4.1 Epidemiology

4.1.1 Incidence

Ependymomas are relatively rare gliomas arising from the differentiated ependymal cell layer lining the ventricular system and central canal of the spinal cord. Intracranial ependymomas account for approximately 9% of all brain tumors in the population under 20 years of age, and are the third most common primary brain tumor in children (following astrocytomas and primitive neuroectodermal tumors). According to SEER (Surveillance, Epidemiology and End Results) data from 1975 until 1998, the annual incidence of ependymoma is 2.6 per million for the 0 to 14 age group, and 2.2 per million for the 0 to 20 age group (Ries et al. 1999). Population-based measurements of the incidence of spinal cord ependymoma in children are available from the Connecticut Tumor Registry. Between 1935 and 1973, 5 spinal cord ependymomas and 44 intracranial ependymomas were identified in the Connecticut population under 20 years of age; suggesting that spinal cord ependymoma represents approximately 10% of all ependymal tumors in children and young adults (Dohrmann et al. 1976). Another large institutional series confirmed that spinal cord ependymomas are rare in children under 10 years of age, accounting for less than 1% of all spinal tumors. After age 10, the incidence of spinal cord ependymoma increases, and it represents the majority of intramedullary tumors in patients older than 20 years (Constantini et al. 1997).
4.1.2 Age and Sex Distribution

The incidence of intracranial ependymoma peaks in the 0 to 4 age group (5.2 cases per million) and decreases thereafter to 1.5 per million in the 5 to 14 age group, and 0.9 per million in the 15 to 19 age group. Ependymomas are twice as common in males than in females. The average annual incidence is 3 per million in males, and 1.5 per million in females (Ries et al. 1999).

4.1.3 Etiology – Environmental and Viral Causes

The etiology of ependymomas remains obscure. In most epidemiologic studies ependymomas are grouped with other brain tumors, making definitive identification of specific risk factors impossible. One agent that recently received attention and has been studied for its role in oncogenesis is a specific polyomavirus, simian virus 40 (SV40). Contamination of pools of poliovirus and adenovirus vaccines from 1955 until 1963 with SV40 has raised concern about possible increases in overall cancer incidence and increases in the incidence of rare tumors such as ependymoma and choroid plexus papilloma (Carbone et al. 1997). SV40 virus is capable of transforming cells from different species, including normal human cells, into cells with a neoplastic phenotype. Furthermore, in an animal model, intracerebral inoculation of rodents with SV40 virus induces ependymoma formation (Kirschstein and Gerger 1962). SV40 oncogenicity and transforming ability are dependent on the expression of the early region gene product, large tumor antigen (Tag), which complexes with tumor suppressor genes such as p53, pRb, p107, p130, p300 and p400, resulting in their inactivation (Zhen et al. 1999). The SV40 genome can be detected in the tissue of a majority of ependymomas and choroid plexus carcinomas, and also in astrocytomas, meningiomas, glioblastoma multiforme, and medulloblastoma (Bergsagel et al. 1992; Martini et al. 1996). Normal brain tissue is negative for SV40 large tumor antigen. Although provocative, these data are nonspecific and do not provide a causative link for the formation of human tumors. In addition, large epidemiologic studies that evaluated the incidence of neoplasms in patients inoculated with contaminated vaccines after long follow-up periods ranging from 17 to 30 years did not detect an increased overall incidence of ependymoma or other neoplasms (Strickler et al. 1998).

4.1.4 Genetic Predisposition

Neurofibromatosis type 2 (NF2) is the only known genetic defect with a predisposition for development of ependymoma. Patients with NF2 typically develop intramedullary spinal tumors (Lee et al. 1996). NF2 mutations have been found in 25 to 70% of patients with sporadic intraspinal ependymomas. No NF2 mutations were found in ependymomas arising in other locations (Birch et al. 1996; Lamszus et al. 2001). Familial intracranial ependymoma is very rare; however, in one family with four cousins who developed ependymoma, a suspected tumor-suppressor gene locus was located by a segregation analysis to the 22pter–22q11.2 region (Hulsebos et al. 1999). There is currently no evidence that this gene plays a role in sporadic ependymoma. Although there is a case report of a child with a germ-line mutation in the p53 gene and intracranial ependymoma, ependymoma is usually not considered to be one of the neoplasms associated with Li-Fraumeni syndrome (Hamilton and Pollack 1997). One large population study indicated that parents of children with ependymoma may be at an increased risk of colon cancer (relative risk 3.7; Hemminki et al. 2000). However, another large study did not identify increased risk of any cancer in families of children with brain tumors (Gold et al. 1994).

4.2 Pathology

4.2.1 Histopathological Characteristics

Ependymomas arise from ependymal epithelium, which lines the ventricles of the brain and central canal of the spinal cord. Therefore, the most common