Simultaneous choroid plexus carcinoma and pilocytic astrocytoma in a pediatric patient

Case report

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Simultaneous primary brain tumors in pediatric patients without prior chemotherapy or radiotherapy, phacomatoses, or known familial history are a rare occurrence. The authors report the case of a 4-year-old boy with simultaneous choroid plexus carcinoma and pilocytic astrocytoma with features of oligodendroglioma. Magnetic resonance imaging studies revealed diffuse heterogeneously enhancing left intraventricular and posterior fossa tumors initially believed most consistent with multicentric choroid plexus carcinomas. A multiple staged resection was carried out for each tumor and gross-total resection was achieved. Upon gross inspection intraoperatively as well as postoperative histological analysis, 2 distinct simultaneous tumors were identified: choroid plexus carcinoma and pilocytic astrocytoma. To the authors’ knowledge this is the first case report published identifying 2 distinct tumor types with similar radiological appearances in a pediatric patient with no prior history of radiotherapy, chemotherapy, or phacomatoses. (DOI: 10.3171/2009.8.PEDS09117)

KEY WORDS • simultaneous pediatric tumors • choroid plexus carcinoma • multiple tumors • multicentric tumors

The clinical dilemmas faced by neurosurgeons in the treatment of multiple intracranial tumors were first thoroughly described by McCormick and colleagues52 and Malamud and Batzdorf27 over 50 years ago after a landmark study by Bailey and Cushing1 contributed significantly to our arsenal of knowledge about the mode of growth and spread of gliomas. At that time, simultaneously occurring primary tumors were usually found in postmortem examinations and even then considered a rare occurrence. Several smaller reports followed, but Courville1 was the first to focus attention on multiple primary brain tumors during the modern medicine era; and at the time he was only able to account for 25 cases of multicentric or multiple gliomas in his entire review. Much confusion existed surrounding the best classification of multiple tumors until a report by Russell and Rubinstein47 classified multiple intracranial tumors into 2 categories that are still used today: multiple tumors and multicentric tumors. Multiple tumors were interpreted to result from dissemination by an “established” route such as via the commissural or other pathways, spread via the CSF or through local metastasis through satellite formation in the immediate vicinity of the initial tumor. Multicentric tumors are widely separated lesions in different locations that do not easily fit into one of the aforementioned pathways of dissemination. More recent published reports document multiple or multicentric intracranial neoplasms usually occurring in patients who had been treated with chemotherapy or radiotherapy, patients with known genetic histories putting them at increased risk, or those with multiple tumors occurring at different times.4,9,46,49

Phacomatoses, such as neurofibromatosis and tuberous sclerosis, have been shown to be associated with an

Abbreviation used in this paper: NF = neurofibromatosis.
increased incidence of multiple tumors.26,46 Recently, genetic analysis has allowed patients with germline mutations to be identified. Mutations in several genes including TP53, hSNF5/INI-1, as well as other chromosomal abnormalities have led to the identification of several genes involved with multiple tumor syndromes such as Li-Fraumeni, Aicardi X, and Turcot Syndromes.38,48,50

We conducted a MEDLINE/PubMed review utilizing the search terms “simultaneous tumors,” “multicentric tumors,” “multiple tumors,” and “two primary intracranial tumors” and found only approximately 50 documented cases of simultaneously occurring primary brain tumors. In this group of cases, only a handful has been documented as occurring in the pediatric population. The incidence of multiple and multicentric tumors reported in the literature varies greatly. Much of the data on the incidence of these tumors was obtained from poorly controlled studies in the pre-imaging era, excluding all but gliomas. From these studies, multiple primary intracranial neoplasms have been inferred to occur with an incidence rate of 2–10%, with the incidence of 2 simultaneously occurring tumors of different histology occurring simultaneously estimated to be far less. From 1896 to 1959, an analysis of 12 series including a total of over 1200 patients reported an incidence ranging from 1 to 10%.27 Choroid plexus carcinomas are decidedly of neuroectodermal origin and are even more rare, representing < 0.5% of all central nervous system tumors with an annual incidence of 0.3 cases per 1 million population.16,31,60 The following case is the first published report of 2 simultaneously occurring brain tumors with similar imaging appearances in a pediatric patient without prior history of radiation, chemotherapy, or known phacomatoses.

Case Report

**History and Examination.** This 4-year-old boy was transferred to our institution from another hospital with a 5-day history of headache, anorexia, nausea, and emesis. He had been doing well until 1 week prior to admission, when he began to develop symptoms of an upper respiratory infection in the form of nasal congestion and low-grade fevers for which his mother had been giving him an over-the-counter nasal decongestant with minimal relief. A few days prior to his presentation, his symptoms worsened and he began to develop intractable nonprojectile vomiting associated with headache. The headache was frontally located, was sharp in quality, and caused fussiness and irritability and eventually inconsolable crying. The child’s mother noted that after each episode of emesis there were brief periods of headache relief; however, the frequency of these episodes was increasing to as many as 4–5 times daily. The child was observed to be sleepier and less active, with a clumsy gait, and he exhibited periodic bizarre truncal body movements. Weakness, numbness, paresthesias, night sweats, weight loss, rashes, back pain, and recent trauma were denied.

