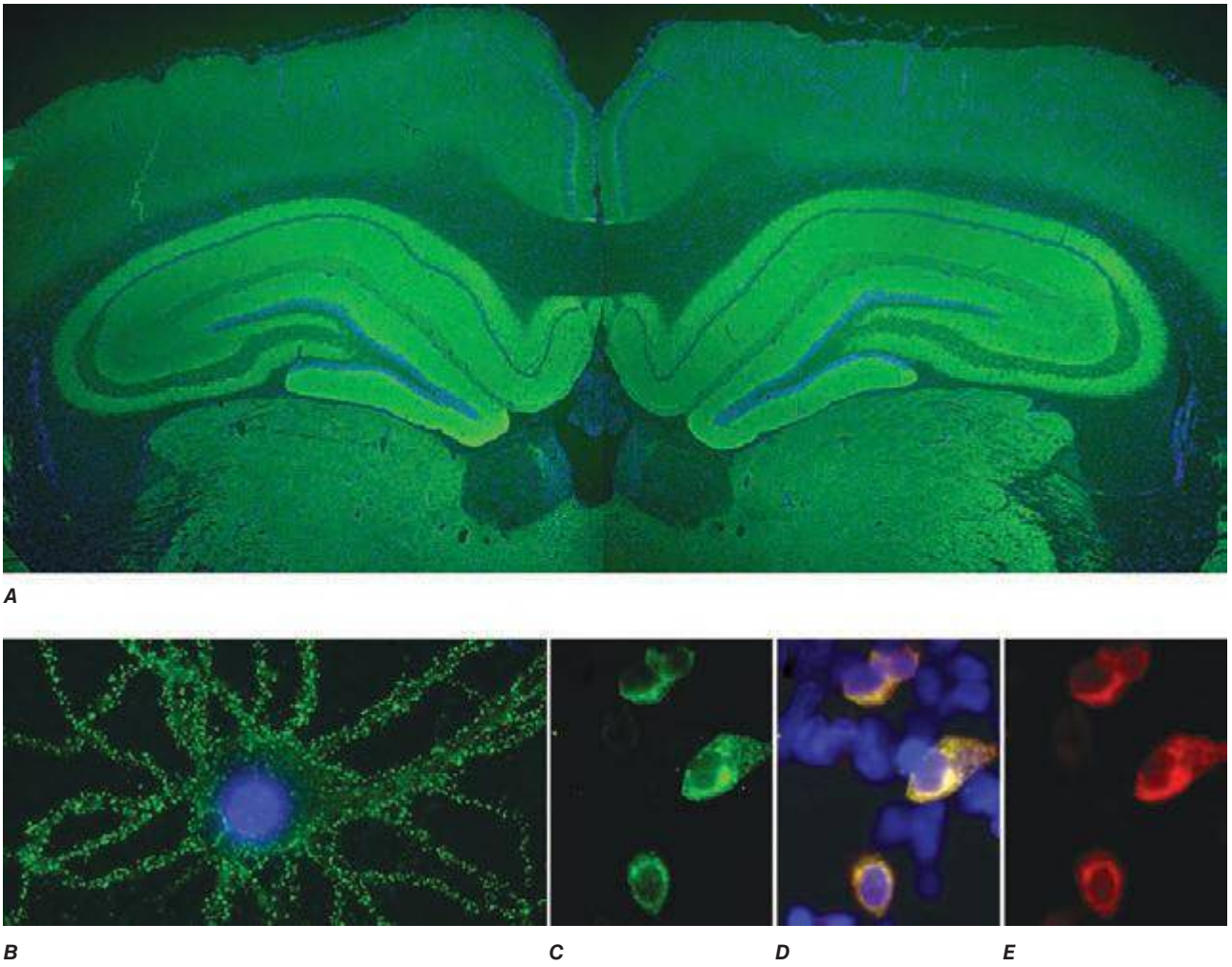

FIGURE 122-1 Antibodies to the GluN1 subunit of the *N*-methyl-D-aspartate (NMDA) receptor in a patient with anti-NMDA receptor encephalitis and ovarian teratoma. (***A***) Coronal section of rat brain immunolabeled (green fluorescence) with the patient's antibodies. The reactivity predominates in the hippocampus, which is highly enriched in NMDA receptors. (***B***) This image shows the antibody reactivity with cultures of rat hippocampal neurons; the intense green immunolabeling is due to the antibodies against the GluN1 subunit of NMDA receptors. (***C–E***) Images of HEK cells (a human kidney cell line) transfected to express NMDA receptors, showing reactivity with patient's antibodies (***C***) and with a commercial monoclonal antibody against NMDA receptors (***E***); the patient's antibody reactivity co-labels only the cells that express NMDA receptors (***D***). *(From J Dalmau et al: Lancet Neurol 7:1091, 2008; with permission.)*

For still other PNDs, the cause remains quite obscure. These include, among others, several neuropathies that occur in the terminal stages of cancer and a number of neuropathies associated with plasma cell dyscrasias or lymphoma without evidence of inflammatory infiltrates or deposits of immunoglobulin, cryoglobulin, or amyloid.

APPROACH TO THE PATIENT: Paraneoplastic Neurologic Disorders

Three key concepts are important for the diagnosis and management of PNDs. First, it is common for symptoms to appear before the presence of a tumor is known; second, the neurologic syndrome usually develops rapidly, producing severe deficits in a short period of time; and third, there is evidence that prompt tumor control improves the neurologic outcome. Therefore, the major concern of the physician is to recognize a disorder promptly as paraneoplastic and to identify and treat the tumor.

PND OF THE CENTRAL NERVOUS SYSTEM AND DORSAL ROOT GANGLIA

When symptoms involve brain, spinal cord, or dorsal root ganglia, the suspicion of PND is usually based on a combination of clinical, radiologic, and CSF findings. Presence of antineuronal antibodies (Tables 122-2 and 122-3) may help in the diagnosis, but only 60–70% of PNDs of the CNS and less than 20% of those involving the peripheral nervous system have neuronal or neuromuscular junction antibodies that can be used as diagnostic tests.

Magnetic resonance imaging (MRI) and CSF studies are important to rule out neurologic complications due to the direct spread of cancer, particularly metastatic and leptomeningeal disease. In most PNDs, the MRI findings are nonspecific. Paraneoplastic limbic encephalitis is usually associated with characteristic MRI abnormalities in the mesial temporal lobes (see below), but similar findings can occur with other disorders (e.g., nonparaneoplastic autoimmune limbic encephalitis and human herpesvirus type 6 [HHV-6] encephalitis) (Fig. 122-2). The CSF profile of patients with PND of the CNS or dorsal root ganglia typically consists of mild to moderate pleocytosis (<200 mononuclear cells, predominantly lymphocytes), an increase in the protein concentration, and a variable presence of oligoclonal bands. There are no specific electrophysiologic tests that are diagnostic of PND. Moreover, a biopsy of the affected tissue is often difficult to obtain, and although useful to rule out other disorders (e.g., metastasis) the pathologic findings are not specific for PND.

PND OF NERVE AND MUSCLE

If symptoms involve peripheral nerve, neuromuscular junction, or muscle, the diagnosis of a specific PND is usually established on clinical, electrophysiologic, and pathologic grounds. The clinical