hearing loss.

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INTRODUCTION

Case Report

When we studied this family, we found that 3 sons of the index patient had typical migraine according to the HIS classification. Many other siblings had symptoms from migraine alone to full blown Menière's syndrome. To answer the second question, we started collecting patients with typical Menière's syndrome in our Otology Clinic and finding out about their family history. At 2 years end we had 8 patients with the full-blown syndrome and 6 of them had many siblings with symptoms going from migraine alone to full blown Menière's syndrome. Therefore Typical Menière's syndrome was not very frequent among us and the presence of family history in patients with Menière's syndrome was quite frequent. Next, we followed up for 12 years one large family in order to describe the natural history of the association of migraine and Menière's syndrome. Finally, we studied the molecular genetics of this family. At this point we have the chromosome and the probable exon where the gene for this disease is located. We do believe it is very worthwhile to keep, looking for the gene in the identified locus. All these families had an autosomal dominant mode of genetic transmission with variable penetrance. In this communication we describe in detail our findings and comment upon the relationship between Menière's disease and vertiginous migraine. This research line started up in 1992[1]. By that time, we saw a patient who was 69 years old and had a full blown Menière's syndrome: severe episodic rotatory vertigo with drop (falling) attacks, tinnitus and fluctuating hearing loss in his right year. These symptoms started up 5 years before we saw him. His drop attacks were severe and several times he hurt himself during falls. Right sided headaches usually preceded the crisis. Audiogram showed low tone sensorineural hearing loss bilateral and flat severe sensorineural hearing loss on the right ear. Left ear had hearing preserved in the frequencies above 500 Hz. (Figure 1) VDRL test was negative and glycerol test was positive bilaterally. An end lymphatic sac procedure was performed in his right ear and the drop attacks disappeared. Mild dizziness attacks and headache continued but were controlled on medication. Ten years later in June 2002 his hearing in

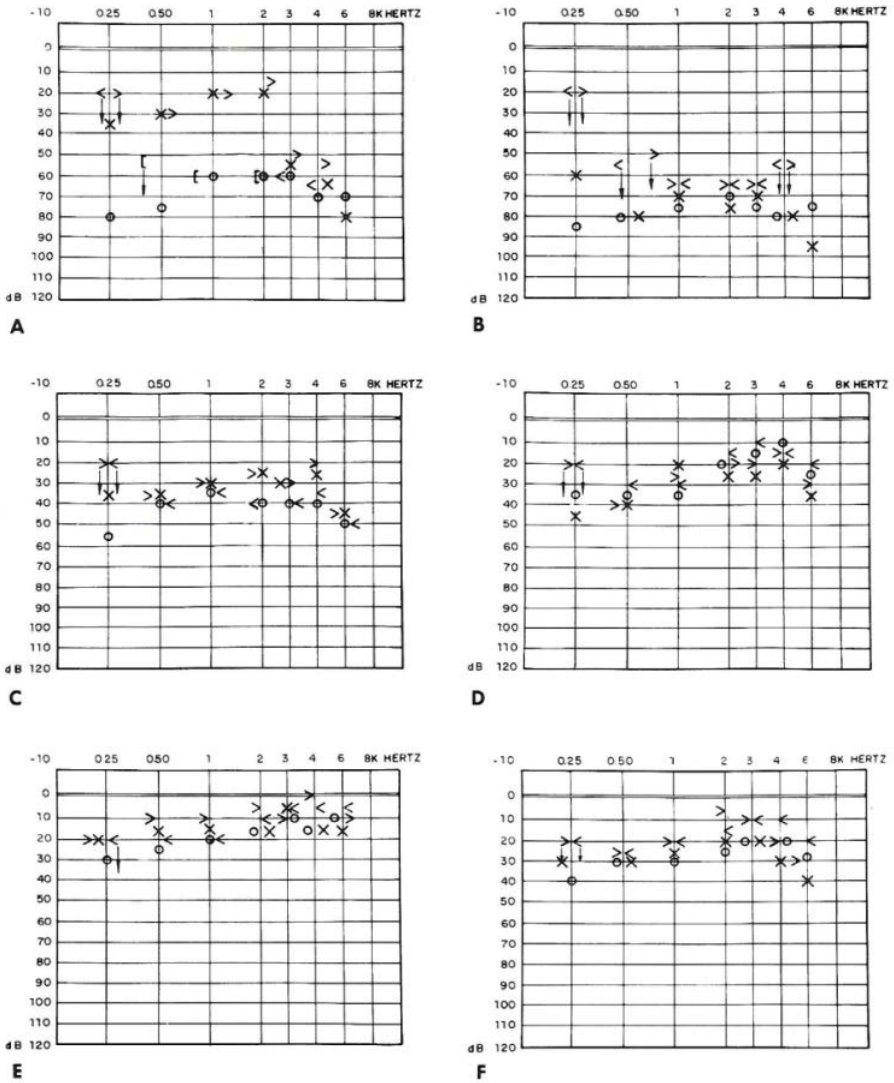

Figure 1: Graphs Showing the Left ear hearing preserved in the frequencies.

