Acta Otorrinolaringol Esp. 2009;**60(5):**318-324

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

ORIGINAL ARTICLE

CSF fistulae following surgery for cerebellopontine angle tumours and their relationship with the body mass index

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Received January 13, 2009; accepted March 24, 2009
Available online July 24, 2009

KEYWORDS
Vestibular schwannoma;
Cerebrospinal fluid leak fistula;
Body mass index

Abstract
Introduction: The most frequent complication after vestibular schwannoma surgery is cerebrospinal fluid (CSF) fistula.
Material and methods: Retrospective study of 170 patients who had vestibular schwannoma (163) or other tumours in the cerebellopontine angle (CPA) (7). Resection was carried out using different approaches: retrosigmoid (66%), translabyrinthine (24%), middle cranial fossa (5%), and others (5%). We studied the day of onset, location and treatment of the CSF leaks, and the influence of demographic, radiological and clinical variables, including body mass index.
Results: Twenty-seven patients developed a CSF fistula (15.9%): fifteen were incisional (8.8%), 8 patients developed CSF rhinorrhea (4.7%), 1 CSF otorrhea (0.6%), and 3 a combination of the above (1.8%). We controlled 11 CSF fistulae with bed rest and compressive dressings (6.5%), 7 required lumbar drainage (4.1%), 2 lumbar drainage and wound closure with local anaesthesia (1.2%), and 7 patients required returning to the operating room under general anaesthesia (4.1%). There was not a significant relationship between the apparition of CSF and tumour size, type of approach, age, or body mass index (BMI).
Conclusions: Despite the great development and new surgical techniques, CSF fistulae are still a frequent complication after VS surgery. There might be other aetiological factors such as intracranial pressure. There was no significant relationship between CSF fistula and BMI. Adequate management and early conservative measures led to reduced reintervention rates of less than 5% in all patients.

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0001-6519/$ - see front matter

PALABRAS CLAVE
Schwannoma vestibular;
Fístula del líquido cefalorraquídeo;
Índice de masa corporal

Fístulas de LCR tras la cirugía de tumores del ángulo pontocerebeloso y su relación con el índice de masa corporal

Resumen
Introducción: La complicación más frecuente tras la cirugía del schwannoma vestibular (SV) es la fístula de líquido cefalorraquídeo.
Métodos: Estudio retrospectivo de 170 pacientes intervenidos por SV (163) y otros tumores del ángulo pontocerebeloso (7). La resección se realiza por las vías retrosigmoidea (66%), translaberíntica (24%), fosa media (5%) y otras (5%). Se estudiaron día de aparición, localización, tratamiento e influencia de variables demográficas, clínicas (incluido el índice de masa corporal [IMC]) y radiológicas.
Resultados: Se desarrolló fístula de líquido cefalorraquídeo (LCR) en 27 pacientes (15,9%), de las cuales 15 fueron incisionales (8,8%), 8 fueron rinolicuorreas (4,7%), 1 fue otolicuorrea (0,6%) y 3 fueron una combinación de éstas (1,8%). Se controlaron 11 fístulas con medidas conservadoras (6,5%), 7 pacientes mediante colocación de drenaje lumbar (4,1%), 2 pacientes precisaron drenaje lumbar y cierre con anestesia local (1,2%) y 7 pacientes requirieron reintervención bajo anestesia general (el 4,1% del total). No se demuestra relación significativa entre la aparición de las fístulas de LCR y la vía de abordaje, el tamaño tumoral, la edad ni el IMC.
Conclusiones: A pesar de los avances técnicos, la fístula de LCR continúa siendo una complicación frecuente tras la cirugía del SV, no habiéndose desarrollado una técnica que garantice su desaparición. Podría haber otros factores implicados en su etiología, como la presión intracraneal. No se ha demostrado una relación entre las fístulas de LCR y el IMC. El empleo precoz de medidas conservadoras nos ha permitido reducir la tasa de reintervenciones bajo anestesia general a cifras inferiores al 5% de todos los pacientes intervenidos.

