Clinical History:
The patient is a 62-year-old man with a history of coronary artery disease and hypertension who was in his usual state of health until 2 weeks prior to admission, when he developed decreased appetite, neck and back pain, nausea, and vomiting. Shortly after admission to an outside hospital, he had a tonic-clonic seizure and was intubated. MRI showed extensive irregular gyriform parenchymal abnormalities in the bilateral cerebral hemispheres and extensive leptomeningeal enhancement throughout the basilar cisterns as well as coating the surface and insinuating the sulci of the bilateral cerebral hemispheres. A lumbar puncture was significant for elevated protein (539 mg/dL, normal range = 15 – 45 mg/dL); a Gram stain was negative. He was treated for meningitis, including tuberculous meningitis, for several days. He showed minimal clinical improvement and was extubated. One week after extubation, he developed altered mental status and was re-intubated. MRI demonstrated communicating hydrocephalus with persistent diffuse leptomeningeal enhancement. A repeat lumbar puncture showed an elevated opening pressure. A VP shunt was placed and he was transferred to our hospital for further care. Upon admission, his physical exam was significant for an inability to follow commands and a mild left-sided facial droop. He moved all extremities spontaneously and withdrew to pain. He remained intubated while his work-up continued. His intracranial pressure remained elevated. Eleven days after admission, he underwent a left frontal craniotomy for subdural and intraparenchymal biopsies (provided for your review). After the brain biopsies, he experienced a slow but progressive decline in his neurological status. His mental status fluctuated between coma and minimal consciousness. He required serial aspirations of CSF to control his intracranial pressure. A repeat MRI thirteen days after admission revealed persistent hydrocephalus, diffuse leptomeningeal enhancement, progressive areas of cortical restricted diffusion, and vascular irregularities on MR angiography. Two weeks later, he was transitioned to comfort care and died the following day. An autopsy was requested by his family.

Material submitted:
One representative hematoxylin and eosin-stained slide from the left frontal brain biopsy.
One representative UNSTAINED slide from the dorsal brainstem (post-mortem).

Points for discussion:
1. Discuss the differential diagnosis.
2. Discuss the process seen in the biopsy and correlate it with the autopsy findings.
3. Review the clinical settings in which these features can be seen.