Subependymoma of the Lateral Ventricles: Report of Two Cases

Lateral Ventrikül Subependimoması: İki Vaka Sunumu

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Abstract: Subependymoma is a rare benign tumor of the ventricular system. It was described as a distinct entity by Scheinker in 1945. The fourth ventricle is the most common location. Many cases are asymptomatic and discovered at autopsy. Symptomatic cases often present with hydrocephalus.We present two cases of subependymoma located in lateral ventricles.

Case 1 was a 69-year-old male with non-Hodgkin's large B- cell lymphoma. He died following seizures and respiratory depression while he was receiving chemotherapy. At autopsy brain oedema and a small nodular mass located in the right lateral ventricular wall were discovered.

Case 2 was a 38-year-old female presenting with headache. MR revealed a mass, approximately 2.5cm in diameter in the right lateral ventricle extending to the third ventricle. Both tumors were diagnosed as subependymoma.

Microscopically, a fibrillary background, cell clusters with small uniform nuclei and microcysts were the main histopathological characteristics. Microcysts contained slightly basophilic material stained with alcian blue pH2.5 and toluidine blue pH7. This material was interpreted as extracellular mucin.

Tumoral infiltration was positive for GFAP and S-100 protein. Ki-67 (MIB-1) proliferation index was lower than 1%. P53 was negative in both cases.

Key Words: Subependymoma, autopsy, lateral ventricle, mucin, p53

Özet: Subependimom, ventriküler sistemin nadir görülen benign bir tümörüdür. Scheinker tarafından, 1945 yılında ayrı bir antite olarak tanımlanmıştır. En sık yerleşim yeri 4. ventriküldür. Vakaların çoğu asemptomatiktir ve otopside tesadüfen bulunurlar. Semptom veren vakalar, çoğunlukla hidrosefali ile karşımıza çıkarlar.

Bu çalışmada, lateral ventrikül yerleşimli 2 subependimom vakası sunulmaktadır. İlk vaka 69 yaşında, B hücreli non-Hodgkin lenfomalı erkek hastadır. Kemoterapi altında, konvülziyon ve solunum yetmezliği ile kaybedilmiştir. Otopside beyin ödemi ve sağ ventrikül duvarında küçük nodüler lezyon saptanmıştır. İkinci vaka 38 yaşında kadındır ve başağrısı şikayeti ile kliniğe başvurmuştur. Radyolojik incelemede MR'da sağ ventrikülde, üçüncü ventriküle uzanım gösteren, 2.5 cm çapında kitle görülmüştür. Mikroskopik olarak her iki vakada da benzer morfoloji saptanmıştır: fibriler zemin, küçük ve uniform çekirdekli hücrelerin oluşturduğu hücre grupları ve mikrokistler. Mikrokistlerin içindeki materyel, alcian blue pH2.5 ve toluidine blue pH7 ile pozitif boyanarak müsin olarak yorumlanmıştır. Tümörde GFAP ve S-100 protein pozitiftir. Proliferasyon indeksi Ki-67(MIB-1) % 1'den az ve p53 negatiftir.

Anahtar Kelimeler: Subependimom, otopsi, lateral ventrikül, müsin, p53.

INTRODUCTION

Subependymoma is a rare benign glial tumor of the ventricular system.

The fourth ventricle is the most common location. They are often found incidentally at autopsy in elderly patients. Symptomatic cases occur primarily in middle-aged patients and often present with hidrocephalus.

Prognosis is good even with subtotal resection (1, 23).

We present a symptomatic case of subependymoma and an incidental case found at autopsy.

CASE 1:

A 69-year-old male was admitted to hospital in January 2001 with complaints

of weight loss and fatigue. Following physical examination and laboratory investigation, cervical lymph node and trephine bone marrow biopsies were performed. Both material showed neoplastic infiltration. Histopathological diagnosis was a large B-cell non-Hodgkin's lymphoma rich in T-cells. The bone marrow was infiltrated by the same tumor. The patient received a regimen of

CHOP chemotherapy and his status began to improve clinically. Three weeks after the first chemotherapy he developed focal seizures and soon after a respiratory depression. Following intubation and anticonvulsive therapy spontaneous breathing was achieved. A few days later the convulsive status reappeared and the patient died. In this period MR and CT revealed no infiltration or hemorrhage.

To explain his neurological status a brain dissection was done. The brain was fixed in 10%formalin for 4 weeks. The fixed brain weighed 1500g. It was cut in

1cm thick coronal slices. Macroscopically, no hemorrhage or mass lesion was detected. The brain was heavy and oedematous. A small nodular lesion, 0.8 cm in diameter was observed in the anterior horn of the right lateral ventricle (Fig 1).

