Intracranial Meningeal Enhancement Characterization

José Luis Mera C.1
Ana María Granados 2
Juan Sebastián Toro 3
Daniel Ospina Delgado 4
Andrés Felipe Borrero González 4

Summary

Objective: To describe the characteristics of intracranial meningeal enhancement (IME) as magnetic resonance imaging findings and their behavior under different associated conditions as described in the scientific literature. Materials and methods: Descriptive cross-sectional study with data collected from the images archive between January and December of 2011, obtaining 89 eligible studies in which it was determined, in the original reading, presence of IME as positive finding. Each study was subjected to further review by a neuroradiologist of the institution for morphological characterization of the IME. Results: The most common causes of IME were: metastatic disease (21.3%), infectious etiology (21.3%), history of intracranial surgery (20.2%) and primary neoplasms (13.5%). Of total CNS infections (19 cases), HIV infection was documented in 12 patients (70.6%). The patient with the oldest surgical history underwent craniotomy 17 years before performing the MRI included in the study, with persistance of IME with no signs of recurrence defined by image or clinical manifestations up to 2015. The most frequent IME type was leptomeningeal (LME) (46.1%), followed by mixed (MME) (43.8%) and pachymeningeal (PME) (10.1%) enhancements. In the subgroup of LME, the most common etiologies were: infectious (31.7%), metastatic disease (19.5%) and primary neoplasms (17.1%). This trend persisted in the subgroup of PME. In the subgroup of MME, post-surgical etiology was the leading cause (35.9%), followed by metastatic disease (23.1%) and infections etiologies (18%). Conclusion: Although a particular pattern of meningeal enhancement is not indicative of a specific pathology, detailed study of its features can provide information that allow the proposal of diagnostic groups, particularly in cases of neoplastic or infectious etiology, relevant contribution in cases where the abnormal meningeal enhancement is the only anormality in MRI.
Introduction

In neuroimaging, intravenous contrast and the resulting information of the enhancement produced after its administration is fundamental to reach the diagnosis of multiple pathologies by means of findings such as abnormal meningeal enhancement; however, its detection is inconsistent and its interpretation may vary depending on the experience of the radiologist and the technique of image acquisition.

Pathologic enhancement is the result of abnormal distribution of contrast medium in the intravascular and extracellular space (1). In general, we describe three locations in which pathologic enhancement occurs and their respective pathophysiological mechanisms.

Abnormal intravascular enhancement, without disruption of the blood-brain barrier (BBB) as a result of neovascularization, vasodilation, or abnormal arteriovenous communications that decrease mean transit time.

Extravascular, without disruption of BBB secondary to menigiomas, schwannomas or granulomatous diseases.

Extravascular, by disruption of BBB and filtration or leakage of the contrast medium in cases of neoplastic disease, infections, infarctions, inflammation with demyelination and trauma (2).

There is usually meningeal enhancement; however, when the integrity of the BBB is compromised as a consequence of some inflammatory process (3), a pathological meningeal enhancement pattern of the nodular and continuous type can be observed (3).

The meningeal enhancement pattern can be divided into two types, pachymeningeal and leptomeningeal; the first refers to enhancement of the dura mater and is identified in the dural reflections of the cerebral sickle, the tentorium, the sicle of the cerebellum and the cavernous sinus. It is typically thick and can be linear or nodular. The leptomeningeal is due to the enhancement of the pia and arachnoid, following the pial surface of the brain and covering the subarachnoid space of the grooves and cisterns. It is recognized by a gyriform or serpentine appearance (1).

The literature specifies some characteristics that allow the description of the meningeal enhancement pattern to guide differential diagnoses, such as the particular case of nodular enhancement and meningeal tuberculosis or sarcoidosis; however, in everyday practice, other different features are recognized that could further aid the practice of imaging diagnosis.

The visualization of the intracranial enhancement with contrast medium and therefore the meningeal enhancement in magnetic resonance (MRI) with the use of spin echo sequences has traditionally allowed an adequate characterization of the same; however, gradient echo sequences with volumetric acquisitions allow better spatial resolution, improving performance to visualize abnormal enhancement and small brain lesions (4-6). As for strategies to improve the sensitivity of intracranial enhancement, the 3 Teslas equipment has allowed the acquisition of images with better signal-to-noise ratio, less time and lower doses of contrast medium (2, 7-9).

Justification

Meningeal enhancement has been described as a radiological sign of multiple pathologies and, depending on its characterization and interpretation, may lead to a clinical diagnosis. However, the literature is scarce and subgroups of patients are described, mostly with a diagnosis of meningiomas, post-surgical changes or meningeal infection (1, 3, 10-13), so their usefulness as a sign is limited to a reduced spectrum of patients.

