Brain Tumors

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KEYWORDS

• Medulloblastoma • Glioblastoma • Anaplastic astrocytoma
• Diffuse intrinsic pontine glioma • Ependymoma

KEY POINTS

- The past 2 decades have witnessed a revolution in the management of childhood brain tumors, with the establishment of multidisciplinary teams and national and international consortiums.
- Unprecedented cooperation within the pediatric neuro-oncology community and sophisticated rapidly evolving technology have led to advances that are likely to revolutionize treatment strategies and improve outcomes.

Brain tumors in children represent the second most common malignancy in children. The number of children, adolescents, and young adults (0–19 years) with a diagnosis of a brain tumor is approximately 4350 per year.[1] The cause for most of these tumors is unknown, but there are some predisposing conditions that give rise to certain types of brain tumors. Turcot syndrome, Li-Fraumeni syndrome, and Gorlin syndrome are examples that can give rise to high-grade glioma (HGG) and medulloblastoma.[2–4]

Management of children with brain tumors requires a multidisciplinary approach, and these children are best served at pediatric hospitals, which are equipped with the necessary resources and personnel. Pediatric neurosurgeon, oncologist, neuropathologist, neuroradiologist, radiation oncologist, endocrinologist, and physical rehabilitation services among others should be available.

These children present most commonly with symptoms related to increased intracranial pressure or one or several of the following: cranial nerve palsies, incoordination, seizures, loss of vision, and short stature.

A few of the more common brain tumors and recent advances in their management are discussed in the following sections.

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MEDULLOBLASTOMA

Medulloblastoma is the most common malignancy in children and represents approximately 20% of all malignant brain tumors that affect children between the ages of 0 and 14 years.[5,6] There is a bimodal distribution peak between 3 and 4 years and again between 8 and 10 years of age. It can occur in teenagers and young adults, but less frequently.

The cause of medulloblastoma is unknown. However several familial syndromes like Gorlin syndrome, Turcot syndrome, and Li-Fraumeni syndrome, which have a genetic predisposition to development of medulloblastoma, offer clues to the molecular pathologic mechanisms that can lead to growth of medulloblastoma. About 3% to 5% of children with Gorlin syndrome develop medulloblastoma. Gorlin syndrome is characterized by an inherited germline mutation of the PATCHED1 gene on chromosome 9, which encodes the sonic hedgehog (SHH) receptor PTCH1 and normally suppresses SHH signaling by inhibiting the SMO receptor.[2,7] Approximately 40% of medulloblastomas show evidence of mutations in the PTCH1, and these tumors are mostly associated with the desmoplastic variant of medulloblastoma.[2,8,9] Children with Turcot syndrome have mutations in the adenomatosis polyposis coli gene (type 2) or mutations in the DNA mismatch repair genes HPS2 and MLH1 (type 1). Patients with type 2 disease are at increased risk for developing medulloblastoma.[2,10] Approximately 10% of children with medulloblastoma have a favorable prognosis and have abnormalities in the WNT molecular pathway, which is also aberrant in Turcot syndrome. Patients with Li-Fraumeni syndrome with germline mutations in the TP53 gene can develop medulloblastoma, particularly of the SHH subtype, although gliomas are more common in this syndrome.[2,11]

Clinical Presentation

The symptoms at presentation caused by medulloblastoma are related to obstruction of cerebrospinal fluid (CSF) pathways and direct involvement of the cerebellum or the brainstem. Headaches and vomiting as a result of raised intracranial pressure, constant features later in the course of the disease, are often nonspecific in the early stages. Unsteadiness, mostly truncal, is present in about 50% to 80% of children with medulloblastoma. Esotropia in 1 or both eyes and papilledema are common. Clumsiness, dropping things frequently, and declining academic performance are other symptoms that can indicate the presence of a cerebellar lesion like medulloblastoma. Macrocephaly, unexplained lethargy, and head tilt are more common in infants.

Diagnosis

The diagnosis of medulloblastoma is initially suspected based on imaging studies, which include MRI of the brain. A typical radiographic presentation is the presence of a solid midline posterior fossa mass that seems to arise from the cerebellum and occupies the fourth ventricle. It shows variable and heterogeneous enhancement pattern. Occasionally, it may arise from the lateral aspect of either cerebellar hemisphere and often indicates a specific subtype of medulloblastoma that shows activation of the SHH pathway. The differential diagnosis of a midline posterior fossa mass includes ependymoma and pilocytic astrocytoma. The former is a solid tumor, which tends to spread toward the cerebellopontine angle via the foramen of Luschka or toward the spinal cord via the foramen of Magendie. The latter consists of solid and cystic components, with often a uniform enhancement of the solid component. In the younger child, the differential diagnosis includes atypical teratoid rhabdoid tumor, which may show involvement of the cerebellopontine angle. A complete MRI