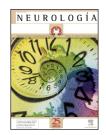


NEUROLOGÍA



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ORIGINAL ARTICLE

Study of neurovascular contact in essential hemifacial spasm: an example of CISS sequence and magnetic resonance angiography

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Received on 24th March 2009; accepted on 11th January 2010

KEYWORDS

Constructive interference at steady state;

Neurovascular contact; Essential hemifacial spasm;

Magnetic resonance imaging;

Time of flight

Abstract

Background and purpose: The purpose of this article is to assess the validity of the magnetic resonance imaging (MRI) CISS 3D sequence associated with 3D time of flight (TOF) angiographic sequence in order to detect neurovascular contact (NVC) between the facial nerve and neighbouring arteries in patients with essential hemifacial spasm (HFS) and to determine the relationship between HFS symptoms and NVC and NVC image features (type, number and site).

Materials and methods: We prospectively enrolled 120 cerebellopontine angle (CPA) MRI studies, 44 cases with HFS symptoms and 76 which were asymptomatic (controls), using axial T2-weighted (CISS) and axial 3D TOF series with associated Maximal intensity (MIP) reconstructions. Prior TOF angiographic studies were available for 56 cases without associated CISS images and the results obtained from that study were compared with the results of the current study.

Results: The diagnostic values obtained significantly favoured the protocol used in this study, which demonstrated a sensitivity of 77.27% and a specificity of 75% There was a statistically significant relationship between the presence of NVC and HFS symptoms (p<0.0001). Only one statistically significant relationship was found between facial nerve displacement (in type of NVC) and HFS symptoms (p=0.019).

Conclusions: The proposed MRI protocol is sensitive and valid for detecting NVC in patients with HFS. The results of our study support a relationship between NVC and HFS symptoms. It is not a simple relationship, however. It may be influenced by other factors, such as displacement of the facial nerve due to NVC.

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PALABRAS CLAVE

Constructive
interference at steady
state;
Contacto
neurovascular;
Espasmo hemifacial
esencial;
Resonancia magnética;
Time of flight

Estudio por resonancia magnética del contacto neurovascular en el espasmo hemifacial esencial: empleo de secuencia CISS y angiografía por resonancia magnética

Resumen

Objetivos: Evaluar la validez de la secuencia CISS 3D de resonancia magnética (RM) en relación con secuencias angiográficas TOF 3D para la detección del contacto neurovascular (CNV) entre el nervio facial y las arterias vecinas en pacientes con espasmo hemifacial esencial (EHE) y determinar la asociación entre la presencia de síntomas de EHE y el CNV y las características de imagen del CNV (tipo, número y localización).

Material y métodos: Se han estudiado prospectivamente 120 ángulos pontocerebelosos (APC), 44 con clínica de EHE y 76 asintomáticos (controles), mediante el empleo de una serie axial potenciada en T2 (CISS) y una serie axial con técnica angiográfica TOF 3D con reconstrucciones MIP; 56 de estos APC tenían un estudio angiográfico TOF previo y se compararon sus resultados con los del estudio actual.

Result ados: Los valores diagnósticos obtenidos fueron significativos a favor del protocolo del presente trabajo que mostró una sensibilidad del 77,27% y una especificidad del 75%. Se demostró una asociación estadísticamente significativa entre la presencia de CNV y la clínica de EHE (p < 0,0001). Entre las características del CNV estudiadas, únicamente se halló una asociación estadísticamente significativa entre el desplazamiento del nervio facial (dentro de tipo de CNV) y la clínica de EHE (p = 0,019).

Conclusiones: El protocolo de RM propuesto es sensible y válido para detectar CNV en pacientes con EHE. Los resultados de nuestro estudio apoyan la asociación entre el CNV y la clínica de EHE, si bien no se trata de una asociación simple, sino que puede estar influida por otros factores, como el desplazamiento del nervio facial producido por el CNV.

