Can sudden sensorineural hearing loss predict stroke? A long-term study

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ABSTRACT

Introduction: Previous studies suggest that vascular diseases as stroke may occur in a high percentage of patients with idiopathic sudden sensorineural hearing loss.

Objective: To report the relationship between SHL and stroke in order to be used as an early risk marker for stroke.

Material and Methods: We carried out a long-term follow-up study of all idiopathic sudden sensorineural hearing loss patients admitted to a tertiary referral center, between January 1994 and December 2006. All the patients were followed up on an outpatient basis until March 2019. Work-up study included history, otomicroscopy, audiometry, tympanometry, laboratory, and the development of vascular diseases, and specifically stroke. Stroke and transient ischemic attack were defined according to the WHO criteria.

Results: A total of 214 patients were diagnosed with idiopathic sudden hearing loss, and 64 patients were assessed for stroke. Stroke after idiopathic sudden hearing loss was reported in 7 patients. Lacunar stroke or small-artery occlusion was the most frequent form of stroke presentation. The majority of cases occurred within the first 10 years after idiopathic sudden hearing loss, although two cases occurred at 14 and 20 years.

Conclusion: There seems to be a relationship between SHL and stroke, especially in patients with cardiovascular risk factors. We recommend a longer follow-up in such a patients since stroke may develop several years after the onset of the hearing loss episode.

Keywords: Sensorineural hearing loss; Sudden hearing loss; Stroke; Vascular diseases; Risk factors.

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INTRODUCTION

Sudden deafness or sudden hearing loss (SHL) is a sensorineural hearing loss which develops suddenly over a period of hours or a few days (72 hours or less)[1,2]. It varies in severity from mild to total deafness, and is true emergency in Otorhinolaryngology and Neurotology.

SHL can be due to head trauma, vascular diseases, viral infections, immune response inside the inner ear or can appear without obvious cause or warning. Despite thorough investigation of its etiology, a specific cause is identifiable in less than 5% of SHL cases. Attempts to look for a consensus in the management of SHL are recommended[3]. Patients with SHL may also experience tinnitus or vertigo.

Although the incidence of stroke presenting as SHL is very low, stroke is a serious situation that must be identified and treated as soon as possible. Stroke has an important socioeconomic impact. The annual incidence for all cerebrovascular events is 187 per 100,000 in Spain[4]. This incidence of stroke is moderate compared to other European countries.

Two studies developed in Taiwan showed that stroke appeared in 12.7% patients with SHL within 5 years of onset of the SHL[5] and prior stroke was the most important risk factor for stroke after SHL[6]. Two other studies carried out in the Republic of Korea found a hazard ratio of stroke 2.02 times[7] and 1.22 times[8] greater for patients with SHL.

We carried out a long-term follow-up study to report the relationship between SHL and stroke. A comparison between the incidence of stroke in the general population and after SHL was performed in order to be used as an early risk marker for stroke.

MATERIAL AND METHODS

We conducted a retrospective analysis of all patients affected by SHL attended in a tertiary referral center, between January 1994 and December 2006. All the patients were followed up on an outpatient basis until March 2019.

Inclusion criteria included: (a) SHL, defined as a sudden sensorineural hearing loss of greater than 30 dB over 3 contiguous pure-tone frequencies occurring within 72 hours; (b) the time from hearing loss to treatment must be within 14 days; (c) no history of ear diseases; (d) no specific causes for the SHL after proper investigation.

Exclusion criteria included: (a) SHL of known cause; (b)

recent chemotherapy, radiation therapy or ototoxic drops; (c) cochlear malformations or the presence of otitis media; (d) pregnancy and (e) those patients who failed to complete at least 10 years of follow-up.

Diagnosis was based on the history, otomicroscopy, pure-tone audiometry, extendend high-frequency audiometry, speech audiometry, and tympanometry. Searching for systemic diseases was performed. Laboratory tests included a complete blood cell count; glucose levels, lipid profiles, erythrocyte sedimentation rate, C-reactive protein levels, immunologic work-up study, and thyroid function tests. Magnetic resonance imaging of the brain were arranged to rule out internal auditory canal, cerebellopontine angle tumors, multiple sclerosis, or cerebrovascular causes.

Patients were treated with oral Methylprednisolone 1mg/kg/day tapered in three weeks. Patients who had failure of oral therapy received intravenous Methylprednisolone (Solu-Moderín, Pfizer, New York, USA) 125-500 mg for 72 hours or injections as a rescue line (4 Methylprednisolone injections through the tympanic membrane within a 1-week period)[9].

