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Incidence of intralabyrinthine schwannoma: A population-based study within the United States

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Abstract

Objective—To describe the incidence of intralabyrinthine schwannoma (ILS) utilizing the Rochester Epidemiology Project (REP), a unique medical consortium in the United States that covers a complete population of all ages in a well-defined geographic area over the past half-century.

Patients—All patients with ILS diagnosed between 1/1/1966 and 12/31/2016 in Olmsted County, Minnesota, identified using the REP medical records-linkage system.

Main Outcome Measures—Incidence of ILS.

Results—Fourteen incident cases of ILS were identified in Olmsted County since 1966 – a period spanning 5.9 million person-years. Over the past decade, the incidence rate of ILS was 0.81 per 100,000 person-years and 1.1 over the last five years. Since 1966, the cumulative incidence rate of ILS over the past 50 years was 0.26 per 100,000 person-years. The median age at diagnosis was 60 years (*IQR*, 39–70). Incidence increased with age: over the last five years, those aged 60–69 exhibited an incidence rate of 2.7 per 100,000 person-years and those 70+ displayed a rate of 4.1. All cases had varying levels of asymmetrical sensorineural hearing loss with 64% of patients presenting with class D hearing. Four (29%) patients had a history of sudden sensorineural hearing loss, 5 (36%) reported imbalance and/or vertigo, and 4 (29%) reported aural fullness. Three of the 14 (21%) patients had neurofibromatosis type 2.

Conclusions—The incidence of ILS exceeds 1 per 100,000 person-years with modern diagnostic imaging. The rising incidence of ILS in recent years most likely reflects improved capacity for disease detection rather than a true growth in sporadic cases. Given the reputability of

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The currently submitted manuscript represents original research that has not been previously submitted and is not under consideration for publication elsewhere. The associated abstract was submitted for poster presentation at the 2018 AAO-HNS meeting. We performed this research with approval from the Mayo Clinic and Olmsted County Medical Center Institutional Review Boards (IRB 15-006036 and 050-OMC-15, respectively).

the REP consortium, these data suggest that ILS comprises a more common entity than previously considered.

Keywords

cochlear schwannoma; intralabyrinthine schwannoma; primary inner ear schwannoma; vestibular schwannoma; acoustic neuroma; epidemiology; incidence; Rochester Epidemiology Project

INTRODUCTION

Primary intralabyrinthine schwannomas (ILS) arise from progenitor Schwann cells of the distal portion of the eighth cranial nerve within the cochlea, vestibule, or semicircular canals.(1) Initially described in 1917 by Mayer,(2) ILS was historically diagnosed incidentally at autopsy or during otologic surgery for other indications such as Ménière's disease.(3) More recently, the advent of modern diagnostic imaging capabilities, such as thinly-sliced contrast-enhanced magnetic resonance imaging (MRI), has enabled preoperative diagnosis of ILS while evaluating for retrocochlear pathology in the setting of asymmetrical sensorineural hearing loss.(4,5) Nevertheless, the literature suggests that ILS remains extremely rare – a recent systematic review identified only 234 cases reported between 1933 and 2011.(6) As a consequence of this rarity, no population-based studies exist surrounding the epidemiology of ILS.

First established in 1966, the Rochester Epidemiology Project (REP) comprises a unique medical records-linkage system that covers a complete population in a well-defined geographic area over the past half-century.(7) The primary objective of this study was to characterize the incidence of ILS in Olmsted County, Minnesota over this extended period of time using the REP medical records-linkage system.