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Introduction

Hemifacial spasm is a syndrome characterised by involuntary, tonic and clonic contractions of muscles innervated by the homolateral facial nerve. Some cases may be secondary to peripheral facial paralysis or to expansive processes of the posterior cranial fossa that compress the facial nerve, However, the majority of cases are considered to be idiopathic or essential (essential hemifacial spasm, HFS). To date, the most widely accepted, best developed hypothesis to explain these essential forms is that of neurovascular contact (NVC) between the facial nerve and adjacent vessels of the cerebellopontine angle (CPA) cistern, 1-4 which would produce a microscopic myelin lesion in the nerve and subsequently lead to abnormal nervous stimulation dissemination and muscular hyperactivity.

This hypothesis, formulated from a neurosurgery standpoint, is not without controversy, mainly from that same environment.⁵ There are questions, not as to the pathogenic role of NVC, but concerning its consideration as simple and unique.

There have been technological advances in magnetic resonance imaging (MRI), with the development of different sequences and improvements that make possible images with higher spatial resolution and contrast. Thanks to these advances, we can currently use this imaging technique to study NVC, its image characteristics and potential diagnostic and clinical correlations in an attempt to better understand the pathogenesis of HFS. To do this, it is necessary to use

appropriate sequences that make it possible to identify those small structures involved in NVC. Therefore, T2-weighted sequences with high spatial resolution, such as the constructive interference at steady-state (CISS) sequence, are effective tools. 6-10

The CISS sequence is a 3D gradient echo sequence which, through the use of very thin sections (0.7-1mm), provides high spatial resolution. Due to its high T2-weighing, it also offers excellent contrast between cerebrospinal fluid (CSF) and soft tissues. For these reasons, it is an ideal sequence for the study of the cisternal segment of cranial nerves. 11-15 In the images obtained by this sequence, cranial nerves and vessels are visualised as hypointense linear structures surrounded by the hyperintense CSF, so that their contours are very well defined (fig. 1). The combination with angiographic sequences also enables correct, easy identification of the vessels causing the NVC. 16-19

One purpose of this study was to evaluate the validity of the MRI protocol for 3D CISS sequences with 3D TOF (time of flight) angiographic sequences used for NVC detection. A second objective was to determine the relationship between NVC, its imaging characteristics (type, number and location) and HFS symptoms.

Material and methods

We conducted a clinical and radiological descriptive study with prospective patient recruitment. The target population

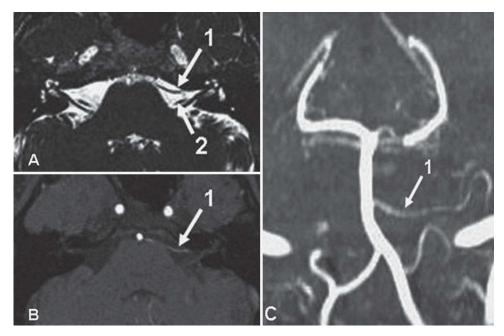


Figure 1 Patient with left essential hemifacial spasm: neurovascular contact between the anterior inferior cerebellar artery (1) and the distal cisternal portion of the facial nerve (2) of the left side. A: CISS sequence. B: TOF angiographic sequence. C: coronal MIP reconstruction of the vertebrobasilar system.

comprised the set of patients *a*) with HFS diagnosis; *b*) with clinical monitoring for a period of at least 3 months at the Movement Disorders Unit at the Neurology Department in the Basurto Hospital, in Bilbao; and *c*) who attended from November 2005 until November 2006. This included 42 patients with HFS (40 with unilateral clinical manifestations and 2 with bilateral), and 18 asymptomatic subjects (controls); in total, 60 patients were included in the study. Table 1 lists the characteristics of the studied series.

Either two anatomical sides or the CPA were studied for each patient, making a total of 120. The symptomatic CPA of patients with HFS were used as cases (n=44). As the control group, we used the asymptomatic CPA of these same

 Table 1 Demographic characteristics of patients included

	HFS	Controls
Patients	42	18
Male	16 (38.1%)	8 (44.44%)
Females	26 (61.9%)	10 (55.55%)
Age (years)	64.45±12.86	51.27±14.58
	[38-85]	[29-74]
Time until HFS diagnostic	52.92±0.05	_
(months)	[1-240]	
Clinical laterality		
Right	15 (35.7%)	_
Left	25 (59.5%)	_
Bilateral	2 (4.8%)	_

The data express n (%, mean±standard deviation [interquartile range].

patients (n=40) plus the 2 CPA of the control subjects (2 ? 18=36), thus having a total of 76 controls.