Stroke and transient ischemic attack (TIA) were defined according to the WHO criteria. Stroke and TIA diagnosis was carried out by a neurologist based on clinical and imaging findings. The Lausanne Stroke Registry was used to classify ischemic stroke subtypes: (1) large-artery atherosclerosis (LAA); (2) cardioembolism (CE); (3) lacunar stroke or small-artery occlusion (SAO); (4) stroke of other infrequent cause (SIC), and (5) stroke of undetermined cause (UND)[10].

The SHL patients were matched 1:4 with subjects no diagnosed with SHL from the same time period. The control participants were selected from patients who were treated at the hospital for different reasons not suspected of causing stroke. A total of 256 patients were randomly selected and matched with the SHL group in terms of age and gender.

The Statistical Package for the Social Sciences (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.) was used for statistical analysis. Quantitative and qualitative statistical methods of data analysis were used. The Chi-square test was used. For the quantitative variables the Student´s t-test and the Mann-Whitney U-test were used. To control the possible confounding variables and possible interactions a logistic regression adjustment analysis was performed, taking into consideration the possible associations related to the patient, auditory findings, and being the dependent variable sensorineural hearing loss. The estimate was established with 95% confidence intervals, and a p-value of < 0.05 was accepted as the statistical significance level.

RESULTS

Between January 1994 and December 2006, a total of 214 patients were diagnosed with SHL. The primary outcome was evaluated (cardiovascular disease risk factors) in 188 patients who signed the informed consent. Of these patients, 64 patients in whom a known cause of the hearing loss such as an immune-mediated disorder and/or viral infection was ruled-out (37 male, 57.81%; 27 female, 42.19%) were assessed for

FIGURE 1
Trial profile scheme carried out in the present study.

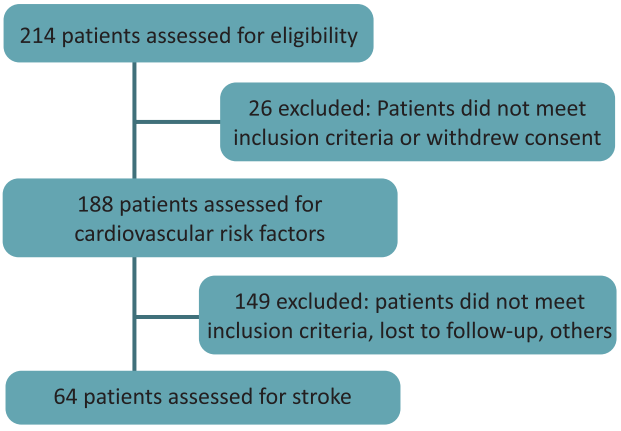

TABLE 1
Clinical characteristics and comorbidities in patients with SHL in different series.

	Chang et al.[6] (n=349)	Lin et al.[5] (n=1432)	Rudack et al.[20] (n=142)	Ballesteros et al.[27] (n=99)	Kim et al.[8] (n=4944)	Present study (n=64)
Gender M/F (%)	64.8/35.2	54.5/45.5	54.2/45.8	1/1	44.1/55.9	57.81/42.19
Age (yr)	60.2 ± 16.6	—	51.2 ± 17.2	51.7 ± 16.4	5-85+	61.4 ± 30.6
Ear: R/L/B(%)	47.3/50.1/2.6	—	47.9/52.1/0	46.8/53.2/2	—	43.75/43.75/12.5
Dizziness(%)	16.9	—	31.7	27	—	29.7
High blood pressure(%)	47.9	8.4	14.1	21.1	34.8	42.2
Diabetes mellitus(%)	19.8	10.1	5.6	7	20.7	12.50
Dyslipidemia(%)	40.1	0.8	—	—	30.2	31.25
Coronary heart disease(%)	8.9	—	3.5	8.8	7.6	4.7
Stroke after SHL (%)	4.9	12.7	—	—	4.9	10.94

TABLE 2
Characteristics of patients with stroke after SHL.

