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Choroid plexus carcinoma: A case report

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Background. *The opinions on the value of adjuvant therapy in choroid plexus carcinomas vary. The aim of present report is to present a case of successful therapy of this rare tumor.*

Result. *A fourteen-year-old girl with third ventricle tumor had non-radical surgery and adjuvant chemotherapy and irradiation. She is alive with no evidence of disease 8.5 years after diagnosis. The role of adjuvant therapy in the context of literature data is discussed.*

Conclusion. *For choroids plexus carcinomas, adjuvant multiagent chemotherapy and craniospinal radiotherapy following surgery should be considered.*

Key words: choroid plexus neoplasms; chemotherapy, adjuvant; radioteraphy; survival analysis

Introduction

Choroid plexus tumor (CPT) is a rare neoplasm, arising from the neuroepithelial lining.[1] After its first description in 1832, more than 500 CPT patients have been described in literature.[2] Three quarters of the patients are children, with tumors most often found in the lateral ventricles. In adults, the fourth ventricle and its recesses are the most common sites of origin.[1] The histopathology of CPT ranges from a well - demarcated benign papilloma (WHO grade I) to highly anaplastic, infiltrative carcinoma (WHO grade III, choroid plexus carcinoma [CPC]). Surgical resection alone is curative for benign tumors, but the optimal adjuvant therapy for the malignant ones has not yet been defined and the prognosis is poor.[1,3] Our experience in successfully treating such a patient is therefore of interest.

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Case report

The patient was previously healty 13.8-year old girl who was admitted to the hospital in January 1996, with a six months complaint of headache and double vision when reading. Two months prior to admission she became progressively lethargic and dull resulting in a deterioration of school performance. Neurologic examination revealed bilateral papilledema, ataxia, positive bilateral Babinski