Introduction

Surgery of vestibular schwannoma (VS) was started in the late 19th century. At that time it was characterized by high morbidity, with mortality reaching more than 20%. Thanks to advances in surgical techniques, mortality in this surgery has dropped significantly, achieving complete tumour resection and preservation of facial and auditory functions in many cases. One of the complications caused by this surgery, the most frequent in most series, is the fistula of cerebrospinal fluid (CSF). The incidence of this complication has declined very significantly in recent decades. Despite this, it remains a common and potentially dangerous complication, since it can promote the development of meningitis and thus may prolong hospital stay.

There are many studies which investigate the risk factors for development of a fistula and among them a recent meta-analysis which reviewed 25 studies, conducted by Selesnick et al[1] stands out. This work studied the relationship between the surgical approach, tumour size, age and gender and the possibility of developing a CSF fistula, without a demonstration of a clear influence of these factors. Many techniques have been described in the medical literature, which aim to decrease the rate of fistulas, such as the closure of translabyrinthine approaches with abdominal fat.[2] In another work[3] it was concluded that the systematic obliteration of the Eustachian tube after VS resections by translabyrinthine approach did not significantly diminish the rate of postoperative rhinoliquorrhea. Other techniques have been developed to help to minimize the incidence of CSF fistulas, among them the use of fascia, tissue adhesives, bone cements of hydroxyapatite,[4,5] and other biomaterials.

Despite all these factors, none has been described which clearly influences the presentation of CSF fistulas. A demographic datum which has hardly been studied as a possible factor related to the appearance of CSF fistulas is the body mass index (BMI) of Quetelet, which has been shown to relate to the occurrence of spontaneous CSF fistulas.

This study aims to analyze our incidence of CSF fistulas, the management and the influence of different clinical, radiographic, and demographic variables, including BMI.

Patients and methods

This retrospective study includes 170 patients operated on between July 1990 and November 2007 in our department. In 163 patients, the pathology of the lesion was of SV, in 5 of meningioma and the 2 remaining cases were treated for choristoma and an arachnoid cyst.

Among the patients, 94 were women and 76 men, with ages between 14 and 78 years and an average age of 49 years. The tumours were on the right side in 81 cases and on the left in 89 cases.

The average size of the component in the cerebellopontine angle (CPA) was 17.7 mm, ranging between 0 and 60 mm. The average maximum tumour diameter, considering the 2 components, internal auditory canal and CPA, was 23 mm (5-60 mm).

The most frequent cause for consultation was unilateral hearing loss in 49% of cases, followed by tinnitus (21%), dizziness (11%), vertigo (6%), and other causes in 12%

Surgical technique

The approach used to access CPA tumours was the retrosigmoidal pathway in 112 cases (66%), the translabyrinthine in 41 cases (24%), the middle fossa in 9 patients (5%), and in 8 cases (5%) a suboccipital or combined approach in the case of petroclival meningiomas. Factors considered to decide between one or another approach included tumour size, size on the CPA, and preoperative hearing.

Factors analyzed

We studied the possible relationship between the development of CSF fistula and tumour size, both the maximum diameter and the diameter in the CPA, the relationship with the type of approach and a possible relationship between type of approach and type of CSF fistula. We analyzed the influence of age and gender on the development of this complication and whether this influenced the length of hospital stay.

Finally, we studied the relationship between the incidence of CSF fistulas and BMI values of our patients. BMI is found by dividing the weight of the patient (kg) by the height squared (m^2). These data were obtained by reviewing medical records and through a telephone survey to confirm the records, obtaining data from 19 patients with CSF fistulas and from 81 patients who did not develop this complication. We subsequently analyzed data from both groups.