the right ear had worsened (Figure 1) considerably but the drop attacks had not come back and his dizziness was under control. His headache was unchanged. The heredogram of this family (Figure 2) shows that 6 of 7 sons and daughters of this man had the same complaints as their father and the audiograms on 4 available siblings showed low tone sensorineural hearing loss. One offspring of a second marriage of the index patients also had the same complaints. We did not give attention to the headache these patients complained about so we could not classify the headache properly. We found several reports of headache associated with both familial and sporadic Menière's syndrome[2-4] but the headache was not well characterized in any. Two questions were in our minds after we studied the family described above: How often a family history could be elicited from patients with classic Menière's syndrome What kind of headache was associated with Menière's syndrome We started to apply to all the Patients with Menière's syndrome seen in our Clinic a questionnaire with questions about the presence of similar symptoms in their family members as well as about the characteristics of the headache. Through this questionnaire we identified a large family who had typical Menière's syndrome present in some siblings, migraine and Menière's syndrome in others, and only migraine symptoms in others. Considering all siblings affected with these symptoms we arrived to the heredogram displayed in (Figure 3). The mode of genetic transmission was clearly autosomal dominant[5]. Of course, we knew that in every day clinic work we find more patients with incomplete than full blown Menière's syndrome. To consider patients with migraine only as affected siblings was an assumption that was supported by continuing the line of thought. The summary of all symptoms present on 19 affected members of the family is in (Table 1a and Table 1b). It can be seen there the spectrum of symptoms with some of them present and others absent in different patients. The index patient had full blown Menière's syndrome and fluctuating low tone sensorineural hearing loss (Figure 4). Three of his sons had intractable migraine who needed hospitalization for treatment sometimes but they lacked Menière's syndrome symptoms at that point. We concluded that there was a strong association between migraine and Menière's syndrome in this family and both seemed to be transmitted by a single gene in an autosomal dominant mode. From a physiopathologic

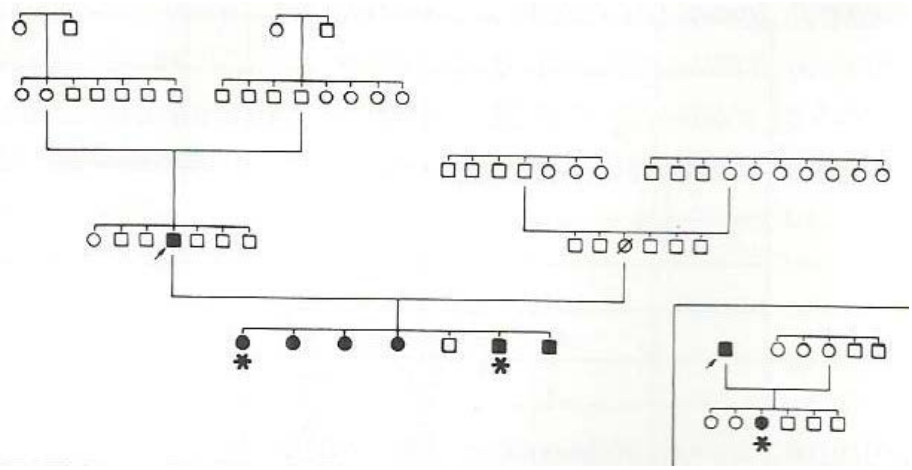

Figure 2: Showing 6 of 7 sons and daughters of Audiograms.

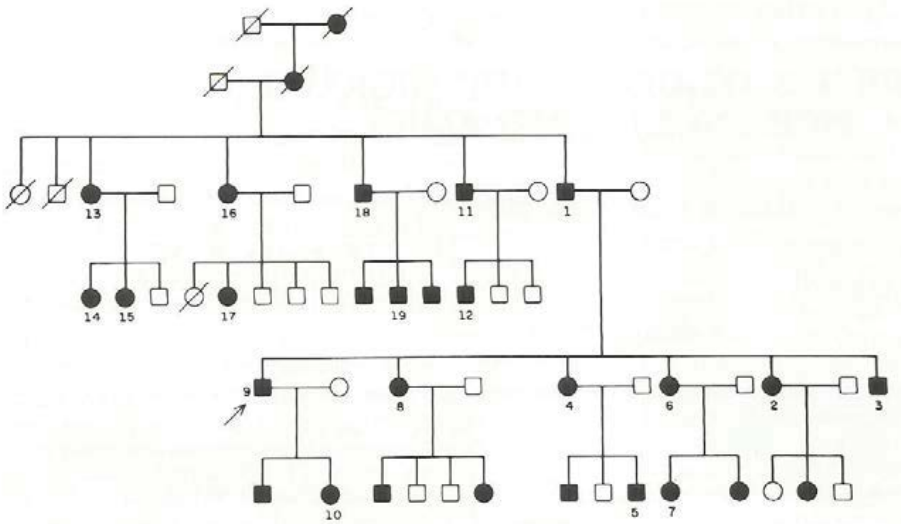

Figure 3: symptoms of the heredogram.

Table 1a: Summary of clinical, laboratory, audiometric, and electronystagmography findings in affected members of family studies.