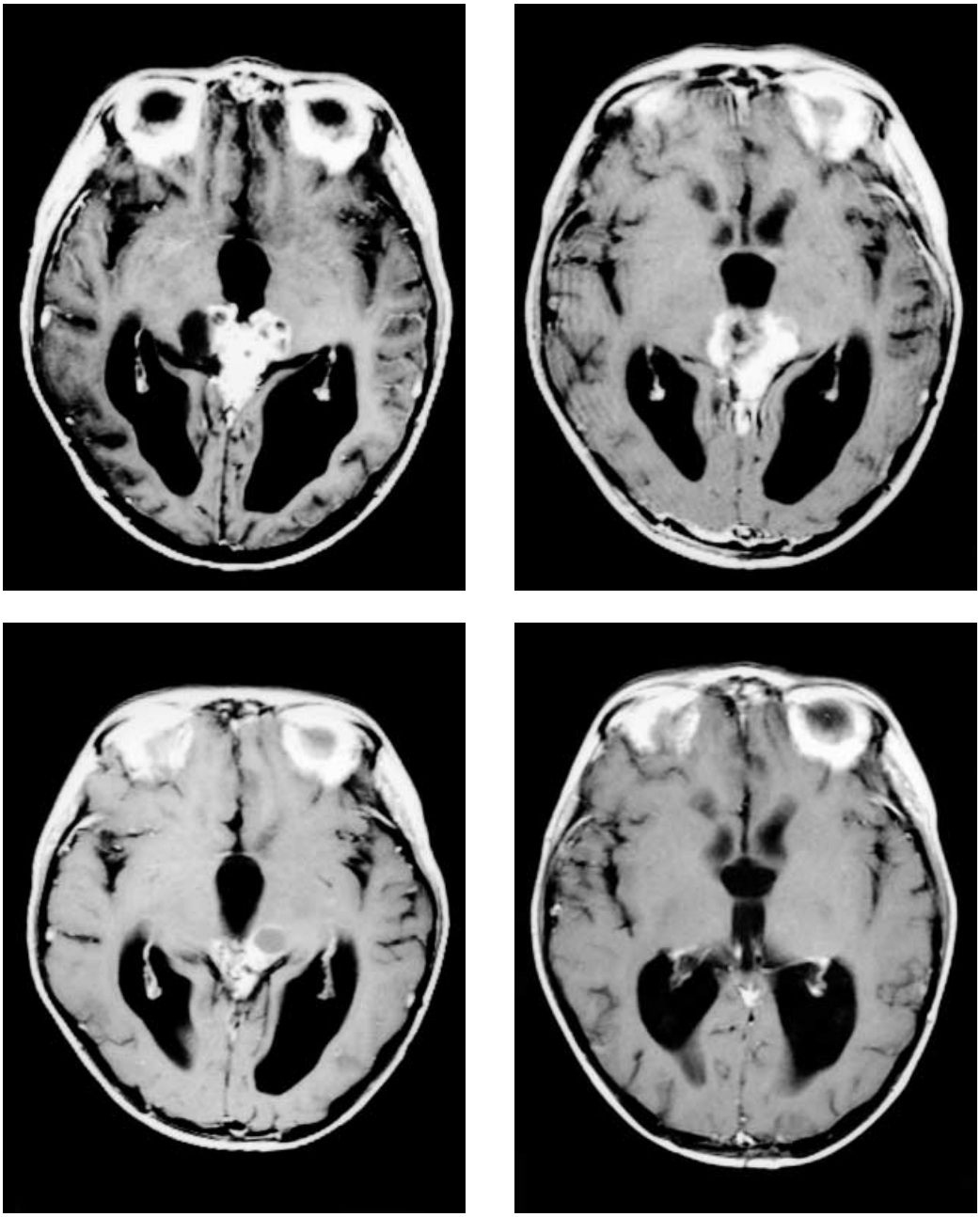

Figure 1. T1-weighted transverse postcontrast MRIs of the patient.
(A) Before surgery: partially cystic tumor mass of the third ventricle with the extension to thalamus, and dilatation of ventricular system.
(B) Two weeks after surgery and before chemotherapy: residual tumor in the third ventricle.
(C) After the second cycle of multiagent chemotherapy: marked regression of residual tumor.
(D) Five months after radiotherapy: even after gadolinium application, there is no pathologic enhancement suspicious for residual tumor mass.

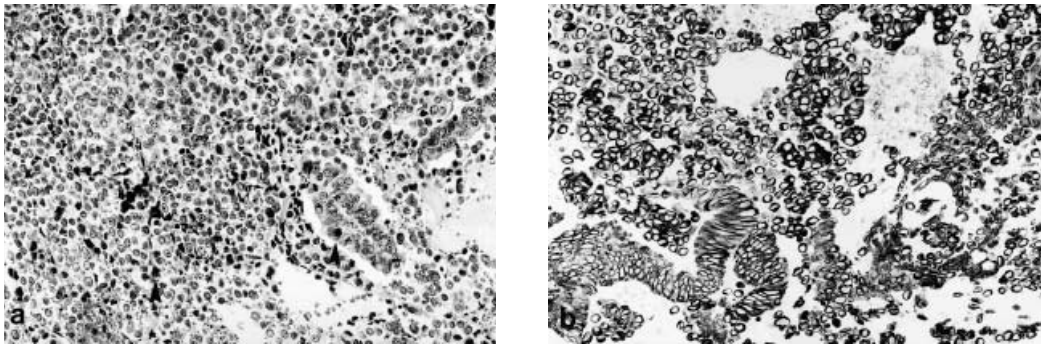

Figure 2. Histologic characteristic of resected tumor.
(A) Solid growth of carcinoma with focal papillary structures. Mitotic figures are present (arrowheads). H&E, magnification 190x.
(B) Strong cytokeratin immunoreaction is evident in all tumor cells. Immunohistochemistry, DAKO's CK 18 monoclonal antibody, magnification 190x.

signs and right-sided hyperreflexia. Two days before surgery, Parinaud syndrome developed. Computed tomography (CT) and magnetic resonance (MR) scans of the brain showed a contrast-enhancing lesion in the pineal region with extension to the thalamus and the lamina quadrigemina and dilatation of the supratentorial ventricles (Figure 1A).

External ventricular drainage was introduced first. No tumor cells were found in the cerebrospinal fluid. Tumor resection was performed one week later and a reddish granular tumor tissue overgrowing the posterior part of the third ventricle was found. It infiltrated locally and extended to the lamina quadrigemina. Histologic examination revealed a highly cellular, focally necrotic tumor composed of polygonal cells with moderately polymorphic nuclei and scattered mitoses. Tumor cells were organized in sheets or formed papillary structures lined with multiple epithelial layers. Due to pineal location, embryonal carcinoma was also taken into consideration. Strong cytokeratin and NSE labelling of tumor cells, in addition to negative AFP and PLAP, confirmed the diagnosis of CPC (Figure 2). Two days after surgery, external ventricular drainage was removed. On postoperative imaging, tumor residue was seen in the postero-inferior part of the third ventricle (Figure 1B).