For statistical analysis, data were treated by the Section of Biostatistics at our centre using SPSS 9.0 (SPSS Inc.). The comparison of quantitative data between 2 groups was performed by the Student *t* test for independent data and the Mann-Whitney *U* test according to the distribution of the variables. The qualitative data was analyzed using the ^{2} test or Fisher exact test. The Pearson correlation coefficient was calculated as a bivariate correlation coefficient. All statistical tests were considered bilateral and as significant values for *P* less than .05.

Results

From the series of 170 patients operated on through different approaches for VS and other CPA tumours, 27 patients (15.9%) presented CSF fistula sometime in the postoperative period. The fistula was diagnosed clinically, requiring no routine studies on the beta-2-transferrin content of the fluid. Most of the fistulas appeared on the 8th postoperative day. In 11 patients (41%) the fistula appeared during the first week after the operation, in another 11 patients (41 %) during the 2nd week, and in 5 patients (18.5 %) during the 3rd week. In 3 cases (7.4%) diagnosis of fistula took place on the same day of surgery and in 1 case (3.7%) 21 days after it.

The most frequent CSF fistulas were of incisional type, appearing in 15 cases, representing 8.8% of the whole series, followed by 8 cases rhinoliquorrhea (4.7%) and one case of otoliquorrhea (0.6%). In 3 patients (1.8%) a combination of these types of fistula appeared.

Eleven of the 27 fistulas (40.7%) were controlled with conservative treatment, which consisted of rest and compressive bandages. In 7 patients (25.9%) the complication was resolved after placement of a lumbar drain, in 2 of these cases (7.4%) in addition to a lumbar drain a new closure with suture under local anaesthesia was required. Only 7 patients required reoperation under general anaesthesia to resolve the fistula (25.9%), representing 4.1% of all patients operated. In 6 cases the primary approach was retrosigmoidal, 5 of these patients underwent mastoidectomy with closure using abdominal fat and in one case a closure of the dura mater with periosteum was carried out (Figure 1). In the case of the reoperation of the translabyrinthine approach it was reviewed surgically, extracting the head of the hammer and resealing with abdominal fat. There was no need to close the Eustachian tube to stop the fistula in any patient and in all cases the fistula was controlled with a single intervention.

In analyzing the data from this series of patients, no significant difference in the presentation of CSF fistulas was observed according to the surgical approach (retrosigmoidal, 17%; translabyrinthine, 17.1%; middle fossa, 0%; and other routes, 12.5%), tumour size (average size with presentation of the fistula 23.3 mm and without it 22.9 mm), CPA size (18.4 mm with fistula and 17.5 mm without fistula), age (51 years of average with fistula and 48.7 years without fistula), or gender of the patients (14.5% men and 17% of women presented fistula). Nor was there any causal association observed between the surgical approach employed, and a predominance of a particular type of fistula.

We analyzed BMI data of 100 patients (19 of them presented CSF fistulas) to study the existence of a relationship between BMI and an increased likelihood of development of CSF fistulas. The average BMI of patients who did not develop fistula was 26.85 and that of patients who developed this complication was 27.63, with no significant difference being found.

The average stay for patients undergoing surgery was 13 days, ranging from a minimum of 3 to a maximum of

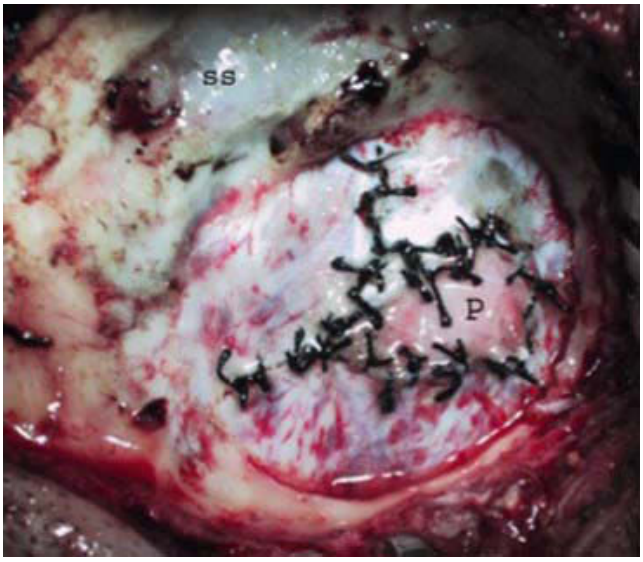

Figure 1 Closure of dura mater defect with periosteum after retrosigmoidal approach. P indicates periosteum; SS, sigmoid sinus.