Patients were studied using the 1.5 Tesla MRI device (Semens Symphony) at the Radiology Department in the Basurto Hospital. To rule out disease processes that could cause the symptoms, contrast-enhanced T1, T2 and FLAIR series were obtained and a diffusion study of the entire brain was carried out. A 3D ClSS axial series (TR, 11.92 ms; TE 5.96 ms; section thickness, 0.70 mm; field of view (FOV), 190 mm; matrix 192 ? 256; flip angle, 70°; sections per block, 40) was performed to identify the facial nerve and the CNV. In addition, a 3D TOF angiographic technique axial series (TR, 39ms; TE, 5.02 ms; section thickness, 0.80 mm; FOV, 200 mm; matrix 192 ? 256; sections per block, 32) with MIP reconstructions in the axial and coronal planes (fig. 1) was performed to identify the artery causing the NVC.

Two radiologists blinded to clinical diagnosis and laterality carried out an independent double reading of the MRI study; in cases of disagreement, they made a joint reading and the final conclusion was decided by consensus. We calculated the degree of non-random agreement between the two radiologists for NVC presence and causal artery through the kappa coefficient.

We determined NVC presence or absence between the facial nerve and adjacent CPA arteries and analysed the following image characteristics of the NVC in those cases in which it was present:

 NVC Type: simple NVC was defined as the situation where the facial nerve and artery come into contact and the course of the nerve is normal; nerve displacement is considered when the artery produces a displacement or deformity in its exit from the protuberance or in its cisternal pathway (fig. 2).

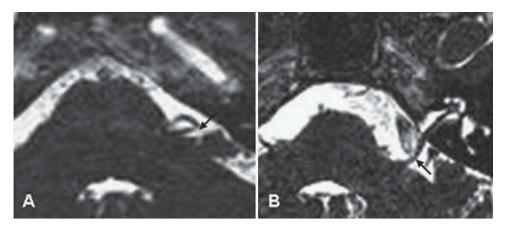


Figure 2 Type of neurovascular contact (NVC). A: Simple NVC. B: NVC with facial nerve displacement. Arrows indicate the point of NVC.

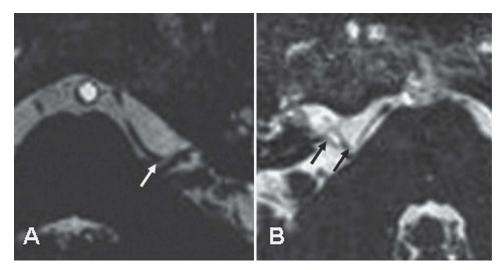


Figure 3 Number of neurovascular contacts (NVC) per nerve. A: Single NVC. B: Multiple NVC. The arrows indicate the points of NVC.

- Number of NVC per nerve: single NVC was defined when only a single point of contact with the facial nerve is detected; multiple CNV is considered when several points of contact are identified in the same nerve (produced by the same artery or by different arteries) (fig. 3).
- NVC location: the pathway of the facial nerve (divided into two parts) in which the NVC occurred was determined. The proximal cisternal segment extends from the exit of the nerve from the protuberance to the proximal third of its cisternal pathway; the distal cisternal segment includes the distal two thirds of the cisternal segment of the nerve and its intracanalicular course within the internal auditory canal (fig. 4).

The imaging findings were then correlated with clinical data. The associations between NVC presence in MRI, its imaging characteristics and the presence of HFS symptoms were determined by the Pearson χ^2 test or the Fisher exact test, as appropriate; p<0.05 was considered significant.

Among the 60 patients included in the study, 28 (corresponding to 56 CPA) with HFS had also had a previous

3D TOF angiography performed to search for NVC between the facial nerve and surrounding arteries, without the use of a CISS sequence. Their results were compared with those of the current study (CISS + TOF sequences) by calculating 95% confidence intervals (CI) for the difference of proportions; we considered the difference statistically significant when the interval did not include the value 0.

