MRI for detecting neoplastic and non-neoplastic meningitis: a comparison with cerebrospinal fluid cytology

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**Purpose**

- The spread of cancer cells into the cerebrospinal fluid (CSF) is a devastating complication of solid tumours with an incidence of 5-15%.
- An early diagnosis of a meningeal involvement of the disease is important to improve patients’ survival.
- Cerebrospinal fluid cytology is the gold-standard to diagnose neoplastic and non-neoplastic meningitis. Contrast-enhanced magnetic resonance imaging (MRI) is also routinely performed in patients with typical clinical symptoms. In the literature for both methods the sensitivity is reported to be limited, however for the CSF-cytology the reported specificity is around 95%, for MRI the reported specificity is as low as 50%.
- Published data reporting about a direct comparison of these two diagnostic modalities are very limited. Therefore, the aim of the study was to compare the diagnostic value of MRI with the results from CSF cytology in patients with neoplastic and non-neoplastic meningitis.

**Methods and Materials**

*Patients*

Between 2000 and 2010 we performed both cytology and contrast enhanced MRI in patients suspicious for neoplastic meningitis. Patients were primarily recruited from the department of haematology. All patients gave written informed consent for both examinations. In all cases, MRI was performed before lumbar puncture. This retrospective study was conducted in accordance with the principles of the Helsinki Declaration. The local institutional review board approved the study protocol.

*Magnetic resonance imaging (MRI)*

All patients underwent MRI using a 1.5 Tesla scanner (Avanto®, Siemens, Erlangen, Germany) with a standard head coil. Brain MR images were obtained in the axial, sagittal, and coronal planes by using three sequences including a T2-weighted axial turbo spin-echo pulse sequence with fat suppression, a pre-contrast fluid-attenuation inversion-recovery (FLAIR) spin-echo sequence and a non-contrast enhanced and a contrast-enhanced T1-weighted spin-echo sequence. Slice thickness was 5 mm for all sequences. Before acquisition of contrast enhanced images, all patients underwent diffusion-based echo-planar MRI. The b values were 0, 500, and 1000. At b values differing from 0, diffusion gradients were applied in three orthogonal directions in order to calculate the diffusion trace value.
The contrast-enhanced sequence was obtained after bolus injection of a dose of 0.2 ml/kg contrast agent with a flow rate of 2 ml/s (Magnevist®, BayerHealthcare, Leverkusen, Germany). All imaging studies were reviewed by two experienced radiologists and decisions on findings were made by consensus.

All sequences were evaluated independently from each other regarding the presence of a meningeal, pial or intraparenchymal signal or contrast enhancement to refer to an inflammatory or malignant intracerebral process. Additionally, all sequences were evaluated together to make a MRI diagnosis. These findings were correlated to the final diagnosis.

Meningeal findings were described with the following characteristics: Nodular meningeal tumour, meningeal thickening > 3 mm and a subjectively strong contrast enhancement were suspicious for neoplastic meningitis. A smooth contrast enhancement of the meninges was judged to be typical for inflammatory meningitis.

**CSF processing**

Cerebrospinal fluid (CSF) was obtained by lumbar puncture. The fresh specimens for cytology were centrifuged, re-suspended in phosphate buffered saline (PBS) and diluted according to cell count. The specimens were morphologically categorized to be either malignant, suspicious of malignancy, reactive/normal or non-diagnostic. The term "malignant" was used only in cases with clear morphologic changes consistent with lymphoma, leukaemia or carcinoma. Samples with small lymphocytes, macrophages and ependymal cells were judged as "reactive/normal". All samples with doubtful cell morphology were classified as "suspicious".

**Statistical analysis**

Statistical analysis was performed using GraphPad® software fisher`s exact test. Diagnostic findings of CSF and MRI were compared to the final clinical diagnosis. The sensitivity for diagnosing meningeal involvement of the disease with CSF cytology and with MRI was calculated. Additionally, the results were evaluated separately for patients with leukaemia, lymphoma, solid tumours and for patients with inflammatory meningitis. Positive predictive value (ppv) for MRI to differentiate infectious meningitis from neoplastic meningitis was calculated. Additionally, ppv was calculated for MRI to specify neoplastic meningitis in dependence to different tumour types. Statistical significance was tested on a 95% significance level.

