Imaging of Cancer Therapy–Induced Central Nervous System Toxicity

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KEYWORDS

• Neurotoxicity • Cancer • Chemotherapy • Radiation therapy
• Central nervous system • Imaging

KEY POINTS

- Cancer treatment–related neurotoxicity can occur in patients with both central nervous system and non-central nervous system cancers, and clinical symptoms are nonspecific.
- On structural imaging techniques, such as computed tomography and magnetic resonance imaging, distinguishing volume gain versus volume loss can be helpful in differentiating edema, inflammation, and tumor growth from gliosis, necrosis, and atrophy.
- Comparison of a current imaging study with recent and more remote prior imaging is crucial for recognizing subtle changes that occur over time.
- Radiation necrosis, leukoencephalopathy, hydrocephalus, and ischemic and hemorrhagic vascular events can occur with highly variable delay following treatment.
- Perfusion imaging and positron emission tomography can potentially help differentiate tumor progression versus necrosis and leukoencephalopathy, and functional magnetic resonance imaging can be helpful in surgical planning.
- Recent advanced imaging research studies in patients with cancer have provided novel insights into the cause of cognitive impairment and other neurotoxic syndromes in patients with cancer.

INTRODUCTION

Cancer therapies can cause a wide range of acute and delayed treatment complications involving the central nervous system (CNS),[1,2] causing significant morbidity and mortality. Notably, these syndromes occur not only in patients with brain tumors but

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also in patients treated for cancer outside the CNS, such as systemic lymphoma, breast, and lung cancer.[3] With improved survival rates in patients with cancer and more aggressive and combined treatment modalities, neurologic treatment complications have been observed with increasing frequency. The clinical presentation of patients experiencing neurotoxicity is commonly nonspecific. Therefore, the diagnosis of neurotoxic syndromes often poses a major challenge to the treating physician. However, recognition of treatment-related neurologic complications is critically important to avoid unnecessary procedures, such as brain biopsy and lumbar puncture, and because symptoms may be confused with metastatic disease, tumor progression, paraneoplastic disorders, and infections of the CNS. Neuroimaging, including computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), is an important diagnostic tool in patient evaluation and guidance of patient management. Moreover, advanced neuroimaging techniques with resting state and diffusion tensor MRI and functional MRI (fMRI) have most recently provided compelling evidence that both structural and functional brain changes occur in a substantial number of patients with cancer treated with chemotherapy and radiation.

In this review various imaging techniques and modalities that can be used in patients with cancer with suspected neurotoxic syndromes are highlighted and advantages and limitations of each imaging modality in the context of classical neurotoxic syndromes encountered in patients with cancer are discussed.

CT IN THE ASSESSMENT OF CANCER THERAPY–ASSOCIATED NEUROTOXIC SYNDROMES

CT is a technique that measures the attenuation of X-rays by different substances. Higher density materials absorb more x-rays than lower density materials and thus appear brighter (whiter). Two-dimensional images are reconstructed to display cross-sectional anatomy, and these individual images can be stacked so that one can view sequential images and appreciate the 3-dimensional contours of normal and abnormal structures. CT images can be acquired in any plane; for the brain, images are typically acquired in horizontal slices from the skull base to vertex. Slice thickness is variable, but most often approximately 5 mm per slice. Reformatted images in orthogonal planes (ie, coronal and sagittal) can be very useful in characterizing lesions. CT contrast is iodine-based; enhancement following contrast administration is seen in vascular structures and at sites of disruption of the blood-brain barrier.

The appearance of tumor on CT, as well as the effects of its treatment, depends on many variables. The contents of the tumor and the presence of surrounding edema, hemorrhage, necrosis, and postsurgical changes attenuate radiographs to a different extent. The degree of attenuation is measured on a scale of Hounsfield units (HU), which ranges from −1000 (air) to 0 (water) to +1000 (dense bone or metal). Intracranially, cerebrospinal fluid (CSF) measures about 15 HU; white matter measures 20 to 30 HU, and gray matter measures 35 to 45 (HU). Fat, as in myelin, does not strongly attenuate radiographs and has an HU range of −30 to −70; thus, white matter appears darker than gray matter. Vasogenic edema in tissue appears dark on CT because water has a lower Hounsfield unit value than normal brain tissue. Vasogenic edema will most often be associated with local or regional mass effect. Subtle evidence of mass effect includes effacement of cortical sulci and compression of ventricles. With more severe mass effect, loss of gray-white matter differentiation and herniation of brain tissue is seen.