Results

Using our study protocol, the facial nerve was identified and the eighth cranial nerve was singled out correctly in 100% of cases. The relationship to neighbouring arteries was also established (that is, whether or not there was NVC). In cases of CNV, the causal artery was determined in 100%

Figure 5 shows the relationship between NVC presence and HFS symptoms. Among the 120 CPA explored, there were a total of 53 NVC, 34 symptomatic and 19 asymptomatic (false positives). In the remaining CPA, no NVC was detected; among these, 57 corresponded to asymptomatic nerves and 10 to symptomatic nerves (false negatives).

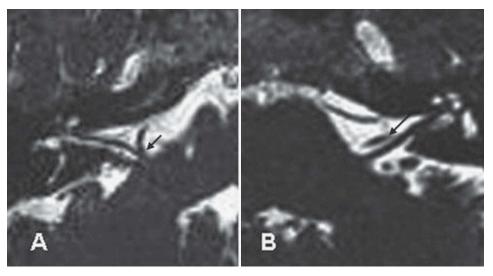


Figure 4 Location of neurovascular contact (NVC). A: NVC in the proximal cisternal segment of the facial nerve. B: NVC in the distal cisternal segment of the facial nerve. Arrows indicate the point of NVC.

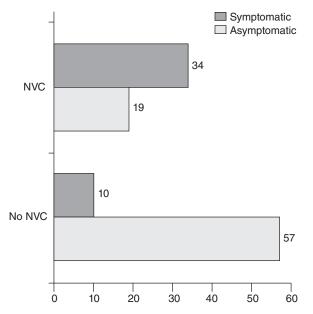


Figure 5 Association between the presence of neurovascular contact on MRI and symptoms of essential hemifacial spasm in the 120 cerebellopontine angles explored.

The anterior inferior cerebellar artery (AICA) was the artery most frequently involved in cases of NVC (in 60.37%), followed at a distance by the posterior inferior cerebellar

The data express median [interquartile range].

artery (PICA) (15.1% of cases) and the vertebral artery (13.2% of cases). In the rest, NVC was produced by the basilar artery (5.66%), superior cerebellar artery (1.9%) and by combinations of AICA and PICA (1.9%) and of AICA and basilar artery (1.9%).

The concordance obtained for the interpretation of the MRI between the two independent observers was very good, with a kappa value of 0.828 for the presence of NVC and 0.962 for the identification of the causal artery.

Table 2 compares the diagnostic values for NVC detection obtained with this study protocol (CISS + TOF sequences) and those obtained in previous TOF angiography studies. The sensitivity, negative predictive value (NPV) and global test value (GTV) were significantly higher with the protocol including the CISS sequence (95% CI for sensitivity, 24.4-63.9; for NPV, 14.5-47.5; for GTV, 2.3-31.6). However, the specificity and positive predictive value (PPV) were higher in the previous TOF angiographic study, although the difference did not reach statistical significance (for specificity, -1.1-29.4; for PPV, -14-36.4).

When correlating the imaging findings with clinical data, we detected a statistically significant association between MRI findings of NVC and the presence of HFS symptoms (p<0.0001). With respect to imaging characteristics of NVC and its association with the presence of HFS symptoms, the findings obtained by analysing the 53 cases of MRI-detected NVC were the following:

Table 2 Diagnostic values of the present study protocol (CISS+TOF) and of the prior angiography study Sensitivity Specificity **PPV** NPV **GTV** CISS+TOF (n=120) 77.27 [63-87.2] 75 [64.2-83.4] 64.15 [50.7-75.7] 85.1 [74.7-91.7] 75.83 [67.4-82.6] TOF (n=56) 30 [16.7-47.9] 92.3 [75.9-97.9] 81.81 [52.3-94.9] 53.33 [39.1-67.1] 58.92 [45.9-70.8] GTV: global test value; NPV: negative predictive value; PPV: positive predictive value.

