MR findings in Creutzfeldt-Jakob disease.

Award: Cum Laude
Poster No.: C-1808
Congress: ECR 2012
Type: Educational Exhibit
Authors: S. Alfonso Cerdan¹, F. Nunez¹, B. Gómez-Anson¹, P. Alcaide Leon², I. Sala Matavera¹, M. de Juan-Delago¹, J. L. Munuera del Cerro¹, E. Granell³, A. Lleo¹;¹Barcelona/ES, ²Sevilla/ES, ³Hospitalet De Llobregat/ES
Keywords: Neuroradiology brain, MR, Diagnostic procedure, Dementia
DOI: 10.1594/ecr2012/C-1808

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

Illustrate Magnetic Resonance (MR) findings in 12 patients with Creutzfeldt-Jakob disease (CJD).
Background

CJD is a rapidly progressive neurodegenerative disease that is invariably fatal [1, 2]. It is one of spongiform encephalopathies, caused by prions (infectious protein agents), group in which sporadic CJD, fatal familial insomnia, familial CJD, Gertsmann-Straussler-Scheinker disease, iatrogenic CJD, kuru and variant-CJD are included [2].

A prevalence of 1 case per million and an incidence of approximately 2 new cases per million have been estimated [2, 3]. About 90% of cases are classified as sporadic CJD, with no known precipitating cause [4]. In sporadic CJD the average age of onset is 60 years, with a mean course of 5 months [1].

Symptoms may vary depending on the stage of the disease, often being nonspecific in early stages [5]. Rapid and progressive cognitive impairment is the main feature, progressing to pyramidal and extrapyramidal symptoms, periodic synchronous discharges on EEG and myoclonus, resulting in a state of akinetic mutism and death, often within one year after the onset of symptoms [2]. At present, no specific treatments for prionic diseases are available.

Diagnosis of CJD is based in clinical, electroencephalographic and imaging findings, though definitive diagnosis can only be made after histological study of affected brain tissue. Classical histological findings in CJD are neuronal loss, spongiform changes and astrocytic gliosis [1]. Under circumstances above, CJD is extremely difficult to diagnose in its early stages. Early diagnosis/suspicion is important in order to differentiate from other causes of rapidly progressive dementia which are potentially treatable (ie. Hashimoto encephalopathy) and to prevent human-to-human transmission [5]. Regarding imaging techniques, head CT has been traditionally used for excluding potentially treatable causes for cognitive impairment [2]. Studies do not show specific CT findings in CJD, only different degrees of atrophy in advanced cases [1]. MR has become the main imaging technique in early diagnosis of CJD.

CJD criteria in MR have been classified into three characteristic patterns [1, 6, 7]:

- Extensive cortical ribboning high signal (more than 3 gyri) without adjacent white matter involvement on FLAIR or DWI sequences.
- Head of caudate nucleus and putamen (unilateral or bilateral) high signal in T2, FLAIR and/or DWI sequences.
- High signal (unilateral or bilateral) involving the striatum AND more than one cortical gyrus in FLAIR and/or DWI sequences.

Other criteria are the absence of contrast enhancement, the absence of T1 signal changes in the affected regions, the absence of artifacts that explain the high signal and the absence of incidental findings that may explain the clinical features (tumour, encephalitis).
Thalamic high signal (pulvinar sign) is characteristic of patients with variant CJD, although it has also been described in sporadic CJD [1, 7].

Cortical and basal ganglia changes are more clearly seen and appear earlier in DWI sequences than in FLAIR [5] (combining both techniques a sensitivity and specificity over 91% has been estimated [1, 7]). DWI sequence can be the only showing signal abnormalities, and can be used to follow progression of the disease [5]. It has been suggested that high signal lesions depicted by DWI are related to spongiform changes rather than to prionic protein deposition [5].

Published series have shown that mixed pattern (cortical and basal ganglia) is the most frequently observed (68%), followed by pure cortical pattern (24%) [7]. Involvement of basal ganglia without cortical involvement is rare. The cortical high signal can affect any area, being frontal lobes the most often affected [1].

Final stages of the disease can show normalization of the signal and, in some cases, parenchymal atrophy.
Imaging findings OR Procedure details

We reviewed cases of rapidly progressive dementia between 1994 and 2011 at our institution (n = 81, 40 women, mean age at diagnosis 69.9 ± 13). Twelve patients were diagnosed of CJD (all of them had positive immunoassay for the 14.3.3 protein in cerebrospinal fluid and typical EEG changes establishing diagnosis with the revised WHO criteria. Four cases were histologically proven).

The diagnosis of CJD was made according to the revised WHO criteria [8] (definitive diagnosis is made after histological confirmation; probable diagnosis is made when rapidly progressive dementia is associated with two of the following: myoclonus, visual/cerebellar signs, pyramidal/extrapyramidal signs, akinetic mutism and typical EEG pattern and/or a positive 14-3-3 protein in CSF). European CJD consortium criteria [6] (which also include radiological criteria) were also applied in patients with MR available.

Table 1 summarizes the data of the reviewed patients.

Patterns of cortical and subcortical (basal ganglia and thalami) high signal intensity in fluid attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) sequences are described in Table 2.