Patient	Age	Sex	Tinnitus	Hearing	Vertigo	Headache	Vomiting	Nausea	Scotomas
1	50	M	+	+	+	+lt	+	+	+
2	46	F	+	+	+	4.*	+	+	+
3	17	M	—	—	—	+*	+	+	+
4	19	F	—	—	—	+*	+	+	+
5	56	F	+	—	+	+	—	+	+
6	58	M	+	+	+	4-*	+	+	+
7	15	F	+	—		4-*	+	+	+
8	77	M	+	+		—	+	+	—
9	51	M	+			-1-*	—	—	+
10	80	F	+	—	+	+	—	—	—
11	59	F	+	+	+	+*	—	+	+
12	75	M	+	+	+	+	+	+	+
13	45	M	—	—	—	+*	—	—	—

Table 1b: Summary of clinical, laboratory, audiometric, and electronystagmography findings in affected members of family studies.

Patient	Age	Variables	Blood Tests	Audiometry	Tympa-nometry	ENG
1	30	-	N	SNHL, bilateral, down-sloping	N	ND
2	10	Headache precedes vertigo	ND	ND	ND	ND
3	10	Variable	ND	ND	ND	ND
4	13	Migraine only for 17 years, MS only afterward	N	Mild SNHL, bilateral, 500 and 1,000 Hz	N	N
5	15	-	ND	Mild SNHL, bilateral, 500 and	ND	-
6	14	Headache precedes vertigo	N	Bilateral moderate SNHL, down-sloping	N	HL left side
7	10	-	ND	ND	N	N
8	9	Headache and scotomas precede vertigo	N	Mild SNHL, 500 and 1,000 Hz,	N	HL left side
9	39	Headache precedes vertigo	N	Bilateral moderate SNHL, down-sloping	N	HL left side
10	7	Headache precedes vertigo	ND	ND	ND	ND
11	18	-	ND	Bilateral moderate SNHL, down-sloping	N	HL left side
12	17	Migraine only for	ND	Bilateral moderate	N	HL
13	32	8 years, then MS only	-	SNHL, down-sloping	-	bilateral
14	30	Variable	N	Bilateral mixed hearing loss, worse on left	ND	HL bilateral
15	20	Variable	ND	ND	ND	ND
16	35	Variable	N	Mild SNHL, left	N	HL bilateral
17	21	Variable	ND	ND	ND	ND
18	43	Variable	ND	ND	ND	ND
19	15	Headache precedes vertigo	ND	ND	ND	ND

ENG — electronystagmography N — normal, SNHL — sensorineural hearing loss, ND — not done, MS — Meniere's syndrome, HL — hyperactive labyrinth.
*Headache was described by patient as typical migraine.

standpoint we don`t know how the migraine (central) relates to the Menière's symptoms (peripheral). Now we had a hypothesis: migraine and Menière's syndrome are related and transmitted in an autosomal dominant mode. To further this hypothesis, we set up to answer two questions i,e How often is the occurrence of familial Migraine-Menière's syndrome in our population How is the evolution of these symptoms as time goes by In

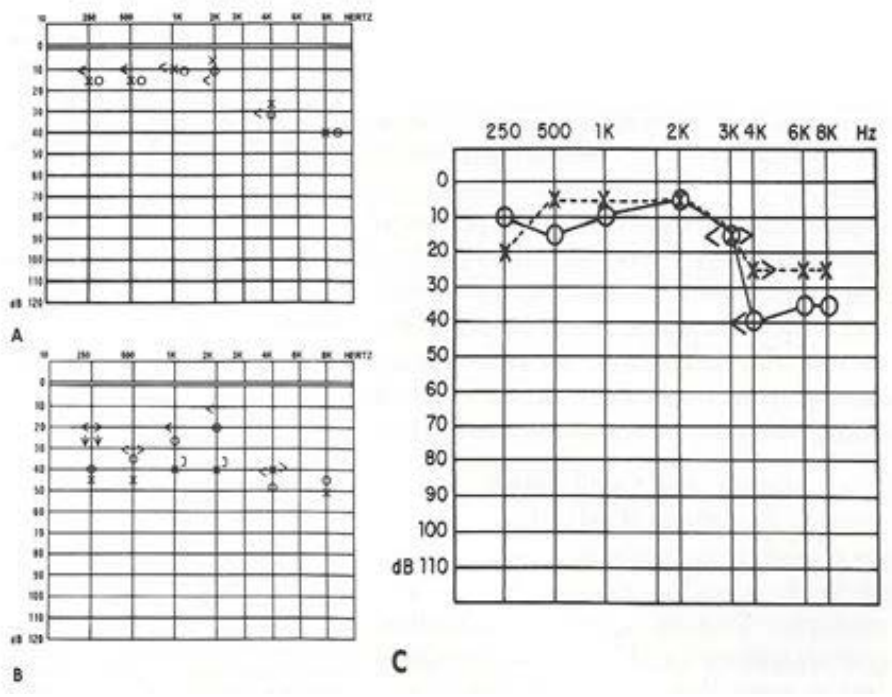

Figure 4: Menière's syndrome and fluctuating low tone sensorineural hearing loss.

