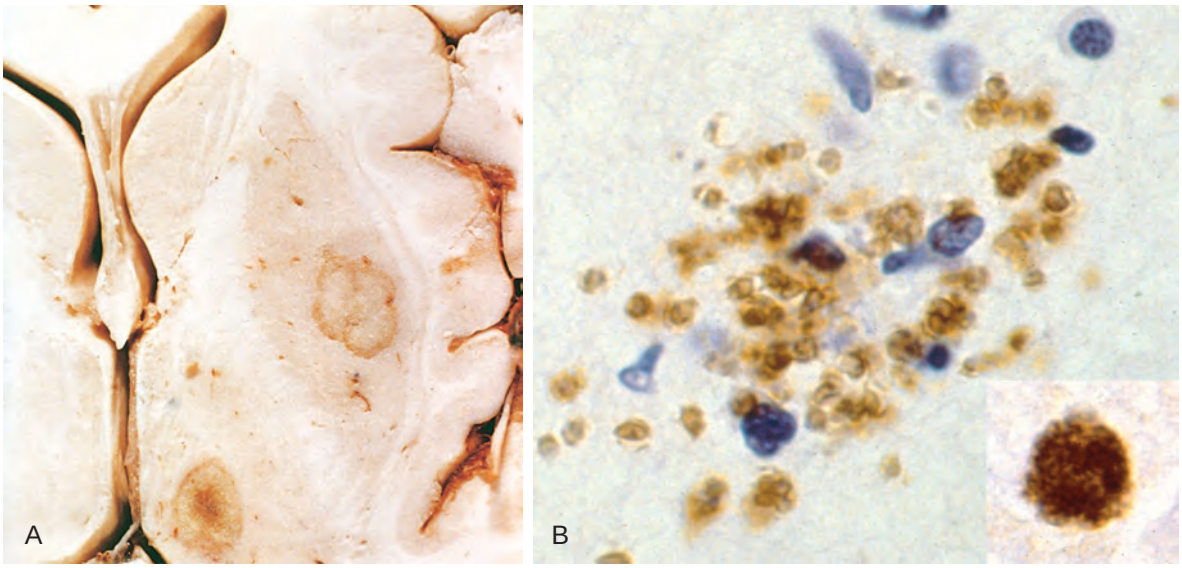

Figure 28-29 **A,** *Toxoplasma* abscesses in the putamen and thalamus. **B,** Free tachyzoites demonstrated by immunostaining; *inset*: *Toxoplasma* pseudocyst with bradyzoites highlighted by immunostaining.

infection (HSV-1 in the temporal lobes, polio in anterior horn).

- HIV can directly cause meningoencephalitis, or indirectly affect the brain by increasing the risk of opportunistic infections (toxoplasmosis, CMV) or EBV-positive CNS lymphoma.

Prion Diseases

Prions are abnormal forms of a cellular protein that cause rapidly progressive neurodegenerative disorders that may be sporadic, familial or transmitted. This group of diseases includes Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia, and kuru in humans; scrapie in sheep and goats; mink-transmissible encephalopathy; chronic wasting disease of deer and elk; and bovine spongiform encephalopathy. These disorders share an etiologic basis as they are all associated with abnormal forms of a specific protein termed *prion protein* (PrP). They are all characterized morphologically by "spongiform change" caused by intracellular vacuoles in neurons and glia, and clinically by a rapidly progressive dementia.

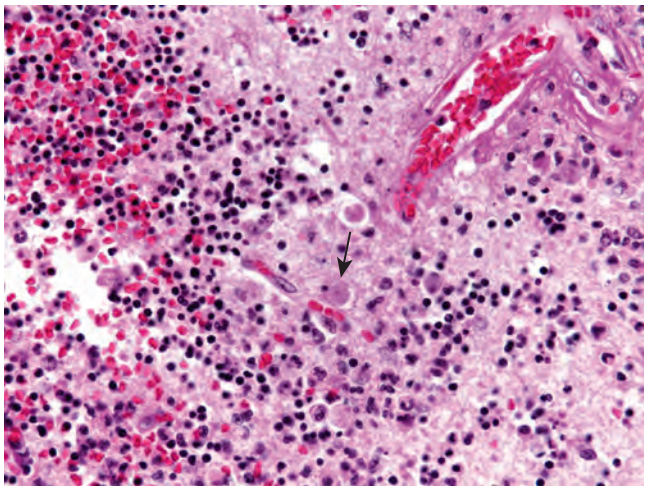

Figure 28-30 Necrotizing amebic meningoencephalitis involving the cerebellum (organism highlighted by *arrow*).

Pathogenesis and Molecular Genetics. **Prion diseases are conceptually important because they exemplify degenerative disorders that are caused by "spreading" of misfolded proteins, a remarkable phenomenon that allows a pathogenic protein to acquire many of the characteristics of an infectious organism**. Normal PrP is a 30-kD cytoplasmic protein present in neurons. Disease occurs when PrP undergoes a conformational change from its normal α-helix-containing isoform (PrP^c) to an abnormal β-pleated sheet isoform, usually termed PrP^{sc} (for scrapie) (Fig. 28-31). Associated with the conformational change, PrP acquires resistance to digestion with proteases, such as proteinase K. Accumulation of PrP^{sc} in neural tissue seems to be the cause of the pathologic changes in these diseases, but how this material induces the development of cytoplasmic vacuoles and eventual neuronal death is still unknown. Western blotting of tissue extracts after partial digestion with proteinase K allows detection of PrP^{sc}, which is diagnostic.

The conformational change resulting in PrP^{sc} may occur spontaneously at an extremely low rate (resulting in sporadic cases) or at a higher rate if various mutations are present in PrP^c, such as occurs in familial forms of Creutzfeldt-Jakob disease (CJD) and in Gerstmann-Sträussler-Scheinker syndrome (GSS) and fatal familial insomnia (FFI). PrP^{sc}, independent of the means by which it originates, then facilitates, in a cooperative fashion, the conversion of other PrP^c molecules to PrP^{sc} molecules. It is this propagation of PrP^{sc} that accounts for the transmissible nature of prion diseases. This capacity for a protein in an abnormal conformation to induce similar structural change in other molecules as a self-propagating process has recently been demonstrated for many of the aggregating proteins associated with traditional neurodegenerative diseases. The suggestion that, at least within an individual, there may be