**Results**
68 patients were included in this study. 44 patients (64.7%) had neoplastic meningitis, 21 patients (30.9%) had non-neoplastic meningitis. The sensitivity to diagnose meningeal disease was 49.2% for MRI and 95.4% for cytology (p<0.001), fig. 1. In patients with neoplastic meningitis, sensitivity was 45.5% for MRI and 93.2% for cytology (p<0.001), fig. 1. In patients with infectious meningitis, sensitivity was 57.1% for MRI and 100% for cytology (p=0.0013). In patients with solid tumours, the sensitivity was 84.6% for both diagnostic methods. The sensitivity for MRI was low in patients with leukaemia (20.0%) and lymphoma (37.5%). The positive predictive value (PPV) for MRI to differentiate infectious from neoplastic meningitis was high in patients with infectious meningitis (75.0%), in patients with lymphoma (83.3%), and in patients with solid tumours (72.7%), fig. 2. Ppv was low in patients with leukaemia (33.3%). FLAIR sequence as well as contrast-enhanced T1-weighted images are the most important sequences to diagnose meningitis, figures 3-5.

Images for this section:

<table>
<thead>
<tr>
<th>Underlying disease</th>
<th>Sensitivity (MRI)</th>
<th>Sensitivity (CNS cytology)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic meningitis (n=44)</td>
<td>45.5 (20/44)</td>
<td>93.2 (41/44)</td>
</tr>
<tr>
<td>Solid tumours (n=13)</td>
<td>84.6 (11/13)</td>
<td>84.6 (11/13)</td>
</tr>
<tr>
<td>Leukaemia (n=15)</td>
<td>20.0 (3/15)</td>
<td>100 (15/15)</td>
</tr>
<tr>
<td>Lymphoma (n=16)</td>
<td>37.5 (6/16)</td>
<td>93.8 (15/16)</td>
</tr>
<tr>
<td>Leukaemia and lymphoma (n=31)</td>
<td>29.0 (9/31)</td>
<td>96.8 (30/31)</td>
</tr>
<tr>
<td>Non-neoplastic meningitis (n=21)</td>
<td>57.1 (12/21)</td>
<td>100 (21/21)</td>
</tr>
</tbody>
</table>

**Fig. 1:** Sensitivity for CSF-cytology and MRI in diagnosing neoplastic and non-neoplastic meningitis as well as results in dependence of tumour origin. Given are the sensitivity in % as well as the absolute number of patients which were correctly diagnosed / all patients with specific meningitis (in brackets).
**Fig. 2:** Positive predictive value (ppv) for MRI in diagnosing neoplastic and non-neoplastic meningitis in dependence of tumour origin. Given are the ppv in % as well as the number of patients which were correctly diagnosed having specific meningitis from all patients with correctly diagnosed as positive for meningitis (in brackets).

<table>
<thead>
<tr>
<th>Meningitis Underlying disease</th>
<th>Correctly interpreted as neoplastic meningitis (ppv) with MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic meningitis (n=44)</td>
<td>70.0 (14/20)</td>
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<tr>
<td>Solid tumours (n=13)</td>
<td>72.7 (8/11)</td>
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<td>Leukaemia (n=15)</td>
<td>33.3 (1/3)</td>
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<td>Lymphoma (n=16)</td>
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<td>Leukaemia and lymphoma (n=31)</td>
<td>66.7 (6/9)</td>
</tr>
<tr>
<td>Non-neoplastic meningitis (n=21)</td>
<td>75.0 (9/12)</td>
</tr>
</tbody>
</table>

**Fig. 3:** Pathological findings on the different MRI sequences within the subgroup of patients with positive MRI findings and neoplastic meningitis (n=20). Given are the absolute number of patients; multiple choices were possible.
**Fig. 4:** Pathological findings on the different MRI sequences within the subgroup of patients with positive MRI findings and non-neoplastic meningitis (n = 12). Given are the absolute number of patients; multiple choices were possible.
Fig. 5: Coronal plane of MRI from a 65 year old patient with prostate cancer (right: FLAIR sequence, left: T1w contrast-enhanced sequence). MRI showed a hyperintense signal of the dura mater (arrows) and diagnosed the meningitis correctly. The FLAIR sequence alone did not allow the differentiation between neoplastic and inflammatory meningitis; this was only possible with the T1w contrast-enhanced sequences showing a dural thickening and a strong dura-arachnoid pachymeningeal contrast enhancement.
Conclusion

In conclusion, diagnostic value of MRI for the diagnosis of meningitis is limited in patients with hematopoietic malignancy. MRI had the same sensitivity in diagnosing neoplastic meningitis compared to CSF cytology in patients with solid tumours. Further studies with a large patient cohort and based on a gold standard such as histopathologic specimen are necessary to evaluate not only the sensitivity but also the diagnostic accuracy of MRI.

References

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