other words: what is the Natural History of this symptoms complex We then started to apply a questionnaire inquiring about the family history of every patient with typical Menière's syndrome seen in our Otology Clinic prospectively beginning in January 1997 and finishing in December 1998. All index patients were required to have typical Menière's syndrome according to the American Academy of Otolaryngology-Head and Neck Surgery criteria. The work up included audiometry, tympanometry, vectoeletronystagmography and a glycerol test in order to seal the diagnosis of idiopathic typical Menière's syndrome (Menière's disease). At this point the included patients were questioned about Migraine symptoms. Next the Questionnaire about their family history regarding Menière's and Migraine's symptoms present in other family members was applied. It is worth to mention that any symptom of one of these syndromes were noted and used to construct the heredogram of each family. Every available affected member of these families went through the same work up as the index patients. Eight patients with typical, complete Menière's syndrome were collected in 2 years from our otology clinic in Brasília. Six of the 8 had positive family history for Menière's and/or Migraine. Table 2 shows that only one index patient had low tone sensorineural hearing loss. All others displayed high tone sensorineural hearing loss in between crisis. Table 3 shows the presence/absence of Menière's and Migraine symptoms in the affected members as well as demographic data. Age of the index patients varied from 26 to 63 years old. Symptoms appeared between 15 and 40 years. Six patients had unilateral symptoms and two had both ears affected. Most of the time migraine occurred before the vestibular symptoms, sometimes it came after the vestibular crisis and a minority had migraine unrelated to the vertiginous attack. In 6 of the 8 index patient's headache fit the classification of the

Table 2: Summary of audiometric findings in eight probands.

S. No.	Proband Age (y)	Sex	Audiometry
1	62	M	Bilateral moderate SNHL, down-sloping on R, flat on L
2	43	F	Bilateral downsloping SNHL, moderate on R, severe on L
3	30	F	Normal
4	46	F	Normal
5	43	F	Flat moderate SNHL on R, normal on L
6	26	F	Normal
7	45	M	Bilateral moderate SNHL low and high tones, worse on L, middle tones normal
8	35	F	Moderate low-tone SNHL on L, normal on R

Speech discrimination score was compatible with pure tone loss in all patients.
SNHL — sensorineural hearing loss.

Table 3: Summary of clinical, audiometric, and findings in affected members of six families.

Affected Family Probands Members		Age (y)	Sex	Aural Tinnitus	Aural Fullness	Fluctuating Hearing Loss	Vertigo	Nausea	Vomiting	Audiom-etry	VENG	Scotoma	Photo-phobia	Atypical Head-ache	Hemi-cranial Head-ache	Pulsatile Head-ache
111-5		30	F	+	+	+	+	+	+	N	PIS R	+	+	-	+	+
(Family 3)	I -2	Deceased	F	+	+	+	+	+	-	ND	ND	+	+		+	+
-	11-2	60	F	-	-	-	-	+	-	ND	ND	+	+		+	+
-	111-6	16	F	+		+	+		-	SNHL bilat	PIS R	+	+	-	+	+
-	111-8	37	F	-	-	-	-	+	-	ND	ND	-	+	-	+	+
-	IV-1	10	M	+	+	+	+			N	N	-	-		-	-
I11-2		46	F	+	+	+	+	+	+	N	PIS R	-	-	+		-
(Family 4)	11-2	60	F	+			+			N	N	-	+	-	+	
-	11-3	58	F	+			+			N	N	+			+	+
-	II-4	65	F	+	+		+	+	+	N	PIS L	-	+	-	+	+
-	111-3	43	F	-	-	-	+	-	-	N	PIS bilat	+	+	-	+	+
-	111-7	33	F							ND	ND	-	+		+	+
-	111-8	32	F						+	ND	ND	-	+	-	-	
	1V-1	25	F				+	+		ND	ND	-	-	-	-	-
III-5-		43	F	+	+	+	+	+	+	SNHL R	ND	+		-	+	+
(Family 5)	111-4	46	F	+			+			N	N			+		-
	IV-3	14	F	+	-			-	-	N	N	-		-		
III-6		26	F	+	+	+	+	+	+	N	PIS bilat	+	+	-	+	+
(Family 6)	11-5	75	M	+			+	+	+	SNHL L	N	-	+	-	+	+
	111-8	32	F	+	-	-	+	-		ND	ND	-	+		+	+
	11-4	65	F	-	-	-	-	+	-	ND	ND	-	+	-	+	+
	111-2	46	M							ND	ND	-	+		-	-
	111-6	36	F	-	-	-	+	+	-	ND	ND	-	+	-	+	+
	II-1	40	F	-		-	-	+	-	ND	ND	+	+	-	+	-
	II-2	50	F	-	-	-	-	-	-	ND	ND	+	-	-	+	+
	11-4	52	F	-	-	-	-	+	+	ND	ND	-	+	-	+	+
11-22		45	M	+	+	+	+	+	+	SNHL L	N	-	-	-		
(Family 7)	11-13	62	M	+	+	-	+	+	-	SNH bilat	ND	+			+	+
	11-18	58	M	-	-	+	+	-	-	SNHL bilat	ND					-
	11-17	56	F	+	-	+	-	-	-	SNHL. bilat	ND	+		+	+	+
	111-4	20	F	+	+	+	-	-	-	ND	ND	-	+	-	+	+
	111-5	12	F	-	-	-	-	-	-	N	N	-	+	-	+	+
111-5		35	F	+	+	+	+	+	+	N	PIS bilat	+	+	-	+	+
(Family 8)	11-5	54	F	+	-	+	-	+	-	ND	ND	+	+	-	+	+
	II-1	50	F	-	-	-	+	+	-	ND	ND	-	-	-	+	+

Tympanometric and stapedial reflex results were normal in all patients who had them done. Proband 1 had full-blown Meniere's syndrome and atypical headache. Proband 2 had both Meniere's and migraine symptoms.
VENG — vectoelectronystagmography, N — normal, PIS — peripheral irritative syndrome, ND — not done.

