Overlap between Creutzfelt-Jakob Disease and Paraneoplastic limbic encephalitis

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Introduction

• Creutzfeldt-Jakob disease (CJD) or Subacute Spongiform Encephalopathy is a very rare neurodegenerative disease of the brain that belongs to the prion diseases category.
• Limbic encephalitis (LE) is frequently associated with neoplasia, 80% of cases are associated with bronchial cancer, typically small cell lung carcinoma. An overlap of those two diseases is incredibly rare. Our patient exhibits signs and symptoms that suggest this rare occurrence.

• The patient was admitted for: major headache, of a very high intensity (8/10), enhanced at occipital level with frontal irradiation, which did not yield to NSAIDs, temporo-spatial disorientation (a few months ago the family reported cognitive impairement) partial motor seizure in the upper right arm (1 month ago) ,physical asthenia, weight loss (10 kg of about 6 months).

• Keeping in mind the similar clinical characteristics (cognitive impairment, personality changes, depression, anxiety, hallucinations, convulsions) sometimes it is difficult to differentiate between CJD and LE, especially at the onset of the disease.

• The spinal fluid can be positive for the "14-3-3" protein in both pathologies but the presence of inflammatory cells and the Hu Antibodies are frequently present in LE.

• On the EEG, high voltage, slow (1-2 Hz) and sharp complexes on an increasingly slow and low-voltage background are suggestive for CJD.

Methodology

• Our patient is a 66 years old female, who in the absence of fever, presented a confusional state and in 6 months developed focal seizures.

Workup:

-To rule out a toxic or a metabolic encephalopathy : Serum CBC count, liver enzymes, ESR, alcohol, sedative (barbiturates, hypnotics), heavy metals, organophosphorus, tricyclic antidepressants, anticholinergics, opioid analgesics, anticonvulsants.

- the thyroid function was evaluated (FT4, TSH), B12 levels, folate levels.

- VDRL test for neurosyphilis.

- HIV testing.

- serum levels of anti-thyroperoxidase antibodies to rule out Hashimoto ncephalopathy.

- spinal tap was performed and the CSF was evaluated for cell count, protein, glucose, bacterial cultures, viral cultures and VDRL.
- antineuronal antibody testinig: CSF samples were tested for autoimmune encephalitis-associated antineuronal (HuD, NMDAR, GABA b1/b2) antibodies
- CSF: 14-3-3 protein.

• An EEG was performed.

• The brain MRI showed hyperintensity in the bitemporal areas including the limbic zone.

• In addition to MRI a chest X ray was performed to rule out the posiibility of a malignancy that could be producing a paraneoplastic syndrome.

Results

• CBC: leukocytosis with neutrophilia; Elevated creatinine level. Increased alkaline phosphatase and CA 15-3.

• The chest X ray examination found micronodules in both pulmonary fields.

• Thoracic CT scan showed diffuse intertitial infiltrates with micronodular appearance.

•The EEG was suggestive for CJD (microvoltage, the appearance of sharp waves complexes).

• The spinal tap identified the Hu antibodies and the 14-3-3 protein.

• The postmortem examination established the diagnosis of pulmonary neoplasia with small cells and the brain showed structural changes suggestive for CJD.

Conclusion

• The particularity of this case consists in the overlap of those two rare neurological pathologies and the difficulty in establishing the accurate diagnosis.

• In retrospect, our patient met the 2010 CDC criteria for possible or probable CJD
• Several other studies have addressed the clinical overlap between prion disorders and autoimmune encephalitis.

• The Dutch surveillance Centre for Prion Diseases performed almost 400 autopsies on patients with suspected CJD over a 14 year period and found out that in 50% of the patients with autoimmune encephalitis tested, 14-3-3-protein was elevated in CSF, this result increasing the difficulty of distinguishing between the two pathologies.

• In general the prognosis of autoimmune encephalitis appears to be determined by the involved immunopathogenic mechanism. Most paraneoplastic neurologic disorders with onconeural antibodies respond poorly to immunotherapy

• CJD is a rapidly progressive neurodegenerative disease and the outcome is fatal.

• It is important to consider both prion and immune-mediated disorders in the differential diagnosis of rapidly progressive cognitive impairment, keeping in mind that EEG and 14-3-3- protein in CSF do not discriminate sufficiently to distinguish the two.

Acknowledgements

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