60 days of hospital stay. It was found that a relationship exists between the occurrence of fistulas and increased hospital stay. Patients in whom the postoperative period passed without complications had an average stay of 11 days. For those who had a complication with a CSF fistula, the average stay was almost 21 days, $P<.05$.

In our series only 2 patients who presented fistula in turn had postoperative complications with meningitis. This diagnosis was made by suggestive clinical findings (febrile illness accompanied by signs of meningitis), based on a CSF sample with an increase in the number of polymorphonuclear cells and a decrease in glucose levels. The causative organism was not isolated in the CSF in any of the 2 cases; therefore, they were cases of aseptic meningitis. The treatment employed was intravenous antibiotics with third-generation cephalosporins.

Discussion

CSF fistulas remain the most common complication after surgical removal of VS, with a reported incidence in some series up to 30%. The rate of CSF fistula presented by our series of patients (15.9%) falls within the range described in the medical literature, although there are case series with lower incidence of this complication.

This study could not demonstrate a relationship between the surgical approach, tumour size, age, and gender with a higher frequency of fistulas. These results agree with those obtained by Selesnick et al.[1] Many of the studies found no significant relationship between the incidence of CSF fistulas and tumour size.[6-10] However, there are authors who have described a relationship between increasing tumour size and increased likelihood of fistulas,[11] type of approach and incidence of fistula[9] and others who, although they do not describe significant relationships, they do describe a tendency towards increased frequency of CSF fistulas in patients older than 50 years.[10] Table 1 shows the results of incidence of CSF fistulas in various studies, and the percentages of fistulas in each type of approach.

Traditionally, in our department there have been more retrosigmoidal approaches, although the current trend is towards using the translabyrinthine approach. Despite this turnaround, we have observed no significant differences in the incidence of fistulas between both approaches.

The treatment for each fistula depends on its type, day of diagnosis, and general condition of the patient. We believe that the rate of reoperation under general anaesthesia in our series (25.9%of fistulas) is a good result compared with other series (Table 2). As a general rule, the management of this complication goes through relative rest, compressive bandage and acetazolamide (carbonic anhydrase inhibitor which reduces the production of CSF) during the first 4 or 5 days. If these measures do not manage to control the situation, we then place a lumbar drain (never prophylactically) for another 5 days. In the case of incisional fistula we evaluate re-suturing under local anaesthesia and if the fistula persists we opt for a reoperation under general anaesthesia. For rhinoliquorrhea, if the fistula does not remit after placement of a lumbar drain for 5 days, the next

Table 1 Incidence of fistulas and percentage of approaches employed

Authors	No. of patients	CSF fistula, %	TL, %	CSF fistula TL, %	RS, %	CSF fistula RS, %	MF, %	CSF fistula MF, %
Shea MC, 1979[11]	80	15	37.5	30	62.5		0	0
Jacob A, 2007[3]	359		64.3	14.2	13.9	13.2	19.5	11.4
Selesnick SH, 2004[1]	5964		–	9.5	–	10.6	–	10.6
Sanna M, 2004[10]	707	2.8	84.9	1.8	5.4	18.4	7.6	3.8
Darrouzet V, 2004[12]	400	6.9	57.2	–	32		–	–
Fishman AI, 2004[13]	215	6.6 17[a]	52	5	36	8.5	12	8.3
Becker SS, 2003[8]	300	11	33.3	13	33.3	10	33.3	10
Kalamarides M, 2004[14]	220	12	63	–	27		10	–
Cueva RA, 2005[15]	343	0.8 1.2[a]	51.6	–	47.1		1.23	–
Coca A, 2007[16]	120	12.5	36.6	–	62.5		0.8	
Leonetti J, 200[19]	589	0.5 0a 6.9[a]	35.5	3.8	32.4		0.51	0
Lee SH, 2002[17]	160	10.5	0		100		0	
Wu H, 1999[2]	277	3 28.2[a]	100		0		0	
Díaz Anadon, 2008	170	15.9	24	17.1	66	17	5	0