The patient had been born after full-term gestation. The pregnancy and delivery had been free of complications. The parents were nonconsanguinous, and the child had no significant medical or surgical history. Developmentally, he was physically appropriate for age except for a speech delay with a 75% understandable speech rate, for which he was undergoing evaluation. His immunizations were current. There was a sporadic family history of stomach and esophageal cancer, lymphoma in a paternal great-grandfather who died at 50 years of age, seizure disorder, and kidney disease. There were no first- or second-degree relatives in whom malignancy had been identified.

Neurological examination revealed a sleepy but arousable child. He followed commands and verbalized a few strings of words with a slow rhythm, but did not form any complex sentences. Fundoscopic examination revealed bilateral papilledema. There were no focal motor or sensory neurological deficits at the time of initial examination.

**Imaging Studies.** Review of a noncontrast axial CT scan of the head performed at the institution from which the child was transferred revealed 2 separate hypodense cystic masses—one located in the left thalamus and lateral ventricle and a second in the posterior fossa adjacent to the fourth ventricle. There was mass effect and midline shift with associated obstructive hydrocephalus (Fig. 1). Initial MR imaging of the brain (with and without gadolinium) revealed a 5 × 2 × 3–cm heterogeneously enhancing, left

![Fig. 1. Preoperative noncontrast axial CT images demonstrating hypodense and cystic lesions of the left lateral ventricle and posterior fossa. Note the presence of obstructive hydrocephalus and midline shift.](image-url)
lateral ventricular lobulated mass with nonenhancing cystic components located laterally and posteriorly. There was associated edema and mass effect upon the thalamus and third ventricle. Within the posterior fossa, a 4 × 4 × 3-cm heterogeneously enhancing midline mass with extension through the fourth ventricle was found. Again, an associated nonenhancing cystic component located within the fourth ventricle was seen (Fig. 2).

Management. Immediate staged resection of the supratentorial tumor followed by the infratentorial tumor was undertaken in view of the patient’s condition, neurological status, hydrocephalus, and associated midline shift. Debulking, resection of the intraventricular tumor, and placement of an external ventricular drain were performed with the assistance of Stealth intraoperative guidance. A high left parietal circular craniotomy and craniectomy were performed. The tumor was found to be vascular, requiring circumferential resection from normal brain tissue prior to intratumoral decompression with use of an ultrasonic aspirator (CUSA). Successful tumor resection and coagulation of the remaining ventricular choroid plexus were achieved. Postoperative MR imaging of the brain (with and without gadolinium) revealed successful resection of the intraventricular tumor (Fig. 3). Next, our attention shifted to the posterior fossa tumor. On the following day, a suboccipital craniotomy and microsurgical resection were performed. Grossly, the tumor appeared grayish, firm, not clearly defined and not as highly vascularized as the supratentorial tumor, leading one to speculate that these might represent tumors of differing pathology. The patient required reoperation for residual tumor 2 days after the second staged resection. Postoperative MR imaging of the brain (with and without gadolinium) revealed successful resection of the posterior fossa tumor (Fig. 4). Neuroelectrophysiological monitoring was used during all resections with no changes from baseline. Tissue samples were sent for pathological analysis. Surveillance MR imaging of the axial spine (with and without gadolinium contrast) did not reveal any evidence of drop metastasis. He had a stable postoperative course and was discharged home 5 days later with minimal ataxia.

Histological Findings. Grossly, the intraventricular tumor revealed tan, ragged tissue; microscopically the tissue showed papillae lined by crowded moderate-sized epithelioid cells as well as sheets of cells with abundant cytoplasm. The tumor cells showed focal atypia. Brain invasion by tumor cells was seen focally at the periphery of the lesion. Mitotic activity was brisk and a high proliferation index was seen with Ki 67 immunostaining. It was felt that this tumor was compatible with a choroid plexus carcinoma (Fig. 5).

Microscopically, the posterior fossa tumor revealed features consistent with both pilocytic astrocytoma and oligodendroglioma. The pilocytic component consisted of mildly pleomorphic astrocytes with oval and minimally tapered nuclei. Rosenthal fibers and densely fibrillar pildial material were also present. A prominent nesting pattern was seen in the tumor fragments that were confined to the subarachnoid space. The oligodendroglial component consisted of cells with more round nuclei, perineural cytoplasmic clearing, abundant capillary network, and calcifications. Tumor cells showed immunoreactivity with glial fibrillary acidic protein (GFAP), and immunnostaining with Ki 67 showed a low proliferative index. It was felt that this tumor was compatible with a pilocytic astrocytoma with oligodendrogial features (Fig. 6).