METHODS

Patient Data and the Rochester Epidemiology Project

After obtaining institutional review board approval (IRB 15-006036 and 050-OMC-15), a retrospective review was performed of all residents of Olmsted County, Minnesota who were diagnosed with primary ILS between January 1, 1966 and December 31, 2016 using the infrastructure provided by the REP medical records-linkage system. Cases of vestibular schwannoma (VS) that invaded the labyrinth were excluded. Patients with ILS were identified through a diagnostic code search, and all cases, residency status, and research authorization were confirmed upon medical record review. Hearing data were reported in accordance with the American Academy of Otolaryngology–Head and Neck Surgery committee guidelines.(8) Tumor classification was performed in accordance with the modified Kennedy system.(6,9) Several studies have validated the accuracy and exhaustibility of the REP consortium.(10,11)

Statistical Methods

Continuous features were summarized with medians and interquartile ranges (IQRs); categorical features were summarized with frequency counts and percentages. Incidence

rates per 100,000 person-years were calculated using incident cases of primary ILS as the numerator and age- and sex-specific counts of the population of Olmsted County, Minnesota as the denominator. The denominators were obtained from a complete enumeration of the Olmsted County population.⁽¹²⁾ Incidence rates were age- and sex-adjusted to the structure of the 2000 United States population.

RESULTS

Patient Characteristics, Presenting Symptomatology, and Tumor Classification

Fourteen incident cases of ILS were identified over a period that spanned 5.9 million person-years. For context, the number of residents and thus number of people at risk for the development of ILS in Olmsted County was 148,201 in 2010. The presenting characteristics, symptomatology, and tumor classification at diagnosis are presented in Table 1 and Figure 1. All cases had varying levels of asymmetrical sensorineural hearing loss with 64% of patients presenting with class D hearing. Four (29%) patients had a history of sudden sensorineural hearing loss, 5 (36%) reported imbalance and/or vertigo, and 4 (29%) reported aural fullness. Intracochlear ILS was the most common classification, and 75% of these (71% of all tumors) involved the basal turn of the cochlea. Three of the 14 (21%) patients had neurofibromatosis type 2 (NF2). One patient (7%) with NF2 exhibited sufficient tumor growth to require treatment, and this was pursued using stereotactic radiosurgery when treating a distinctly separate synchronous ipsilateral vestibular schwannoma. The median time delay from onset of symptoms to diagnosis was 5 months (*IQR*, 5–120).

Incidence of Intralabyrinthine Schwannoma Over the Past 50 years

Despite covering 50 years of population data, the first case of ILS was not diagnosed in Olmsted County until 2006; no cases were incidentally diagnosed at autopsy or during otologic surgery for other indications. Since 2006, the incidence rate of ILS was 0.81 per 100,000 person-years (Table 2). Over the past five years, the incidence rate was 1.1 per 100,000 person-years. Taken since 1966, the cumulative incidence rate of ILS over the past 50 years in Olmsted County was 0.26 per 100,000 person-years. The incidence rate of ILS increased with age: the incidence rate over the past five years for individuals aged 60–69 was 2.7 per 100,000 person-years and 4.1 for individuals 70 years and older (Table 3).

DISCUSSION

The rarity of ILS has previously precluded research into its epidemiology. This study was envisioned to determine the incidence of ILS over the past half-century in Olmsted County, Minnesota using the REP medical records-linkage system and found that the incidence rate over the past five years exceeded 1 per 100,000 person-years. The observed incidence rate has increased over the past decade. This finding is most likely secondary to an increased detection rate of ILS stemming from heightened provider awareness and increased utilization of advanced diagnostic imaging modalities rather than an increase in the true incidence of ILS. Next, despite all patients being diagnosed in an era with MRI, the vast majority of patients still presented with class D hearing at a median time delay to diagnosis from the onset of symptoms of almost 5 years. In this population-based cohort, patients most

commonly presented with intracochlear ILS that arose from the basal turn of the cochlea, and only one patient exhibited sufficient tumor growth to require treatment.