CSF indicates cerebrospinal fluid; MF, middle fossa approach; RS, retrosigmoidal approach; TL, translabyrinthine approach.
[a]Previous series.

step would be surgical review under general anaesthesia. A single surgical intervention was enough to control the process in all reoperated patients.

The time limits given for each type of fistula are approximate and flexible, depending on the individual circumstances of each patient.

CSF fistulas are related, according to Selesnick et al,[1] with higher incidence of meningitis, with this increased incidence not being attributable exclusively to the use of lumbar drains. Thus, they increase the morbidity of the intervention in addition to prolonging the average hospital stay.

A proper closure after tumour resection is fundamental in reducing the incidence of CSF fistulas. Various surgical techniques and materials for closure have been described for the different approaches.

A decrease has been demonstrated[1] in the incidence of fistulas after translabyrinthine approach by placing strips of autologous fat directly into the CPA, without the interposition of the fascia which was performed in the first series of patients.

Another proposed technique for reducing the incidence of postoperative rhinoliquorrhea is obliteration of the Eustachian tube. A retrospective study[2] compared 2 groups of patients operated on for VS via the translabyrinthine approach. In the first group (51 patients) the middle ear, epitympanum and aditus ad antrum were obliterated with muscle and fascia; in the second group (148 patients) in addition the anvil was eliminated, the aditus was extended, the tensor tympani tendon was sectioned and the facial recess was opened in order to view and fill the Eustachian tube and middle ear with muscle, fascia and/or other synthetic materials. The group in which the Eustachian tube was not obliterated presented a rate of rhinoliquorrhea of 5.9%compared to 8.1%presented by the group with obliterated tube, although this difference was not statistically significant. It was concluded therefore that the obliteration of the Eustachian tube does not decrease the incidence of rhinoliquorrhea.

In another article,[19] Sanna describes the closure technique used at his institution, which presents the series of cases with lowest incidence of fistula after translabyrinthine approach in medical literature.[6] The 6 points he emphasizes for prevention of CSF fistulas are: *a)* keep intact the bone of the facial recess; *b)* closure with bone wax of the mastoid cells prior to opening of the dura mater; *c)* extraction of the anvil and obliteration of aditus, attic and middle ear with periosteum; *d)* closure of the dural defect and obliteration of the mastoid cavity with long fat strips placed in "champagne cork" style; and *e)* wound closure in 3 planes.

Other authors[3] conducted a prospective study of a series of patients intervened for VS with retrosigmoidal approach in whom they rebuilt the back wall of the internal auditory canal with hydroxyapatite cement, experiencing a significant decrease in the presentation of rhinoliquorrhea and fistulas in general. Another method of use of hydroxyapatite cement is conducting cranioplasty with it after closing a translabyrinthine approach, in which a decrease in the incidence of this complication has been described[5] in a retrospective study comparing closure with autologous fat and with hydroxyapatite. In it, this complication fell from 12.5%to 3.7%(a difference which was not statistically significant), but with the disadvantage of requiring a lateral drainage to the cement during the first 12 postoperative hours.

Since the results presented are part of a retrospective study over more than 10 years, the rate of closure at our institution has varied slightly.

During a retrosigmoidal approach, we consider it necessary to seal all the mastoid air cells as they arise. Once the tumour has been resected, the reconstruction of the posterior wall of internal auditory canal is performed with grafts of free muscle, fat, and tissucol. The closure of the dura mater is made with 4/0 silk sutures, and then the bone island is restored, sealing it with bone cement and a suture is made in the muscular and subcutaneous plane and finally the cutaneous plane.