International Headache Society of 1988 as Migraine. There were 6 female and 2 male probands[6]. Figures 5-7 show heredograms of the 6 affected families. It is clear from them that the pattern of genetic transmission is autosomal dominant and there is great variability with some siblings having typical Menière's disease and Migraine, others having Migraine alone and others having symptoms of Menière`s syndrome incomplete with or without Migraine. If we assume monogic causation then variable penetrance of the gene is probably the cause of this variability. From these data we reasoned that typical Menière's syndrome is not very frequent in Brasília during two years in a very buzzy Otology Clinic we collected only 8 cases.

On the other hand, the occurrence of familial disease in patients with typical Menière's syndrome (Menière's disease) is quite high (Six of 8 index patients). If we consider Menière's syndrome all the spectrum of symptoms seen in these families then the disease is not so infrequent (Table 4). In other words, we see incomplete Menière's syndrome much more often in our clinics than the typical syndrome. However, Migraine can be associated with all the Menière spectrum of symptoms. We wanted to ask: What happens to this spectrum of symptoms as time goes by the family we published in 1997[5-7] lived in Brasília and we were able to follow them up from 1995 on for 10 years. The following paragraphs will refer to unpublished data from our group. All affected and unaffected siblings in the heredogram in (Figure 3) were carefully interviewed along the ten years follow up. Twenty siblings had no qualitative changes in symptoms from 1995 to 2005. Four had changed from atypical headache in 1995 to typical migraine 10 years later. Two had migraine in

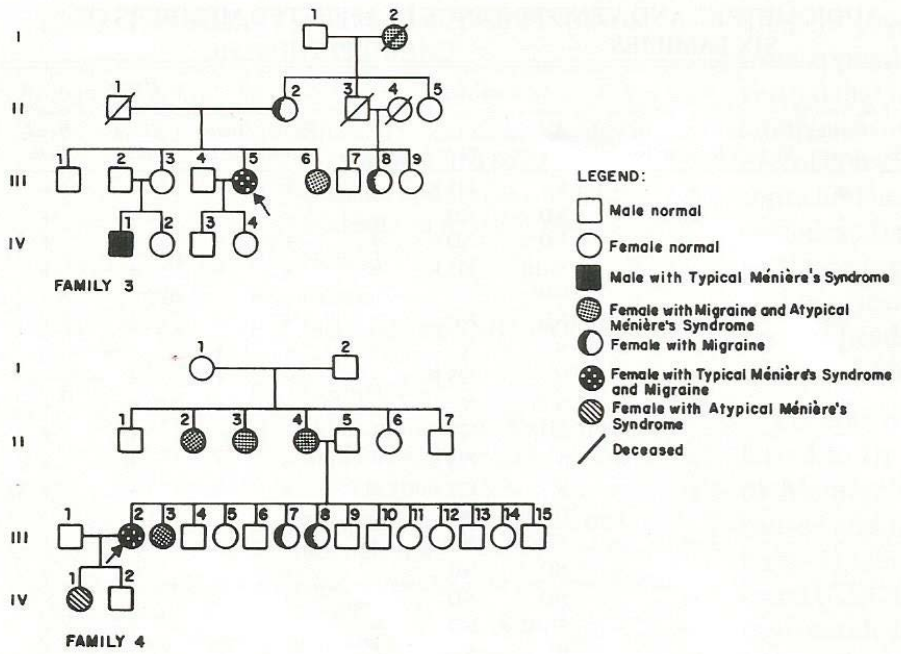

Figure 5: Heredograms of the affected families.

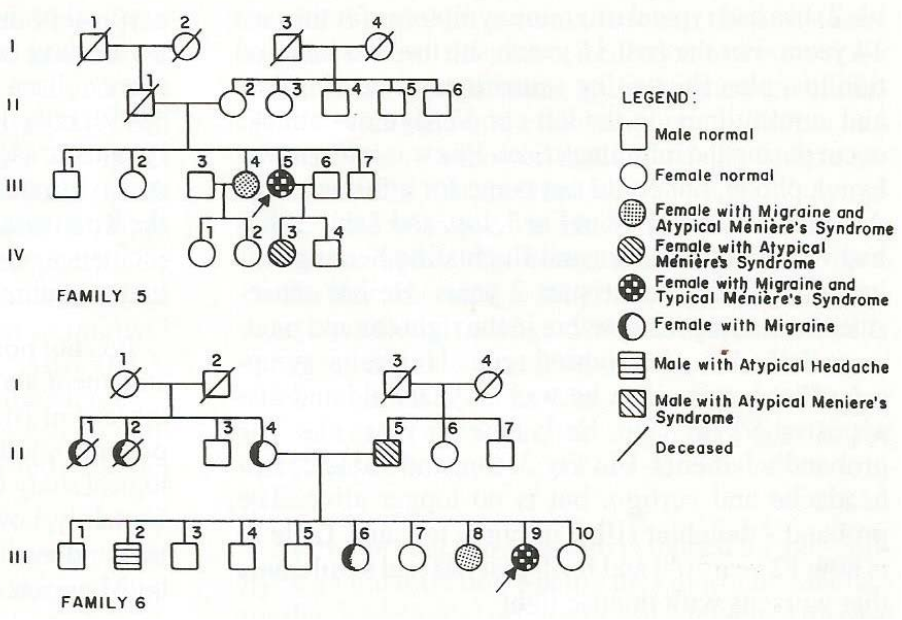

Figure 6: Heredograms of the affected families.