Postoperatively, multiagent chemotherapy was introduced according to the so-called BEP protocol (bleomycin 15 mg/m^2 I.V., days 1-3; etoposide 100 mg/m^2 I.V., days 1-3; cisplatin 20 mg/m^2 I.V., days 4-8). After the second cycle of chemotherapy, the MRI showed a marked regression of the residual tumor (Figure 1C), and an additional two cycles of these drugs resulted in further tumor reduction. The treatment concluded with craniospinal radiotherapy of 31.5 Gy/21 fx and a local tumor boost of 22 Gy/20 fx b.i.d. The patient was irradiated five days per week, using 5 MV linear accelerator photon beams. The treatment technique consisted of posterior spinal fields with moving junction and a combination of two lateral opposing portals and one posterior portal for the brain. Two-field technique was used for boosting the tumor. Complete disappearance of the tumor was confirmed by a subsequent MR scan (Figure 1D).

To date, 8.5 years after diagnosis, there has been no evidence of local tumor recurrence or metastasis. She has no severe neurologic impairment and her Karnofsky index is 100. She finished high school, got married, and gave birth to her first child. So far, the child is normal as was the endocrine testing of his mother.

Discussion

Experience with this extremely rare malignant tumor is scanty. Surgery is, however, unequivocally considered to be the first-line therapy for all histological variants of CPTs. Surgical techniques and possible complications have been widely described in literature.[1] In CPCs, the most significant predictive factor for survival is the extent of surgery. This has been confirmed in several single-institution analyses[4-6] as well as in literature reviews.[2,3] To obtain complete tumor removal, Ellenbogen et al. and others have advocated as many surgical procedures as required.[4-6]

One of the key debates in CPC therapy relates to the value of adjuvant therapy after gross tumor resection. There are both opponents and proponents of the combined treatment approach.[2-5,7,8] A recent literature review by Wolff *et al.* found adjuvant radiotherapy to be of benefit over surgery alone.[2] Similar conclusions with regard to radiotherapy and/or chemotherapy can be drawn from numerous single-institution reports.[5,9,10]

The need for aggressive adjuvant therapy is widely recognized in the patients with residual CPC following surgery since the expected survival is half of that after gross tumor resection.[2,3,8] Even though there are anecdotal reports on successful adjuvant radiotherapy[7,9] or chemotherapy,[10] it is our impression that aggressive combined radio-chemotherapy offers the best chance for survival. Examples of beneficial effect of combined therapy, sometimes incorporating second-look surgery, can be found in the literature.[8,9,11]

The radiotherapy target volume is dictated by the propensity of CPC for subarachnoid seeding which, when confirmed, calls for adjuvant therapy *per se*, irrespective of the degree of completeness of surgical procedure. Subarachnoid seeding was found in 43% of those reported cases that were investigated for dissemination.[3] Thus, craniospinal axis irradiation to a dose of 30 Gy and a boost to the tumor bed up to 50 Gy is indicated if radiotherapy is used,[12] and seems to be more effective than chemotherapy.[3]

Due to the high risk of severe adverse intellectual and endocrinologic sequelae in very young children, early radiotherapy is an option in older age groups only. Two treatment strategies were described in the literature for young patients, both placing emphasis on multiagent chemotherapy, although this also is not entirely free of long-term side-effects.[13] To facilitate complete tumor resection as a main prognostic determinant in CPCs, St Clair *et al.* used preoperative chemotherapy to reduce tumor vascularity and bulk after initial biopsy or limited surgery. Not specifying the postresection therapy, if any, two out of four children from this program were reported to be free of disease for 30 and 39 months from diagnosis.[6] The second option was described by Duffner *et al.* Using chemotherapy for 24 months in children 0-23 months of age and 12 months in those 24-36 months of age and delayed radiotherapy, the autors reported a 3-year survival of 75%, with five of the eight patients surviving a minimum of 48 months following diagnosis.[10] The variety of chemotherapeutic agents and their combinations used by these two groups as well as in other reports indicates that an optimal chemotherapy regimen is yet to be defined.

In conclusion, our recommendation would be that for CPCs, after as extensive surgery as possible, adjuvant therapy consisting of multiagent chemotherapy and craniospinal radiotherapy, delayed in very young children, should be considered. The BEP regimen detailed above plus radiotherapy gave a good result in the patient described.

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