The tumor was attached to the ventricular wall, well circumscribed with no infiltration of the brain parenchyme.

CASE 2:

The patient was a 38-year-old female. She complained of headache for 2 months and MR examination revealed a mass in the right anterior horn of the lateral ventricle which was extending to the 3rd ventricle (Fig 2).

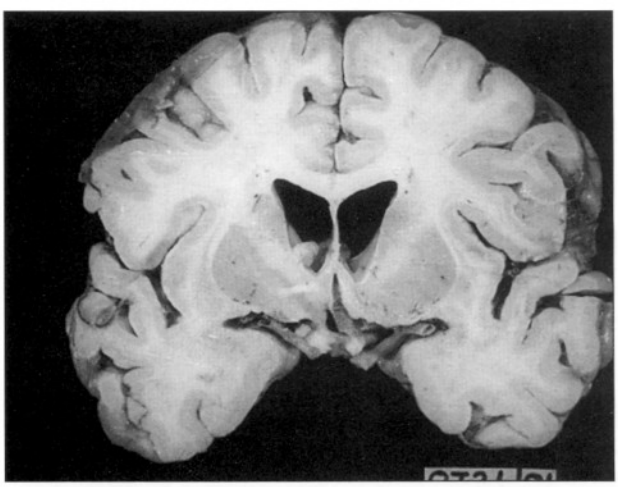

Figure 1: A nodular mass attached to the ventricular wall in case 1

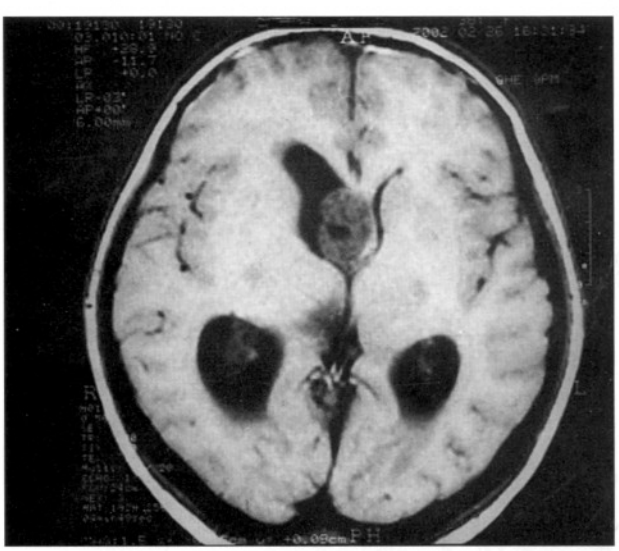

Figure 2: Radiological appearance of the tumor in case 2

Clinical diagnosis was a neurocytoma or a subependymal giant cell astrocytoma.

The lesion was removed gross totally and measured 3x1.8x1cm. The patient has no complaints or recurrence after 6 months.

MICROSCOPICAL FINDINGS

Both tumors had a similar morphology. An infiltration of uniform, small cells having round to oval nuclei was seen. The background was fibrillary and numerous microcysts with basophilic secretory material were observed

(Fig 3,4). This was stained positively with alcian blue pH 2.5, toluidine blue pH 7.

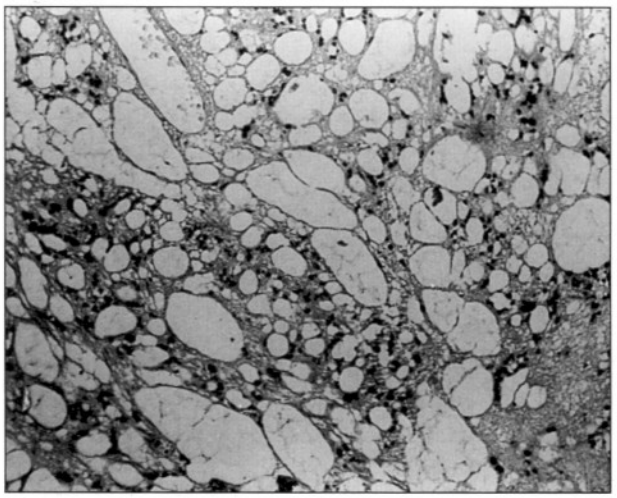

Figure 3: Microcysts and infiltration consisting of uniform, small cells (HEx125)