1995 and progressed to Menière's syndrome in 2005. Four siblings had vertigo and atypical headache in 1995 and progressed to vertigo and typical migraine in 2005. Five unaffected siblings in 1995 had symptoms of the Migraine-Menière's complex 10 years later two with aural fullness, one with migraine, tinnitus, vertigo and hearing loss and two with migraine and vertigo. Three affected siblings had remarkable improvement in migraine and vertigo or complete remission of the symptoms. Fifteen of the 38 affected siblings started out with migraine and the vestibular symptoms appeared in average 17.6 years later. Seven siblings continued with migraine only after 10 years follow up. Over time the intensity and periodicity of the migraine symptoms tended to diminish and the vestibular symptoms tended to become more frequent and intense. (Table 5, Figure 8) Hearing loss worsened in most patients. The loss was in high frequency tones and bilateral (Table 6). We were not able to document low tone fluctuating sensorineural hearing loss during the crisis of vertigo/migraine in all siblings but we did document this feature clearly in the index patient. (Figure 4) Now we had the natural history of this complex of symptoms described. We were therefore able to organize the clinical data in order to define a phenotype of this syndrome in the large family from Brasília. Our hypothesis was that this was a genetically determined symptoms complex and the genetic transmission was monogenic with incomplete penetrance. Next step was to try to find the locus for

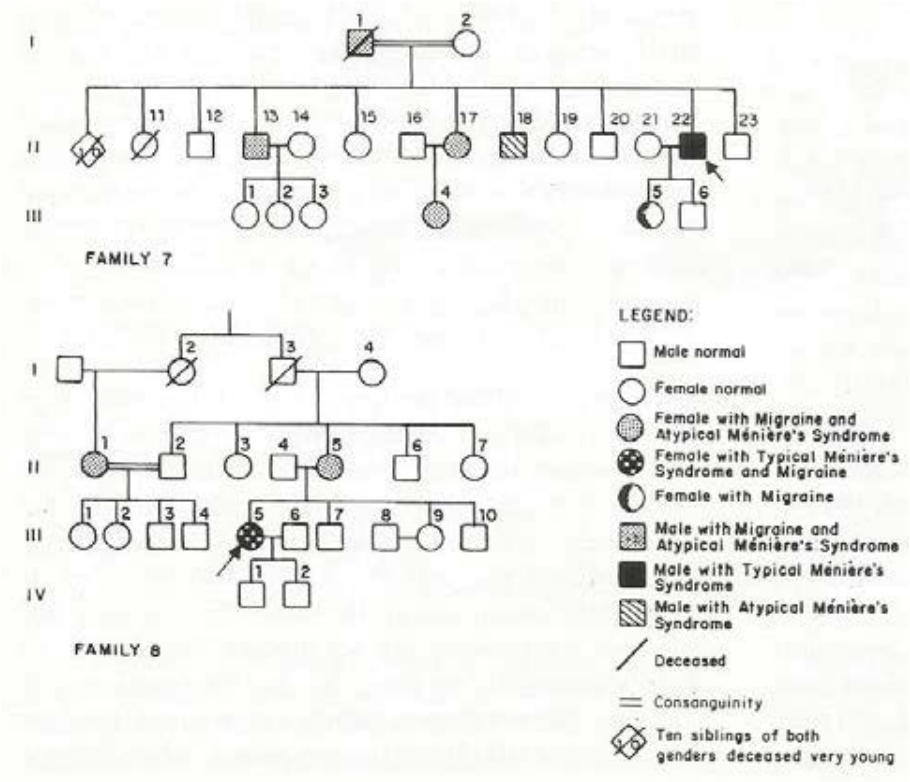

Figure 7: Heredograms of the affected families.

Table 4: Natural history of migraine and vestibular simptoms during 10 years follow-up (n=23 affected siblings).

Patient	Age at the moment	Periodicity* -1995		Periodicity* -2005		Intensity -1995		Intensity -2005	
		Migraine	Menière	Migraine **	Menière	Migraine **	Menière	Migraine	Menière
1	81y	2/w	1/w	1/w	1/w	09-Oct	Moderate	06-Oct	Severe
2	90y	-	-	-	-	-	-	-	-
3	82 y	2/w	2/m	2/m	1/w	08-Oct	Moderate	06-Oct	Severe
4	87y	1/w	1/m	1/m	1/w	06-Oct	Moderate	06-Oct	Severe
5	92y	1/w	1/w	2/m	2/w	09-Oct	Severe	09-Oct	Severe
11	62y	2/m	-	2/m	1/m	08-Oct	-	07-Oct	Severe
12	58y	2/m	-	2/m	-	07-Oct	-	06-Oct	-
21	69y	1/m	1/m	1/m	2/m	08-Oct	Moderate	05-Oct	Moderate
31	61y	1/m	1/m	1/m	2/m	09-Oct	Moderate	06-Oct	Moderate
32	64y	3-4/m	-	2/m	-	09-Oct	-	06-Oct	-
33	63y	1/m	-	1/m	-	10-Oct	-	06-Oct	-
41	61y	2/w	1/w	2/m	2/w	09-Oct	Moderate	07-Oct	Severe
51	68y	1/m	1/m	1/m	2/m	09-Oct	Severe	08-Oct	Severe
52	66y	1/m	-	1/m	-	08-Oct	-	08-Oct	-
53	54y	1/m	2/y	1/m	4/y	07-Oct	Moderate	07-Oct	Severe
54	51y	2/y	3/y	2/y	1/m	08-Oct	Moderate	08-Oct	Moderate
55	51y	3/y	1/y	3/y	3/y	08-Oct	Moderate	06-Oct	Moderate
56	60y	1/m	2/y	1/m	1/m	09-Oct	Moderate	08-Oct	Moderate
512	37y	6/y	1/y	2/m	4/y	08-Oct	Moderate	08-Oct	Moderate
524	37y	1/m	-	1/m	-	08-Oct	-	08-Oct	-
531	32y	3/y	-	3/y	-	07-Oct	-	07-Oct	-
533	25y	3/y	-	3/y	-	07-Oct	-	07-Oct	-
541	29y	4/y	1/y	1/m	4/y	08-Oct	Moderate	08-Oct	Moderate