FVL, as a reference center, serves a wide variety of patients with multiple pathologies of the central nervous system (CNS), which frequently results in the sign of abnormal meningeal enhancement. Therefore, it is important to know how the different patterns of meningeal enhancement with respect to the pathologies that are treated in the institution behave, so that, through the judicious description and the appropriate characterization of the meningeal enhancement pattern, greater security can be obtained and thus make better use of this finding in normal clinical practice.

Objective

To describe the characteristics of intracranial meningeal enhancement (MRI) as a finding in MRI and its behavior according to the different associated pathologies described in the scientific literature.

Materials and methods

Descriptive cross-sectional study, with information obtained in 89 eligible studies, collected between January and December 2011, in which meningeal enhancement was determined as a positive finding in the original reading. Each study was retested by a neuroradiologist with 15 years of experience, for the morphological characterization of the meningeal enhancement.
Inclusion criteria

We included the studies of cerebral MRI with contrast medium, made in the 1.5 teslas equipment, in which the meningeal enhancement was recorded as a finding, with the terms pachymeningeal and leptomeningeal.

Exclusion criteria

Lack of medical history or insufficient information recorded.

Authorization of the medical ethics committee

After the authorization of the Ethics Committee in Biomedical Research of the institution for the study, the studies were assigned a code of identification, without names, surnames or any other data that allowed their identification, in order to guarantee the privacy of patients. The main investigator was in charge of the custody of the data and these were used solely for the purposes of this investigation. Taking into account that no human intervention was done in this research, they did not apply the Helsinki Declaration or the Geneva recommendations given for such research.

Based on Resolution 8430 of 1998, which establishes the scientific, technical and administrative norms for research in Colombia, this study was classified as risk-free since no intervention or modification of biological, physiological, psychological or social variables was required.

Procedure

We performed a search in the registration system (Centricity RIS) to document 982 brain MRIs with contrast medium in 2011; we obtained 259 studies describing meningeal enhancement as an abnormality, of which 89 met the inclusion criteria. Subsequently, the medical records of the patients to whom each study belonged were reviewed and the information was recorded in a database subject to reservation.

In addition, each study was re-examined by a neurosurgeon of the institution, a review performed in DICOM format and in a dedicated workstation, having all acquired MRI sequences available. From this review, we obtained information for the morphological characterization of meningeal enhancement.

Statistical analysis

Frequency distributions were used when the variables were qualitative, and summary measures and central tendency when the variables were quantitative.

Results

The 89 brain MRI studies reviewed belonged to 48 men (53.9%) and 41 women (46.1%), with ages ranging from 1 to 82 years (mean of 42.7 years). The most frequent causes of meningeal enhancement were metastatic disease, infectious etiology, history of intracranial surgery and primary neoplasms of the CNS (Table 1).

Table 1. Etiology of abnormal meningeal enhancement

<table>
<thead>
<tr>
<th>Cause of abnormal meningeal enhancement</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic disease</td>
<td>19</td>
<td>21.3</td>
</tr>
<tr>
<td>Infectious</td>
<td>19</td>
<td>21.3</td>
</tr>
<tr>
<td>Intracranial surgery</td>
<td>18</td>
<td>20.2</td>
</tr>
<tr>
<td>Primary neoplasm of the CNS</td>
<td>12</td>
<td>13.5</td>
</tr>
<tr>
<td>Not determined</td>
<td>6</td>
<td>6.7</td>
</tr>
<tr>
<td>Cerebral ischemia</td>
<td>3</td>
<td>3.4</td>
</tr>
<tr>
<td>Granulomatosis</td>
<td>3</td>
<td>3.4</td>
</tr>
<tr>
<td>Extension of extracranial neoplasia</td>
<td>3</td>
<td>3.4</td>
</tr>
<tr>
<td>Extraaxial bleeding</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Medication</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Primary vasculitis of the CNS</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td>100.0</td>
</tr>
</tbody>
</table>

In the cases of metastatic disease, the main primary neoplasms were breast cancer (Figure 1) in 7 patients (36%), lung cancer in 3 (15%), leukemia in 2 (10.5%) and non-Hodgkin’s lymphoma in 2 (10.5%).

In the 19 cases of infectious etiology, the majority showed HIV-associated CNS infection, 12 patients (70.6%), 7 cases of toxoplasmosis, 3 cases of cryptococcosis (Figure 2) and 2 cases of tuberculosis (TB) were found. The particularity of up to 2 of these opportunistic diseases were found simultaneously in 3 patients.

In the 7 HIV negative patients the etiology was bacterial in 3 cases, viral in 2 and tuberculosis (Figure 3) and toxoplasmosis in the 2 remaining cases.

In order to select the intracranial surgery group, the surgical history was determined as the primary cause of enhancement; patients with active infection at the time of the study or with a diagnosis of recurrent or residual primary neoplasms were excluded from this group. Surgeries were indicated for malignant neoplasm in 12 patients (66%), benign neoplasm represented by meningiomas in 3 (16%) and non-neoplastic pathology (Figure 4) in 3 (16%).