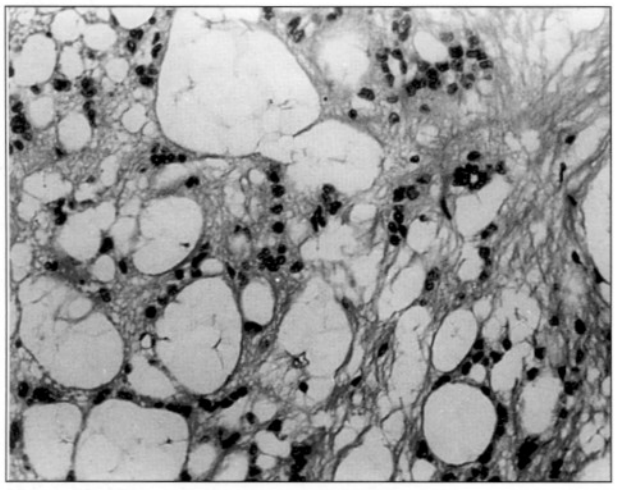

Figure 4: Microcysts containing secretory material and clustering of nuclei in a fibrillary background (HEx310)

Necrosis and mitosis were not found. Cytological atypia was minimal.

Hemosiderin deposition and calcification were not seen. GFAP and S-100 protein were diffuse positive. MIB-1(Ki-67) proliferation index was lower than 1% and p53 (clone D07) was negative in both cases.

DISCUSSION

Subependymoma is a rare benign glial tumor (WHO grade 1). Ultrastructural studies indicate an origin of subependymal layer (11, 18, 22). Some authors suggest that this lesion could be more likely a hamartoma rather than a tumor because of a very low MIB-1 index and lack of telomerase activity (3, 22). The association of subependymoma with another brain tumor or malformations was reported by several authors and they thought that this might have shown that this lesion could be reactive in nature (7, 20, 22, 24, 26).

Case 1 had a large B- cell non-Hodgkin's lymphoma without CNS involvement and a subependymoma coincidentally. A patient who died of colon carcinoma with an incidental subependymoma was reported by Ma (14). The main location of subependymoma is the fourth ventricle followed by lateral ventricles, septum pellicidum, cerebral aquaductus and proximal spinal cord (1, 15, 22, 23). In our two cases, it was located in the anterior horn of the right lateral ventricle. The tumor in the 2nd case was extending through foramen Monroe to the 3rd ventricle. The mean age of symptomatic cases is about 35-40 and elderly patients are affected in asymptomatic cases. Our cases showed this characteristic age distribution. Histopathologically subependymoma has a characteristic morphology: clusters of cells with uniform small nuclei and fibrillary background. Microcysts, calcification, hemosiderin deposition, sclerotic vessels are common features(5, 22). A subependymoma with melanin pigment was also reported(21). Rare cases having an ependymal component with perivascular rosettes and pseudorosettes were described (1, 12). Presented cases had the characteristic appearance of subependymoma. Numerous microcysts

containing basophilic material were observed. This secretory material was stained positive with alcian blue pH 2.5, toluidine blue pH 7 and therefore interpreted as extracellular mucin. There are few tumors in central nervous system with mucin production. Most of them are rare case reports such as a cellular ependymoma, a medulloblastoma, dysembryoblastic neuroepithelial tumor, choroid plexus papilloma and meningioma. Myxopapillary ependymoma is a well known entity with mucin production (4, 9, 16, 25). A recently described entity with 3rd ventricular location the so-called chordoid glioma also has shown to contain extracellular mucin (2). Subependymoma is accepted as a slow growing benign grade I tumor. However the presence of cytological atypia and mitosis has been reported (12, 17). Although no remarkable difference was found between "the pleomorphic variant" and the classical group concerning the behaviour, the possible existence of a more aggressive variant should be considered in the differential diagnosis.(17). Differential diagnosis may include tumors with ventricular location. Neurocytoma is synaptophysin positive. Subependymal giant cell astrocytoma consists of spindle and epithelioid cells having vesicular nuclei and prominent nucleoli. Sarcomatous differentiation is a very uncommon feature of subependymoma, which was described only twice in the literature (13, 27). Tomlinson reported a 52 year-old male with a 4th ventricular mixed tumor consisting of subependymoma and rhabdomyosarcoma. Louis described sarcomatous change in a recurrent subependymoma after 18 months following radiotherapy (27).

Surgical treatment is indicated in symptomatic cases (15). Tumors locating in lateral ventricles usually allow complete resection and in most cases no recurrence was observed (8, 12, 15). Even with partial resection the prognosis is good (6, 19).

Radiotherapy is not indicated; it should be reserved for recurrent , infiltrative lesions.

A rare case of subependymoma in an infant with possible complication of radiotherapy was reported. In this case radiotherapy was administered at 1 year of age. She developed neurologic and mental complications. When she died of cardiovascular failure at the age of 21, more than 20 multiple meningiomas were found at autopsy (10).

In conclusion we present two rare cases of ependymomas with different clinical presentation but with similar histopathological features. In a ventricular tumor, subependymoma should be included in the differential diagnosis.

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