the gene. Because we were not able to document low tone sensorineural hearing loss in most of the siblings and the high frequency sensorineural hearing loss was bilateral in the majority of them the clinical diagnosis of Vertiginous Mograine (VM) was adopted for these patients. The fact that some of them had typical Menière's syndrome including low tone sensorineural hearing loss was however pointed out in the final paper[7]. Twenty-three

Table 5: Hearing during 10 years follow-up (n=19).

Patient	Audiogram Result	Audiogram Result
1	Moderate to Profound Mixed Hearing Loss	Profound Mixed Hearing Loss Bilaterally
2	Mild High Freq. SNHL	Mild to Moderate High Freq. SNHL
3	Moderate High Freq. SNHL	Moderate High Freq. SNHL
4	Moderate Mixed Hearing Loss Bilaterally	Moderate Mixed Hearing Loss Bilaterally
5	Moderate High Frequency SNHL Bilaterally	Moderate to Severe High Frequency SNHL Bilaterally
6	Normal	Normal
7	Normal	Normal
8	Normal	Mild High Frequency SNHL Bilaterally
9	Mild High Freq. SNHL	Mild to Moderate High Frequency SNHL Bilaterally
10	Mild High Frequency SNHL Bilaterally	Mild to Moderate High Frequency SNHL Bilaterally
11	Mild High Frequency SNHL Bilaterally	Mild to Moderate High Frequency SNHL Bilaterally
12	Moderate High Freq. SNHL	Profound High Frequency SNHL Bilaterally
13	Normal	Mild High Frequency SNHL Bilaterally

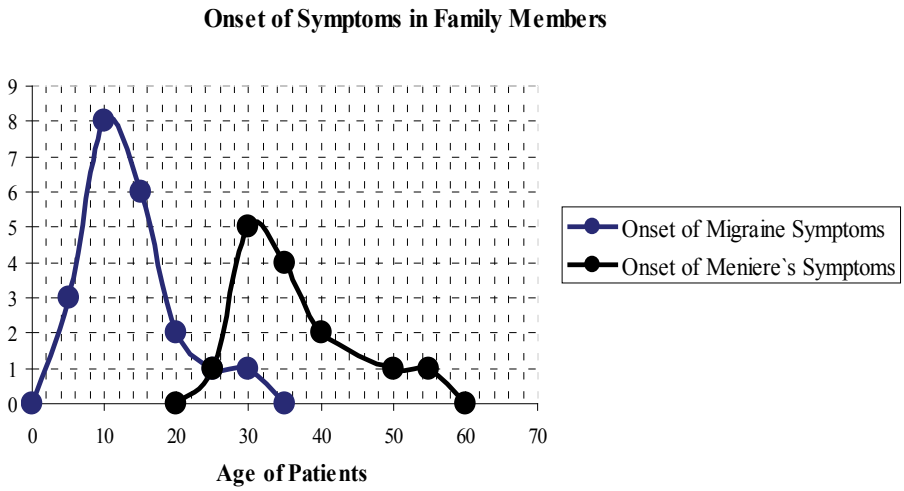

Figure 8: Showing the symptoms tended to diminish and the vestibular symptoms.

family members who were clinically and audiologically evaluated and had image studies also done had genome wide linkage analysis performed with Affymetrix Gene chip Human Mapping 10K microarrays. Genotyping of family members DNA with microsatellite markers was used to further assess candidate loci identified from the whole genome scan. The results of vestibular testing and imaging studies were unremarkable. The genetic analysis defined a 12.0MB interval on chromosome 5q35 between loci rs2448795 and D5S2073 that contained the disease gene (logarithm of odd score 4.21). Molecular genetics studies were performed at the Molecular Genetics laboratory of Harvard Medical School headed by Professor Jonathan Seidman.