Although a recent systematic review identified only 234 reported cases between 1933 and 2011, the incidence of ILS among residents of Olmsted County indicates that ILS affects more individuals than past literature would suggest. To more intuitively understand the estimated incidence of ILS in the current study, these results can be compared with two recent publications that determined the modern incidence of VS in the United States to be 1.1 per 100,000 person-years.(13,14) In a separate study using the REP medical records-linkage system, we found that the incidence rate of sporadic VS from 2012 through 2016 was 4.5 per 100,000 person-years compared to 1.1 for ILS.(15) Taken together, these data acquired using modern diagnostic imaging demonstrate that VS has an incidence rate of only four times greater than ILS.

Contextualizing the observed incidence rates of ILS, it should be noted that there are several demographic characteristics of Olmsted County that render it a unique population of study, particularly in the setting of a pathology such as ILS. First, a recent report found that Rochester, Minnesota possessed the second highest ratio of neurotologists per population in the United States.(16) This finding is uniquely relevant to the detection of ILS when existing pathology can be easily overlooked due to its rarity and often subtle radiologic findings. Indeed, in the authors' experience it is not uncommon that an ILS is identified on secondary review of a scan initially performed elsewhere for sudden or asymmetrical SNHL, after initially being interpreted as normal. Next, Olmsted County's economy is largely driven by healthcare. According to the 2015 American Community Survey of Olmsted County performed by the United States Census, almost 40% of the workforce works in healthcare and social assistance – in contrast, this industry only represents roughly 10% of the national workforce. This demographical feature undoubtedly influences overall health literacy of the population. Further, the healthcare-driven economy facilitates easy access to medical care and thus advanced diagnostic imaging. This claim is substantiated by a study that showed 93% of residents are seen at least once within three years in Olmsted County.(11) The combination of these characteristics likely influenced the high detection rate of ILS that was observed in the present study.

Next, the observed symptomatology within this population-based study parallels past research investigating ILS. For instance, the majority of patients (57%) in this study were found to have intracochlear ILS, most of which arose from the basal turn of the cochlea. This coincides with a past review that found 51% of ILS was intracochlear with the basal turn being most commonly involved. Moreover, the median delay to diagnosis was similar in our study (4.5 years) compared to this review (5 years).(6) However, the present study found that the median age at diagnosis was 60 years – 11 years older than past research suggests. (6) In addition, only 64% of patients in our cohort displayed class D hearing, which contrasts to past research that found 87% of cases present with class D hearing.(1) Interestingly, all patients who presented with vertiginous symptoms possessed tumors that originated within the cochlea and did not extend to the vestibule. This also contrasts past research that suggests only up to 26% of cases display vertiginous symptoms with ILS

confined to the cochlea.(1) Nevertheless, the sample size of the current study limits direct comparisons of these differing rates surrounding presenting symptoms.

There are limitations to the present study. First, cases of ILS were identified through a diagnostic code search. Given inherent limitations to diagnostic coding, it is possible that not every case of ILS was reviewed. Since only 14 incident cases were identified in this study, underinclusion could acutely influence the calculation of incidence rates resulting in an underestimate of the incidence of ILS in Olmsted County. Notwithstanding, the REP consortium has supported over 2,500 publications to-date and several studies have validated its accuracy.(7) For instance, one study found that the rate of underinclusion of at least one medical record in a given patient's chart approximated only 1.3%. (12) Further, the calculation of incidence rates themselves is unaffected by sample size.

CONCLUSION

The incidence of ILS exceeded 1 per 100,000 person-years over the last five years. The incidence rate increased with age, with those aged 70 years and older displaying the highest incidence rate at 4.1 per 100,000 person years. The combination of a high neurotologist to patient ratio, patients' ease-of-access to medical care in Olmsted County, and the comprehensive REP system likely contributed to the high detection rate of ILS in this study.

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a

b

Figure 1.

Magnetic resonance imaging of a left intracochlear intralabyrinthine schwannoma involving the basal turn in a 67-year old man who presented with sudden sensorineural hearing loss.

(A) Left-sided homogeneously enhancing mass on coronal T1-weighted post-contrast imaging and (b) a corresponding cochlear filling defect on coronal heavily T2-weighted imaging.

