Creutzfeldt-Jakob disease is a spongiform encephalopathy affecting 1 individual per million population per year. We report on a previously healthy 43-year-old patient who presented with the simultaneous onset of a movement disorder, encephalopathy, cognitive decline, and dilated cardiomyopathy, and was found to have spongiform encephalopathy on brain biopsy. Although her neurological features could be explained by Creutzfeldt-Jakob disease, the etiology of the dilated cardiomyopathy could not be established. Finally, special staining of the endomyocardial biopsy specimen revealed the presence of abnormal prion, possibly infectious scrapie prion. As an exhaustive search for familial, ischemic, infectious, autoimmune, toxic, and metabolic causes of dilated cardiomyopathy was unrevealing, the presence of abnormal prion in the cardiac muscle suggested the possibility of prion-induced dilated cardiomyopathy in our patient.

Creutzfeldt-Jakob disease (CJD) is a spongiform encephalopathy affecting 1 individual per million population per year. We report on a patient with CJD who had dilated cardiomyopathy associated with an accumulation of abnormally folded prion protein in the heart muscle. To our knowledge, this is the first reported case of this association.

A 43-year-old female dance instructor with no significant medical history presented with symptoms of ataxia, impaired mentation, myoclonic jerks, dyspnea, and a 13.5-kg weight gain, all of which started simultaneously and gradually worsened over 6 months. There was no family history of similar problems, sudden death, or dilated cardiomyopathy (DCM). On examination she was confused and had difficulty with short-term memory and episodic athetotic movements of the hands and legs. Laboratory test results showed serum levels of lactate dehydrogenase of 526 U/L (normal range, 97-190 U/L), aspartate aminotransferase of 269 U/L (normal range, 15-38 U/L), alanine aminotransferase of 307 U/L (normal range, 5-37 U/L), and total bilirubin of 1.5 mg/dL (26 mmol/L) (normal range, 0.2-1.3 mg/dL [3-22 µmol/L]). Complete blood cell count, serum electrolyte and creatinine levels, erythrocyte sedimentation rate, and serum urea nitrogen levels were within normal limits. Human immunodeficiency virus serologic results, along with serologic results for hepatitis A, B, and C, were negative. Results of cerebrospinal fluid studies were normal. A chest radiograph revealed cardiomegaly and a rightsided pleural effusion. An echocardiogram showed severe left ventricular dilation with markedly diminished systolic function and a mildly dilated right ventricle. Cardiac catheterization revealed normal coronary arteries with diffuse hypokinesis and an ejection fraction of 20% to 25%. At 1352 pg/mL (998 pmol/L), the serum level of vitamin B<sub>12</sub> was elevated (normal range, 180-914 pg/mL [133-674 pmol/L]). Imaging studies of the brain and an electroencephalogram were read as normal. Serum levels
Unstained tissue sections of the endomyocardial biopsy specimen were sent to an outside neuropathology laboratory to test for abnormal prion protein (PrP) accumulation. Normal cellular PrPs (PrPc) have the same amino acid building blocks as the abnormal scrapie PrPs (PrPSc) but the amino acids in PrPSc are folded differently, into looser β-sheets instead of tight α-helical structures. Immunohistochemistry studies were performed using the PrP-specific 3F4 monoclonal antibody. No immunostaining of cardiac muscle or peripheral nerve occurred (Figure 1), suggesting an absence of PrPc. Pretreatment of the section with formic acid was then performed, followed by autoclaving in a citrate buffer to expose the 3F4 epitope and look for PrPSc. After pretreatment a weak, diffuse staining and a more intense punctate staining of cardiac muscle fibers were noticed (Figure 2), which was consistent with the presence of abnormally folded prion proteins—possibly PrPSc—in the cardiac tissue. In addition, strong linear immunostaining, which appeared to be adjacent to some of the muscle fibers, suggested immunostaining of peripheral nerve twigs.

As an exhaustive search for familial ischemic, infectious, autoimmune, toxic, and metabolic causes of DCM was unrevealing, the presence of abnormal PrPs in the cardiac muscle suggested the possibility of prion-induced DCM in our patient.

COMMENT

Creutzfeldt-Jakob disease was first described by H. G. Creutzfeldt and A. M. Jakob in 1920 and 1921, respectively. It can be classic CJD, which can be sporadic, familial, iatrogenic, or variant CJD (vCJD), the latter being associated with the bovine spongiform encephalopathy epidemic in Great Britain and Europe. Our patient presented with the clinical triad of dementia, akinetic mutism, and myoclonus, which is considered typical of classic CJD. Typical signs begin with loss of memory or confusion, behavioral aberrations, and gait instability. At autopsy, microscopic sections exhibit widespread spongiform changes accompanied by gliosis and neuronal loss, while immunohistochemical staining reveals numerous protease-resistant PrPs. The definitive diagnosis is usually made by cerebral biopsy, as in our patient. The presentation of vCJD differs from that of classic CJD with younger age of onset, psychiatric symptoms, and different neuropathologic changes. The disease in our patient was most likely sporadic, as she had no history of using pituitary hormones and no family history of CJD, and her presentation was not suggestive of vCJD.

High concentrations of infectious PrPSc have been reported in certain skeletal muscle groups after injecting infective material from hamsters into mice and also in skeletal muscles and spleen at autopsy in patients with established CJD. Mutant PrP in intermediate concentrations has been reported in the skeletal muscles, heart, testes, and stomach of transgenic mice expressing the mouse PrP homologue of the CJD mutation. Western blot analysis did not detect PrPSc in the cardiac muscle of 3 patients with vCJD and there have been no reports of cardiac muscle involvement in classic CJD or scrapie. Our patient had a simultaneous onset of a movement disorder, encephalopathy, cognitive decline, and dilated cardiomyopathy. Although all the other features could be explained by CJD, the etiology of the DCM could not be established. The finding of abnormal PrPs, possibly infectious PrPSc, in the endomyocardial biopsy specimen suggests that the DCM in our patient could have been secondary to infection by the prion causing CJD.

CONCLUSIONS

In conclusion, the simultaneous and rapid cardiac and neurologic decline over a few months in a patient with CJD, combined with the presence of abnormally folded PrPs in the cardiac tissue, suggests an association between PrPSc and DCM.
presence of abnormal PrP in the cardiac muscle raises important questions. First, was this PrP infectious PrPSc, and, if so, can endocardial biopsy be a way of diagnosing CJD instead of carrying out the much more invasive brain biopsy? Second, until further confirmatory studies are available, because of a possible cardiac muscle infection in patients with CJD, safe handling of cardiac muscle in these patients should probably be recommended. Finally, could CJD be a multisystem disease?

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REFERENCES