Patient	Gender	Age	Affected ear	SHL	Stroke	Evolution time (yr)	Stroke subtype a
1	Male	73	Right	1996	2002	6	SAO
2	Male	90	Bilateral	1994	2004	10	LAA
3	Female	46	Left	2008	2014	6	SIC
4	Female	88	Bilateral	2003	2011	8	SAO
5	Female	75	Right	1994	1995	1	CE
6	Male	57	Left	1995	2015	20	SAO
7	Male	69	Left	1997	2011	14	SAO

[a]According to Lausanne Stroke Registry classification[10]: LAA, large-artery atherosclerosis; CE, cardioembolism; SAO, lacunar stroke or small-artery occlusion; SIC, stroke of other infrequent cause.

stroke (secondary outcome analysis). All of the patients included in the secondary outcome analysis presented some cardiovascular disease risk factors (Figure 1). Table 1 shows the clinical characteristics and comorbidities in patients with SHL in different series and the present study. Stroke was reported in 21 patients: 7 (10.94 %) of the SHL patients and 14 (5.46 %) from the control cohort. SHL patients had significantly lower stroke-free survival rates than de control subjects ($p < 0.01$). According to Lausanne Stroke Registry classification 10, lacunar stroke or small-artery occlusion (SAO) was the most frequent form of stroke presentation.
The majority of cases occurred within the first 10 years after SHL, although two cases occurred at 14 and 20 years. Two patients with bilateral SHL had a stroke during follow-up (Table 2).

DISCUSSION

The present study try to consider the risk of stroke within patients in the long-term follow-up after hospitalization for an acute SHL episode.
Age above 65 years, hypertension, coronary artery disease, and history of stroke have been reported as risk factors for stroke after SHL[5-8]. These are also risk factors for stroke in the general population[11,12]. Patent foramen ovale has also been suggested as a cardiovascular risk factor associated with stroke and SHL[13-18].
Previous studies reported that the probability of stroke was 1.64 times[5], 2.02 times[7] and 1.22 times[8] higher in SHL patients. Moreover, 12.7% of the SHL patients had a stroke and almost 50% of patients presented stroke within 2 years after the SHL[5]. Kim et al.[7] found that SHL was associated with increased incidence of cardiocerebrovascular disease, specifically stroke. Kim et al.[8] found that SHL increased the risk of ischemic stroke, but not hemorrhagic stroke.
However, other studies concluded that SHL did not increase the risk of stroke. Chang et al.[6] divided SHL patients into a stroke group and a non-stroke group and its features were compared but there is not a control group. Ciorba et al.[11] found that SHL did not significantly increase the risk of stroke during the observation time period of 6 years.
In the present study stroke was reported between 1 and 20 years after SHL. Therefore, the risk for a stroke remains for several years after an episode of SHL. Two patients with bilateral SHL had a stroke during follow-up. Conversely, none of the patients with bilateral SHL experienced a stroke in Chang et al. study[6].

Although the mechanisms responsible of the relationship between SHL and the subsequent stroke have to be elucidated, elevated plasma fibrinogen and cholesterol could have a role since they can contribute to atherosclerosis and thrombosis[19,20]. Cholesterol may impair cochlear vascularization by reducing the release of nitric oxide from endothelial cells and it can also diminishes motility of outer hair cells[21]. Since fibrinogen increases plasma viscosity and induces aggregation of erythrocytes, thrombocytes, and leucocytes, it may also reduce cochlear blood flow[22]. Fibrinogen/LDL apheresis has been reported to be effective in treatment of SHL since it may reduce the concentration of serum LDL, lipoprotein and fibrinogen[23]. Glycoprotein polymorphisms associated to elevated fibrinogen concentration have been reported in SHL patients[24]. The C807T glycoprotein polymorphism has proved to be a risk factor for SHL and stroke[19,25,26].
The inner ear is especially sensitive to ischemia. Impaired blood flow in the labyrinthine artery is regulated by plasma viscosity and adrenergic receptors. Studies suggest a vascular origin in SHL[27]. Some authors found a high incidence of cardiovascular risk factors in their sample[28]. However, the lack of a clear relationship between SHL and cardiovascular risk factors might suggest a multifactorial origin[28].
The small number of patients affected by SHL of unknown cause who presented cardiovascular disease risk factors is a limitation in the present study. Data from this study suggest a vascular origin of SHL of unknown cause in a group of patients with subsequent development of stroke in a small percentage of them.

CONCLUSION

There seems to be a relationship between SHL and stroke, especially in patients with cardiovascular risk factors, although further research with larger samples would be necessary to confirm the data. Hence we recommend a longer follow-up in such a patients since stroke may develop several years after the onset of the hearing loss episode.

Conflict of Interest

Authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

This article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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