Patient characteristics, symptomatology, and tumor classification of incident cases of intralabyrinthine schwannoma in Olmsted County, Minnesota from 1966 to 2016.

Table 1

Case	Sex	Age at Dx (years)	Delay to Dx* (months)	Hearing Loss(8) [†]	Vertigo	Imbalance	Tinnitus	Aural Fullness	Location(6,9)	Subsite	Treatment
1	F	75	72	D/G	N	Y	Y	Y	IC	BT, MT	N
2	F	74	21	B/G	N	N	Y	N	TM	BT	N
3	F	47	120	B/G	N	N	Y	N	IC	MT	N
4	M	12	154	D/C	N	N	N	N	IV	V	N
5 [‡]	M	67	0	D/S	N	N	Y	N	IC	BT	SRS
6	F	62	36	D/G	N	Y	Y	Y	IC	MT	N
7	F	57	204	D/S	N	N	N	N	IVC	V, BT, MT, AT	N
8	M	33	3	A/S	N	N	Y	Y	TM	BT	N
9	M	58	120	D/G	Y	Y	N	N	TM	BT	N
10	F	70	7	B/G	Y	Y	Y	N	IC	BT	N
11 [‡]	F	39	5	D/S	N	N	N/A	N	IC	BT	N
12	M	66	86	D/G	Y	N	Y	Y	IC	BT	N
13	M	71	180	D/G	N	N	Y	N	IC	BT	N
14 [‡]	F	23	0	A/G	N	N	N	N	TMa	V	N
% Feature	57% F	60 (39–70)	54 (5–120)	64% D	21%	29%	69%	29%	57% IC	71% BT	7% SRS
		Median (IQR)	Median (IQR)								

* Time delay from initial symptom(s) onset to diagnosis of intralabyrinthine schwannoma

[†] Hearing loss by hearing class (A, B, C, D) / rate of loss (G = gradual, S = sudden, C = congenital)

[‡] Patient had neurofibromatosis type 2

Abbreviations: AT = apical turn; BT = basal turn; Dx = diagnosis; F = female; IC = intracochlear; IV = intravestibular; IVC = intravestibular-cochlear; M = male; MT = middle turn; N = No; N/A = information not available; SRS = stereotactic radiosurgery; TM = transmodiolar; TMa = transmacular; V = vestibule; Y = yes

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Table 2
Incidence of intralabyrinthine schwannoma in Olmsted County, Minnesota by period of diagnosis.

Period of diagnosis	Women		Men		Total	
	N	Rate [*]	N	Rate [*]	N	Rate [†]
1966–2016	8	0.27	6	0.24	14	0.26
2007–2016	7	0.80	6	0.79	13	0.81
20012–2016	6	1.3	3	0.79	9	1.1

^{*} Incidence per 100,000 person-years age-adjusted to 2000 United States population.
[†] Incidence per 100,000 person-years age- and sex-adjusted to 2000 United States population.

Table 3

Incidence of intralabyrinthine schwannoma in Olmsted County, Minnesota by age at diagnosis from 2012 through 2016.

Age at diagnosis	Women		Men		Total	
	N	Rate [*]	N	Rate [*]	N	Rate [*]
0–19	0	0.0	0	0.0	0	0.0
20–29	1	1.7	0	0.0	1	0.91
30–39	1	1.7	1	1.9	2	1.8
40–49	0	0.0	0	0.0	0	0.0
50–59	1	1.8	0	0.0	1	0.93
60–69	1	2.5	1	2.9	2	2.7
70+	2	4.8	1	3.2	3	4.1
Total	6	1.3 [†]	3	0.79 [‡]	9	1.1 [‡]

^{*} Incidence per 100,000 person-years.

[†] Incidence per 100,000 person-years age-adjusted to 2000 United States population.

[‡] Incidence per 100,000 person-years age- and sex-adjusted to 2000 United States population.