RESULTS

Here we will blend our results with the current literature on the subject and formulate a new hypothesis. It is important to acknowledge the recently described Vertiginous Migraine (VM) syndrome[8] which is now listed in the Barany Society and the International Headache Society classification of vestibular diseases[9]. This entity is very frequent, second only to benign paroxistic positional vertigo being probably present in 1% of the general population[8]. We are not going to describe in detail the VM symptoms but it is important to point out the differences between Menière's syndrome and VM. One marked difference is the absence of hearing loss that fluctuates in the low frequencies in the beginning and that progress to severe hearing loss along the life in Menière's disease but not in Vertiginous Migraine. Bilaterally of the symptoms seems to be more frequent in familial Menière's syndrome and Vertiginous migraine but it is not different between these two syndromes. There is a significant body of literature dealing with the interfaces of Meniére's Disease (DM) and VM. We will review briefly some papers on this subject. Neuhauser[10] prospectively evaluated Migraine in 200 patients from a dizziness clinic and 200 ones from a migraine clinic. Prevalence of migraine that satisfied the criteria of the International Headache Society(HIS) II was 38% in the dizziness clinic and 24% in sex and age matched controls ($p<0.01$). Vertiginous Migraine was present in 7% of patients in the dizziness clinic and 9% of the ones in the migraine clinic. In 15 of 32 patients's vertigo was always associated with migraine during the acute attacks. In 16 patients this association was sporadic and 2 patients never had both symptoms together. Radke et al.[11] studied 78 patients (40 male and 38 female) aged 29 to 81 years all with idiopathic uni or bilateral Menière's disease according to the AAO-HNS criteria. Lifetime

prevalence of migraine with and without aura was 50% among these patients and 25% among normal control patients ($p<0.001$). Furthermore 45% or the Menière's disease patients always experienced at least one migraine symptom (headache, photophobia, aura) during the acute attacks. They postulated a pathophysiologic link between migraine and MD. Urkur et al.[12] studied VEMPs parameters in VM, MD and migraine patients and found very similar results for all these patients. Gazques et al.[13] published a paper on recent advances in the genetics of recurrent vertigo including familiar episodic ataxias and MD. They found that 20% of MD patients have positive family histories for this disease. Cha et al.[14] described 6 families with index patients affected by MD and migraine. There were 56 affected siblings. Of these 26(41%) met the HIS criteria for migraine. Fifty per cent had migraine with aura. Three patients had typical aura without headache. Sixty-three family members had recurrent spells of spontaneous vertigo. There were 3 twin pairs 2 mono and 1 dizygotic. One of the homozygotic pair had migraine and Menière's syndrome while the other one had migraine and episodic vertigo without auditory involvement. (VM). Bertora and Bergman[15] using quantitative EEG (qEEG) studied 120 patients with MD and migraine and 85 patients with MD and no migraine. Eighty-five per cent of MDs patients had hemodynamic brain variations like the ones found in migraine. Brain electric depolarization's and cortical irrelative focuses are common to migraine and MD. However, MDs patients had important hyperactivity in the limbic lobe.

DISCUSSION

From this brief review of literature, we can see:

- VM and MD are very often present in one single family and therefore have a common-genetic link.
- Hearing involvement in MD and not in VM is the main clinical difference between these two syndromes.
- Migraine is present in both syndromes.

Recently Welfang et al.[16] selected 30 classic MD patients and 30 patients with definite or probable VM matched by age and sex. Three-dimensional real inversion recovery magnetic resonance (3D real IR) was performed in these patients 24 hours after intratympanic gadolinium injection in order to assess Endolymphatic Hydrops (EH). Response rates, amplitudes, latency and response thresholds of cervical and ocular evoked myogenic potentials (c/o VEMP) were tested using air conducted sound. Pure tone audiometry was used to evaluate the level of hearing loss. Different degrees of EH were observed in the cochlea and vestibule of MD patients. Some VM patients had 3D real IR suspicious for cochlea EH and no EH were found in the vestibule of these patients. There was statistically significant correlation between EH and low tone sensorineural hearing loss. Response thresholds for c/oVEMP were no different in VM and MD patients. Therefore, low frequencies sensorineural hearing loss correlate with EH on MD patients 3R-real IR showed more severe degrees of EH in patients with MD but suggestion of EH in the cochlea of VM patients was showed. MD and VM patients behaved similarly in vestibular dysfunction and their transduction pathway. These results suggest a common pathophysiology for MD and VM and that VM may progress to MD as time goes by if EH develops in VM patients[17].

CONCLUSION

At this point we know that the spectrum of symptoms that goes from migraine alone to migraine with full blown MD including Vertigo and Migraine (VM), vertigo alone (atypical Menière's syndrome) has high familial incidence and is genetically transmitted in a monogenic autosomal dominant mode[6]. We have found that the locus for this spectrum of symptoms maps to chromosome 5q35[7]. Studies using VEMP[14] and 3D real IR[15] have shown that EH is present in different degrees in both MD and VM. It may be that absence of low tone sensorineural hearing loss in VM relates to the very small degree of EH present in this entity compared to MD. Based on all this evidence we have up to now we believe that future efforts should be directed to isolate the gene in chromosome 5q35 and follow up longitudinally patients with VM with VEMP and 3D real Ir MRI to test the hypothesis that VM and MD are different stages of the same process. Sporadic MD and VM should be tested for the presence of the gene we are looking for after we have it isolated. Then we might also have a better idea about the etiology of MD and VM. Probably environmental factors[17] will be also important for the full development of the disease (multifactorial etiology). We do believe that this research line should be taken to its future.

CONFLICT OF INTEREST

The Author declares no potential conflict of interest on publishing this paper.

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