In this group, the oldest patient with abnormal enhancement was submitted to meningioma resection 17 years before the MRI included in the study, with no definition of signs of relapse due to imaging or clinical signs.

In the group of primary CNS neoplasms, studies were included in which the patients were not submitted to surgery until the MRI. The neoplasias with histopathological postsurgical diagnosis were 2 glioblastomas, 3 medulloblastomas, 1 anaplastic astrocytoma, 1 rhabdoid tumor of the posterior fossa and 1 ependymoma. Additionally, two studies with lesions in the pontocerebellar angle were included in this group of primary neoplasms, which were not submitted to a surgical procedure or biopsy and showed no signs of malignancy at clinical follow-up.

For the characterization of the meningeal enhancement, the type was determined as leptomeningeal, pachymeningeous or mixed. The morphology of the enhancement was determined as smooth, nodular or mixed and extension as focal and diffuse, defining diffuse enhancement when there is extension to two intracranial anatomical regions (eg, frontal and parietal enhancement) or contralateral extension. Additionally, it was classified as infratentorial, supratentorial or mixed according to the location of the tentorium (Table 2).

Figure 1. Metastasis of infiltrating ductal breast cancer and leptomeningeal carcinomatosis. MRI with T1 information. a) Simple. b) With contrast medium: left temporal intraaxial nodular lesion and smooth and nodular leptomeningeal enhancement.

Figure 2. Cryptococcosis in a patient diagnosed with HIV. MRI with T1 information. a) Simple. b) With contrast medium: nodular leptomeningeal enhancement in the posterior fossa.

Figure 3. Patient diagnosed with tuberculous meningitis associated with HIV. MRI with T1 information. a) Simple. b) With contrast medium: nodular leptomeningitis and pachymeningeal enhancement by empyema drainage craniotomy antecedent.

Figure 4. Background of right temporal arachnoid cyst resection. MRI a) FLAIR sequence. b) Sequence with T1 information with contrast medium of the vertex; diffuse smooth pachymeningeal enhancement.
The most frequent type of enhancement was the leptomeningeal (46.1%), followed by the mixed one (43.8%) and the pachymeningeal one (10.1%). In the subgroup of leptomeningeal enhancement the most frequent etiologies were infectious (31.7%), metastases (19.5%) and primary neoplasias (17.1%), with a prevalence of this tendency in the subgroup of pachymeningeal enhancement. In the mixed enhancement subgroup, postoperative etiology was the first cause (35.9%), followed by metastatic disease (23.1%) and infections (18%).

Postoperative etiology (29%) and metastatic disease (23.7%) were the main causes of smooth enhancement, while infectious etiology (36.4%) was the first cause of nodular enhancement, followed by metastatic disease 21.2%).

In cases of infectious etiology, a predominance of the pattern of leptomeningeal, nodular and diffuse enhancement was found. In the 7 cases diagnosed with HIV and concomitant toxoplasmosis, 5 presented smooth pachymeningeal enhancement. In the cases of metastatic disease and post-surgical etiology, the tendency was diffuse enhancement without identifying a predominant characteristic in cases of primary neoplasia.

Patients with cerebral toxoplasmosis presented, in its majority, a leptomeningeal, nodular, diffuse and supratentorial localization.

In a case of CBT, smooth and localized leptomeningeal enhancement was observed; however, in the more advanced cases (2 cases) the enhancement was predominantly nodular and diffuse (Figure 3).

Table 2. Imaging characterization of abnormal meningeal enhancement according to etiology and number of cases by category

<table>
<thead>
<tr>
<th>Type</th>
<th>Morphology</th>
<th>Extension</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastasis</td>
<td>Focal</td>
<td>Mixed</td>
<td>Infra-</td>
</tr>
<tr>
<td>Infectious</td>
<td>Focal</td>
<td>Mixed</td>
<td>Supra+</td>
</tr>
<tr>
<td>Intracranial surgery</td>
<td>Liso</td>
<td>Mixed</td>
<td>Mixed</td>
</tr>
<tr>
<td>Primary neoplasm of the CNS</td>
<td>-</td>
<td>-</td>
<td>Infra-</td>
</tr>
<tr>
<td>Not determined</td>
<td>-</td>
<td>-</td>
<td>Supra+</td>
</tr>
<tr>
<td>Cerebral ischemia</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Granulomatosis</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Extracranial neoplasia</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Extraaxial bleeding</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Medication</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
<tr>
<td>Primary vasculitis of the CNS</td>
<td>-</td>
<td>-</td>
<td>Mixed</td>
</tr>
</tbody>
</table>