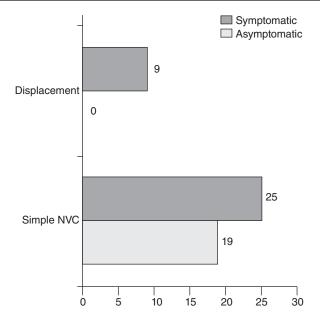


Figure 6 Association between the type of neurovascular contact (NVC) and symptoms of essential hemifacial spasm in the 53 cases of NVC detected.

- NVC type: all cases of MRI-detected facial nerve displacement were symptomatic. However, the simple NVC were both symptomatic and asymptomatic (fig. 6), with a statistically significant association between the presence of facial nerve displacement and the presence of HFS symptoms (p=0.019).
- Number of NVC per nerve: we identified both single and multiple NVC that were symptomatic and asymptomatic (fig. 7), with no statistically significant differences being

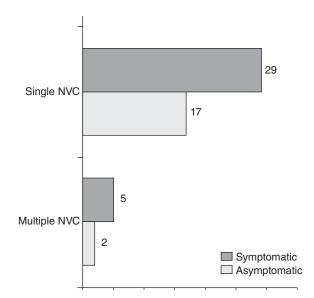


Figure 7 Association between the number of neurovascular contacts (NVC) per nerve and symptoms of essential hemifacial spasm in the 53 cases of NVC detected.

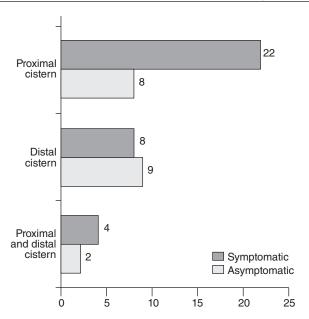


Figure 8 Association between the location of neurovascular contact (NVC) and symptoms of essential hemifacial spasm in the 53 cases of NVC detected.

- observed when associated with the presence of HFS symptoms (p=1).
- NVC location: we observed a greater number of symptomatic NVC in the proximal cisternal portion of the nerve than in the distal or when both locations were present (fig. 8). However, this difference did not reach statistical significance when associated with the presence of HFS symptoms (p=0.194). Neither did we obtain statistically significant differences by grouping the cases of NVC in both locations with those in the proximal cisternal segment (p=0.124) or by grouping them with those in the distal cisternal segment (p=0.151).

Discussion

Currently, the most widely accepted aetiopathogenic hypothesis for HFS is that of NVC between the facial nerve and the adjacent vessels of the CPA cistern. This hypothesis was initially formulated based on surgical findings of ectatic and tortuous arteries that contacted the facial nerve in patients with homolateral HFS symptoms. 1-4 Microvascular decompression to separate these two structures was the proposed treatment then. According to this initial hypothesis, the NVC that caused the symptoms would occur in the root exit zone, which is the portion of the nerve most proximal to its exit from the brain stem, where the myelin coating is thinner because it is a transition point between central myelin and peripheral myelin. It is, therefore, a risk zone where it is easier for the NVC to produce a demyelination that would, in turn, lead to abnormal functional activity, causing the HFS symptoms.

This hypothesis is not without controversy and has received serious criticism, probably the strongest from the neurosurgery field itself. These criticisms are primarily based on the

existence of asymptomatic NVC (the so-called false positives) and on NVC absence in some patients with symptoms (the so-called false negatives). These two facts indicate that this is not a simple hypothesis, nor always present or evident. In addition, it has been observed that HFS symptoms may occur by NVC in a location of the nerve more distal to its root exit zone, 20 which questions the role of NVC in HFS aetiopathogenesis. The truth is that, as of today, the discussion on HFS aetiopathogenesis remains open.