The closure in translabyrinthine approach also includes the sealing of all the mastoid cells which are exposed. Once the tumour is resected, the autologous fat strips are placed in the CPA, reaching the mastoid cavity, the anvil is extracted and fat is placed in the attic to achieve complete

Table 2 Percentage of cerebrospinal fluid fistulas and reoperations

	No. of patients	CSF fistulas, %	Reoperations amongst the total of intervened patients, %	Reoperations amongst the fistulas, %
Becker SS, 2003[8]	300	11	3	27.27
Fishman AJ, 2004[13]	174	6.6 17[a]	2.79	46.15
Coca A, 2007[16]	120	12.5	1.66	16.38
Khrais TH, 2004[7]	710	1.4	1.13	80
Kalamarides M, 2004[14]	220	12	3.18	46.66
Cueva RA, 20051[5]	343	0.8 1.2[a]	0.58	50
Sen A, 2006[18]	24	62.5	41.66	66.7
Díaz Anadon, 2008	170	15.9	4.12	25.92

CSF indicates cerebrospinal fluid.
[a]Previous series.

isolation of the middle ear of the subarachnoid space and mastoid space. Finally, a thorough closure is conducted in three planes (periosteum-temporalis muscle, subcutaneous and cutaneous).

After a middle fossa approach, the closure begins with the placement of muscle or fat in the internal auditory canal, and next the temporal lobe is replaced, along with the bone island of the craniotomy and a closure is performed in 3 planes.

Since, despite advances in surgical techniques, the incidence of CSF fistulas has not been reduced in recent years and taking into account that different approaches have a similar incidence of CSF fistulas, we believe that the development of this complication may be influenced by other factors such as CSF pressure.[8] This increases transiently during the first 24 h after surgery,[20] returning to preoperative values after 48 h. This could be due to difficulty in resorption of CSF caused by surgery, which is recovered at the time commented, without any therapeutic measures. Kalamarides et al[14] propose that CSF pressure values are used as a guide for the management of CSF fistulas, so that low values are a criteria for surgical approach, since in this case the fistula would be attributed to a defect in the surgical closure, whereas high values would indicate a conservative initial treatment, whilst awaiting for the intracranial pressure values to become normalized.

The analysis of the relationship between BMI and the probability of presentation of CSF fistulas seemed interesting, since the relationship between a high BMI, idiopathic intracranial hypertension and the development of spontaneous CSF fistula is well known. In a series of 55 patients with spontaneous CSF fistulas and evidence of intracranial hypertension,[21] the average BMI was 36.2 kg/m^2, 84% of patients were obese (BMI >30 kg/m^2). According to Daniels[22] not only obesity is linked with idiopathic intracranial hypertension, but also modest increases in weight in non-obese patients increase the risk of idiopathic intracranial hypertension. As with fistulas after VS surgery,[14] some authors[23] recommend intracranial pressure measurement as a guide for appropriate therapy of spontaneous CSF fistulas. Despite the apparent similarities, our series showed no significant relationship between BMI and development of fistulas. This could be due to the multifactor aetiology of this complication and to the fact that, although BMI and intracranial pressure are related, they are not strictly consistent.

Conclusions

The new surgical techniques have helped to reduce morbidity and mortality in surgery of the CPA. However, the incidence of CSF fistulas has not changed in recent decades.

There could be other factors that influence their development which explain this fact, such as CSF pressure. This study has not shown any link between high BMI and a higher frequency of fistulas. However, research must continue into new surgical techniques and other pathophysiological factors which may help to reduce the incidence of this complication.

Once a CSF fistula has appeared, an adequate management, with early use of conservative measures has allowed us to reduce, compared to other series, the reoperation rate under general anaesthesia to levels below 5% (25.9% of total patients intervened), thus decreasing perioperative morbidity.

Conflict of interests

The authors have indicated there is no conflict of interests.

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