Two patterns of involvement were identified: 1) cortex, basal ganglia and thalami, and 2) pure cortical, both with and without hippocampal involvement. Demonstrative examples of both patterns are presented (Fig 1-8).

7 cases out of 12 showed cortical and basal ganglia high signal; three of which showed thalamic pulvinar high signal. Four cases showed cortical high signal with normal basal ganglia and thalami. One case showed basal ganglia and thalami high signal with normal cortex. None of the reviewed MR was normal.
**Table 1**

Data of reviewed patients

<table>
<thead>
<tr>
<th>CASE</th>
<th>AGE</th>
<th>GENDER</th>
<th>YEAR</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>77</td>
<td>F</td>
<td>2003</td>
<td>CJD (+ HISTOLOGY)</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
<td>F</td>
<td>2004</td>
<td>CJD (+ HISTOLOGY)</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>F</td>
<td>2006</td>
<td>CJD (+ HISTOLOGY)</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td>F</td>
<td>2001</td>
<td>CJD (+ HISTOLOGY)</td>
</tr>
<tr>
<td>5</td>
<td>78</td>
<td>F</td>
<td>2007</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>6</td>
<td>51</td>
<td>F</td>
<td>2006</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>7</td>
<td>72</td>
<td>M</td>
<td>2006</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>F</td>
<td>2007</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>9</td>
<td>67</td>
<td>F</td>
<td>2005</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>10</td>
<td>81</td>
<td>F</td>
<td>2006</td>
<td>PROBABLE CJD</td>
</tr>
<tr>
<td>11</td>
<td>50</td>
<td>F</td>
<td>2010</td>
<td>PROBABLE CJD (GSS variant)</td>
</tr>
<tr>
<td>12</td>
<td>79</td>
<td>F</td>
<td>2011</td>
<td>PROBABLE CJD</td>
</tr>
</tbody>
</table>

All cases showed positive 14-3-3 protein in CSF and typical EEG changes, establishing diagnosis with WHO revised criteria. Patients died in less than one year in all cases.

**Table 1**: Data of reviewed patients.

© Sant Pau - Barcelona/ES
**Table 2:** FLAIR and DWI findings in reviewed MR.

<table>
<thead>
<tr>
<th>CASE</th>
<th>CORTEX</th>
<th>BASAL GANGLIA</th>
<th>THALAMIC PULVINAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FLAIR + DWI-</td>
<td>FLAIR - DWI-</td>
<td>FLAIR - DWI-</td>
</tr>
<tr>
<td>2</td>
<td>FLAIR ++ DWI ++</td>
<td>FLAIR - DWI-</td>
<td>FLAIR - DWI-</td>
</tr>
<tr>
<td>3</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>4</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>5</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>6</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>7</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>8</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>9</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>10</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>11</td>
<td>FLAIR + DWI +</td>
<td>FLAIR - DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
<tr>
<td>12</td>
<td>FLAIR - DWI-</td>
<td>FLAIR + DWI+</td>
<td>FLAIR + DWI+</td>
</tr>
</tbody>
</table>

© Sant Pau - Barcelona/ES
Case 9: pure cortical pattern. Image above shows asymmetric right parietal-occipital cortical high signal in diffusion and FLAIR. Image below shows normal signal intensity in basal ganglia.

Fig. 1: Pure cortical pattern.

© Sant Pau - Barcelona/ES
Fig. 2: Histologically proven CJD and pattern of cortical involvement.

© Sant Pau - Barcelona/ES
**Fig. 3:** Pure cortical pattern.

© Sant Pau - Barcelona/ES
**Fig. 4:** Pattern of mixed involvement.

Case 11: 51-year-old woman, with positive 14-3-3 protein in CSF and diagnosis of probable prion disease (Gerstmann-Straussler-Scheinker). Pattern of mixed involvement: three images above show basal ganglia high signal of on FLAIR and DWI, with restricted ADC. Bottom image shows faint bilateral hippocampal and asymmetric right lateral temporal cortical high signal (arrow).
**Fig. 5:** Bilateral basal ganglia high signal on diffusion and FLAIR (top images). Bilateral hippocampal high signal on diffusion and FLAIR (bottom images, arrows).

© Sant Pau - Barcelona/ES
**Case 8:** patient diagnosed of probable CJD. On the right, left temporal cortex high signal on FLAIR and diffusion can be seen.

Left image of the same patient shows left temporal-parietal cortex high signal (arrows) on diffusion, as well as mild bilateral high signal in heads of both caudate nuclei.

**Fig. 6:** Probable CJD and pattern of mixed involvement.

© Sant Pau - Barcelona/ES
Fig. 7: Histopathologically proven CJD with pattern of mixed involvement.

© Sant Pau - Barcelona/ES
Fig. 8: Probable CJD with bilateral asymmetrical basal ganglia and slightly bilateral thalamic pulvinar (arrows) high signal.

© Sant Pau - Barcelona/ES
Conclusion

- Prion diseases are a clearly definite group amongst rapidly progressive dementias, which include CJD, and typical brain MR findings can be found, being useful in the difficult diagnosis of this disease in its early stages.

- MRI protocol in patients with suspected CJD must pay special attention to FLAIR and DWI sequences.

- Typical findings include signal abnormalities (cortical and basal ganglia high signal), with characteristic distribution patterns that radiologists must recognize.