Today, neuroimaging (and specifically MRI) may provide additional data to this ongoing clinical debate. To this end, it is necessary to use adequate sequences that provide sufficient spatial and contrast resolution to identify small structures (the facial nerve and the adjacent vessels of the CPA cistern) involved in NVC. Although several MRI sequences have been employed, ²¹⁻²³ the most commonly used sequences are the angiographic ¹⁶⁻¹⁹ and (more recently) T2-weighted sequences with high spatial resolution, such as the CISS sequence. ⁶⁻¹⁰

Various radiological studies have compared CISS and angiographic sequences, and concluded that the former provides higher spatial resolution and greater contrast between nerves and CSF, and that its sensitivity for detecting NVC is higher than that of angiographic sequences. 9,10,24 Our study supports these findings since, in the comparative study we conducted between the protocol that we propose (CISS+ TOF sequences) and the previous angiographic TOF sequence protocol, the diagnostic values obtained were significantly in favour of the former. With our protocol, we identified the cisternal course of the facial nerve, its relationship with adjacent arteries (that is, whether or not there was NVC) and the causal artery in cases of contact in 100% of the CPA explored. In addition, the correlation between the two MRI readers was very good, indicating that the proposed technique is reproducible. These data suggest that the proposed MRI protocol is effective in detecting NVC between the facial nerve and adjacent arteries of the CPA cistern.

Correctly identifying the vessel causing the NVC through MRI is important, especially in preoperative imaging studies within the context of HFS for which microvascular decompression is going to be performed. The reason is that this information helps in planning the surgical approach and can predict the complexity and, in some cases, even the result of the surgical intervention. 9,17,18 The artery involved in the NVC can be identified easily with the use of a 3D TOF angiographic sequence, as we did in our study. In the present study, the AICA was the artery most frequently implicated in NVC, as in other imaging and surgical studies, 16-20 probably due to the path that it follows and to its anatomical proximity to the facial nerve.

The results of this study support the association between NVC and the presence of HFS symptoms, since we found a statistically significant relationship. However, NVC presence does not always predict a HFS clinical manifestation because, as in other studies, 5.8,10,16,23 we detected cases of asymptomatic NVC or false positives at a rate of 25% indicating that NVC itself may not be sufficient to cause the symptoms. It is possible that different factors such as differences in the cortical modulation of the facial motor nucleus, and emotional factors such as stress or genetic susceptibility, may influence the clinical development, as proposed by Tan et al.8

We also detected false negatives or NVC absence in symptomatic nerves at a rate of 22.73% These false negatives could be influenced by the fact of being contacts caused by vessels of very small size or very slow blood flow that the MRI was unable to visualise or by observer errors. However, it is also true that there have been symptomatic cases in which NVC was not observed in surgery, ^{5,9} thus supporting the hypothesis that NVC may be intermittent in nature or that it may not always be necessary and that other, different factors could cause the HFS symptoms.

With respect to the various imaging features of NVC, we found a statistically-significant association with the presence of HFS symptoms only in cases of facial nerve displacement, a fact already pointed out by other authors. 10,16-19 This association suggests that the deformation caused on the facial nerve would produce a larger alteration in the myelin sheath than simple NVC, which would support the development of the manifestations. Chung et al.16 found a statistically-significant association between facial nerve displacement (visualised both by MRI and during surgery) and a better outcome of microvascular decompression, so this finding in MRI studies could help to select candidates for surgical treatment.

We found no statistically-significant differences in the association with the presence of HFS symptoms between single and multiple NVC, as was also the case in the study by Ho et al. ¹⁹ This suggests that a greater number of contact points on the facial nerve do not increase its excitability or that of its nucleus.

No statistically-significant differences between the various locations of NVC in the facial nerve were found either, although we did detect a higher percentage of symptomatic NVC in the proximal cisternal segment of the nerve than in the distal cisternal portion. This proximal cisternal portion of the nerve would include the root exit zone, where the myelin coating is thinner. It is possible that the lack of statistical significance has been affected by the low statistical power of the study and that increasing the sample would demonstrate a significant association between NVC in the proximal cisternal segment of the facial nerve and HFS symptoms.

In short, the MRI protocol integrating CISS sequences associated with 3D TOF sequences is sensitive, reproducible and effective in detecting NVC between the facial nerve and adjacent arteries. This protocol has also demonstrated a statistically-significant relationship between NVC presence and HFS symptoms. However, it is not a simple relationship, as HFS can be the result of the confluence of more factors.

Presentations

Part of this work was presented at the 29th National Padiology Congress of SERAM (Seville, 23-26 May 2008) as an electronic poster. No funding was received.

Conflict of interests

The authors declare no conflict of interests.

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