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Tumor predisposition syndromes represent a heterogeneous group of multiorgan disorders, with many having substantial central nervous system involvement. This article highlights the common and uncommon manifestations of these syndromic disorders, the underlying genetic pathways, and the imaging findings. Radiologists must be aware of the diagnostic criteria, optimal imaging techniques (both for diagnosis and surveillance), as well as the innumerable imaging manifestations of these syndromes. Multidisciplinary approach and teamwork are essential in managing these patients, with imaging having a central role as more of these patients get diagnosed earlier and survive longer.