Carcinomatous meningitis mimicking Creutzfeldt-Jakob disease


Department of Neurology, *Department of Pathology, Goa Medical College, Bombolim, Goa, **Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore, India.

We report a case of carcinomatous meningitis diagnosed at autopsy that was clinically diagnosed as a case of Creutzfeldt-Jakob disease (CJD) because of rapidly evolving dementia. Pathological study revealed diffusely spreading carcinomatous meningitis, infiltrating into cortex along Virchow Robin space. Immunostaining for Prion protein was negative. Despite advances in clinical diagnosis, tissue diagnosis remains a pre-requisite for confirmation of CJD.

Key Words: Carcinomatous meningitis, CJD, Dementia

Introduction

We describe a case of rapidly progressive dementia (over a period of 6 months) with myoclonus associated with pyramidal and extrapyramidal symptoms, clinically diagnosed as a case of sporadic CJD from Goa, South Western India. Autopsy revealed diffuse carcinomatous meningitis and multiple small cerebral and cerebellar metastasis. This exemplifies that despite advances in clinical diagnosis of CJD, confirmation by tissue diagnosis is still essential for a definitive diagnosis and family counseling.

Case Report

A 56-year-old lady presented to Goa Medical College in April 2001, with complaints of disturbed sleep from August 2000, headache and memory impairment from February 2001. According to the informant, she had photophobia, abnormal behavior, emotional lability, hallucinations, incoherent speech and urinary incontinence. She was a non-vegetarian consuming pork, fish and chicken but was allergic to beef. At home she reared cats, dogs and pigs for many years. She had undergone surgery to the knee following trauma, without any tissue grafts or prosthesis. No family history of similar illness was recorded.

She was diagnosed to have type II diabetes mellitus and was receiving human insulin for 3 months (Human Mixtard 10-6 units, Novo Nordisk).

On clinical examination, she had features of dementia, bilateral pyramidal paresis, fasciculations in the hamstrings and quadriceps muscles, extrapyramidal rigidity, ataxia and myoclonus in upper limbs. Mini Mental status examination for evaluation of the cognitive state could not be carried out in ‘Konkani’ language as no standardized battery of tests was available. She was unable to walk and was bed bound. She received alimentation through a nasogastric tube on account of dysphagia for both solids and fluids.

Routine hematological, serological, biochemical and CSF examination were within normal limits, except for raised the CSF protein (140 mg/dl). CSF cytology was negative for AFB, cryptococci and malignant cells. Serum was not tested for HIV. Cranial CT scan revealed bilateral mild cortical atrophy, involving parietal-occipital lobes. EEG carried out after admission revealed diffuse theta activity though the patient was conscious but no periodic triphasic sharp waves were detected.

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In view of rapidly progressive dementia in a 56-year-old lady with myoclonus, extrapyramidal symptoms and ataxia, a diagnosis of Creutzfeldt Jakob disease was considered, though the EEG did not reveal characteristic features. CSF could not be tested for 14-3-3 protein, as the facility is not available in India.

For the terminal three days of the illness, she was stuporous, developed left midzone pneumonia and signs of deep vein thrombosis in the left lower limb. She succumbed to pneumonia 15 days after admission to the hospital and 9 months after the onset of symptoms.

Limited autopsy confined to examination of brain alone, was conducted 3 hours post mortem. On gross examination, moderate diffuse cortical atrophy was the only pathology. There was no evidence of cerebrovascular atherosclerosis. Representative sections from different anatomical areas of the brain embedded in paraffin were submitted to CJD Registry, Department of Neuropathology, National Institute of Mental Health and Neurosciences. All the sections were stained with Haematoxylin-Eosin, Luxol Fast Blue for myelin and Periodic Acid Schiff for preliminary delineation of amyloidotic plaques.

Sections from frontal, occipital cortex and cerebellum were immunostained with monoclonal antibody to prion protein clone, K09
(monoclonal specific to PrP\textsuperscript{\textalpha}, peptide segment, aminoacids 140-180, BBSRC Resource Centre, courtesy Dr. J.W. Ironside, Consultant Neuropathologist, National CJD Surveillance unit, Western Hospital, Edinburgh) using formic acid and hydrolytic autoclaving as pre-treatment and standard immunoperoxidase technique with DAB/H2O2 as chromogen.

Histopathology: Classical spongiform encephalopathy was absent, in all areas of the brain examined. The subarachnoid space both around cerebral and cerebellar cortex, was filled with carcinomatous cells, extending along Virchow Robin spaces (Figure 1) into the cerebral and cerebellar cortex, basal ganglia, thalamus, hippocampus and brain stem, as numerous nodules imparting a spongy appearance at low magnification. The lesions were limited to the cortex and nuclear areas. The tumor nodules had acinar structures, containing PAS positive intracytoplasmic material. Amyloidotic plaques were not seen. PrP immunostain failed to reveal PrP\textsuperscript{\textalpha} positive intracytoplasmic material. Amyloidotic plaques were not seen. PrP immunostain failed to reveal PrP\textsuperscript{\textalpha} deposits in the brain, excluding the diagnosis of CJD. Age related neurofibrillary tangles or senile plaques were not observed, there were no features of limbic encephalitis, viral encephalitis or vascular/ ischemic pathology.

The histological features were characteristic of diffuse metastatic carcinomatous meningitis, extending into the gray areas of the brain. As the autopsy was confined to examination of the brain alone, the source of the primary could not be established.

**Discussion**

CJD affects individuals between 50-70 years of age. Psychiatric symptoms in the form of cognitive impairment, delusions and hallucinations, depression, euphoria and aggression are occasionally described in the literature and may form prodromal symptoms of CJD in 18-39% of cases.\(^1,2,3,4\) A diagnosis of probable CJD of sporadic form\(^5,6\) was considered in the present case on the basis of clinical features. In this case, dementia appears to have been caused by diffuse carcinomatous meningitis and multiple cortical tumor nodules altering the CSF dynamics and deranged cortical activity.\(^7\) The topographic distribution of the lesions in the frontal cortex, hippocampus, striatum account for the clinical features of dementia, ataxia and extrapyramidal symptoms. The diffuse background theta activity on EEG, could be due to multifocal disruption of the synaptic connectivity in the cortex by the tumor deposits. The absence of abnormal prion protein in the brain excluded the diagnosis of CJD. Only one other such report of metastatic disease presenting like CJD is recorded in the literature.\(^8\) Though in cases of rapidly progressive dementia with myelolomas and EEG features, CJD forms an important clinical diagnosis, it is imperative to make efforts to exclude other treatable causes mimicking CJD, as happened in this case. This case report highlights that despite advances in clinical diagnosis, confirmation by tissue diagnosis remains a prerequisite for confirmation of CJD.

**References**


Accepted on 17.12.2003.

**Desmoplastic infantile ganglioglioma - A case report**


Departments of Neurosurgery, *Pathology, **Radiology, Apollo Hospitals, Tondiarpet, Chennai, India.

V. G. Ramesh
350/4, Lloyd’s Road, Gopalapuram, Chennai - 600 086, India. E-mail: drvgrur@vsnl.net or drvgramesh@hotmail.com

**Figure 1:** Section through the frontal cortex shows multiple perivascular metastatic adenocarcinoma deposits in Virchow Robin space and the surface subarachnoid space. HE X 36. Inset: Higher magnification highlighting the adenocarcinoma deposit. HE X 320.