* Leptomeningeal, ** Pachymeningeal, -Infratentorial, + Supratentorial

Discussion and Conclusion

The pathophysiological mechanisms that explain the occurrence of abnormal meningeal enhancement such as BBB disruption, vasodilatation and neovascularization (1, 2) are characteristic of pathologies of inflammatory, infectious and tumor origin. In 55% (49, n = 89) of the cases studied, the etiology of abnormal meningeal enhancement was metastatic disease (21.3%), intracranial surgery (20.2%), and neoplasia (13.5%), which is also expected considering that the institution where the study was developed is a reference center for southwestern Colombia and offers the service of clinical neurology, neurosurgery, oncology and radiotherapy. These results are in accordance with those obtained in a clinical-radiological correlation study that included 34 patients studied by MRI with contrast medium, in whom secondary neoplastic infiltration was the first cause (38%), followed by iatrogenic etiology (30%) and inflammatory causes of infectious type (20%) (14).

As a particular consideration and because the antecedent of intracranial surgery is a recognized cause of pachymeningeal enhancement in up to 99% of patients undergoing surgery without a history of neoplasia (1, 3, 15-17), it was decided to determine this antecedent as the primary cause of enhancement. A pattern was found in which the pachymeningeal and leptomeningeal (mixed) enhancement coexist, tending to be smooth, diffuse and of infra and supratentorial location regardless of the site of the surgery, posterior fossa or not. Another notable finding was the persistence of enhancement for more than 17 years, following intracranial
Primary and secondary CNS tumors share alterations in BBB permeability and angiogenesis, as a mechanism that leads to meningeal enhancement (19, 20). In the present study, none of these etiologies described a distinctive meningeal enhancement pattern. It is noted that most of the primary tumors of the study were of high grade and breast cancer was the leading cause in the metastatic disease group.

The infectious etiology as a cause of abnormal meningeal enhancement is recognized and constitutes a diagnostic tool for the detection of this type of pathologies (1, 11-13, 20-24). It is representative of the number of cases where enhancement is associated with HIV infection and concomitant opportunistic infection (12 cases). In the subgroup of 7 with a diagnosis of toxoplasmosis as the only opportunistic infection, a pituitary-leptomeningeal pattern and nodular lesions in 5 of the cases were observed, a finding consistent with the description of the MRI pattern with typical contrast medium of ring or nodular enhancement of the focal lesions (25-28). An additional finding was that in the 3 patients diagnosed with cryptococcosis the type of enhancement and morphology was different in each, diffuse involvement and supra and infratentorial localization were constant, with nodular morphology enhancement in the mesencephalic region and posterior fossa.

An additional finding in the study was the increase in cerebrospinal fluid (CSF) signal in the FLAIR sequence, associated with leptomeningeal enhancement in cases of infectious etiology, a finding theoretically attributable to the increase in protein concentration as a consequence of the BBB (21, 23, 29). The authors of this study recommend the joint visualization of the T1 sequence with contrast medium and FLAIR (Figure 5) as an alternative to the use of FLAIR with contrast medium.

In the other types of infectious agents, a uniform pattern or tendency of enhancement was not recognized, because the cases studied were few and most were in advanced clinical stages, in which pathologies such as TB tend to present enhancement nodular more evident.

In the other etiological groups, the number of patients does not allow to describe characteristics that are useful for a differential diagnosis; However, in particular cases, such as neurosarcomiosis, meningeal involvement was predominantly basal and of cranial pairs, with nodular enhancement and supra and infratentorial localization (Figure 6), findings consistent with that described in different publications (30-34). One category referred to in the study was the meningeal enhancement of drug etiology, documented in two patients with a diagnosis of reversible posterior leukoencephalopathy syndrome induced by L-asparaginase as treatment of acute lymphoblastic leukemia (35, 36), an entity already described in the literature and, in the particular case of patients in the present study, associated with infratentorial smooth leptomeningeal enhancement (Figure 7).

Although abnormal meningeal enhancement and its characteristics do not allow a diagnosis to be made on its own, postsurgical status, infections, and primary or secondary oncologic disease are established causes of abnormal meningeal enhancement; This is why it is very useful to know the pathophysiological mechanisms that lead to abnormal meningeal enhancement as a finding, which allows the radiologist to propose diagnostic alternatives that are more in line with the requirements of the requesting physician and which, together with sufficient clinical data, allow for a more accurate diagnosis. The detailed study of the characteristics of meningeal enhancement in specific subgroups, such as infectious or neoplastic diseases, provides information that allows a more specific diagnosis or the discarding of less probable pathologies, a fact of special importance in cases in which the abnormal meningeal enhancement is the only obvious abnormality in an MRI.
Referencias


Correspondence
José Luis Mera C.  
Universidad ICESI  
Calle 18 # 122-135  
Cali, Colombia  
jolumeco@hotmail.com

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