Adjunctive Treatment. Chemotherapy was administered according to the CPT SIOP 2000 protocol (choroid plexus tumor study of the Société Internationale d’OncoLOGIE PédiatRIQUE) consisting of the drugs etoposide, carboplatin and vincristine. The child received a total of 6 cycles of etoposide, carboplatin, and vincristine over a span of 8 months and had no hospitalizations for neutropenia or fever. During the fifth cycle of chemotherapy, he developed gross hematuria and proteinuria, and underwent renal biopsy, which revealed immune complex–mediated crescentic necrotizing glomerulonephritis. It was treated with a short course of prednisone and the symptoms resolved promptly. Due to the development of glomerulonephritis, carboplatin and vincristine. The child received a total of 6 cycles of etoposide, carboplatin, and vincristine over a span of 8 months and had no hospitalizations for neutropenia or fever. During the fifth cycle of chemotherapy, he developed gross hematuria and proteinuria, and underwent renal biopsy, which revealed immune complex–mediated crescentic necrotizing glomerulonephritis. It was treated with a short course of prednisone and the symptoms resolved promptly. Due to the development of glomerulonephritis, carboplatin was eliminated from his last cycle of chemotherapy.

Follow-Up and Additional Treatment. Follow-up MR imaging of the brain and complete axial spine (with and without contrast medium) as well as CSF analysis performed after his last cycle of chemotherapy failed to show any evidence or recurrence of malignancy. No further chemotherapy or radiation therapy is planned. Bactrim pro-
Simultaneous carcinoma and astrocytoma in a pediatric patient

Phylaxis against *Pneumocystis carinii* will be continued for 6 months after completion of chemotherapy. Routine immunizations will be delayed until after chemotherapy is completed. Close monitoring of the patient’s neurological status as well as serial MR imaging will dictate future treatment.

As of this writing, approximately 9 months have passed since his initial diagnosis and he is doing well without focal neurological deficits. His cognition, aptitude, and physical development are age appropriate and he is reaching accepted developmental milestones. He continues to undergo physical therapy several times weekly. Language analysis reveals delays similar to those seen preoperatively, although without significant disability. He is able to speak in sentences and comprehend adequately; however, his speech development is reported to be delayed. Speech

![Fig. 3. Gadolinium-enhanced MR images obtained after the first staged resection of the left lateral ventricle lesion. Axial (A), sagittal (B), and coronal (C) images demonstrating gross-total resection of left lateral ventricular supratentorial enhancing lesion with improvement of midline shift.](image)

![Fig. 4. Gadolinium-enhanced MR images obtained after the second staged resection of the posterior fossa lesion. Axial (upper) and sagittal (lower) images demonstrating gross-total resection of posterior fossa enhancing mass.](image)
therapy has been initiated and will be coordinated with his social worker.

Discussion

There have been few reported cases of simultaneously occurring primary brain tumors in patients with no history of radiotherapy, chemotherapy, or phacomatosis. To our knowledge, this is the first documented case that has been reported in a pediatric patient. In patients who present with multiple intracranial neoplasms, diagnosis can be demanding, especially in the pediatric patient population. One must consider that there is not always a clear history and when a history is obtained, it is usually relayed second-hand from involved friends or family members. Additionally, localizing signs may be absent or conflicting. In our patient, the language delay was suggestive of a lesion localized to the left hemisphere, but the ataxic gait suggested a lesion localized to the posterior fossa. In the preimaging era or in areas without CT or MR imaging, diagnoses may be dangerously delayed. Once imaging studies are performed, both neurosurgeon and radiologist must critically analyze their interpretation. Multiple mass lesions with neoplastic, traumatic, or cerebrovascular etiologies, when separated by space, will act independently and, in some cases, balance the mass effects of one another. Paradoxically, for global malignant cerebral edema the additional space created by allowing brain to herniate through the site of a bone defect allows tissues to expand so that CT-demonstrated changes observed preoperatively are minimized or completely resolved in the postoperative period. For example, 2 masses located in contralateral frontal cerebral hemispheres may cancel the mass effect of one another, resulting in what appears to be minimal effect on the midline. In cases involving multiple brain tumors, the mass effect created by some of the tumors may be counterbalanced by the others so that the true mass effect of one tumor is appreciated only after the other is resected. This has important surgical implications that must not be underestimated.

In planning surgery in cases of multiple tumors there are additional variables to be considered. When planning approaches we must be cognizant of the shifts that may occur during surgery. In multiple tumors located in anatomical proximity, this may be a lesser concern, but if a single-stage procedure is used to resect tumors that are not in close proximity, deleterious shifts can occur. Several reports have highlighted this phenomenon with resultant fatal ascending transtentorial herniation. Nonetheless, many advocate removal of both tumors in one session as yielding the best outcomes. If the histological diagnoses are known preoperatively, then those types of tumors with increased likelihood for postoperative edema should be removed after tumors that are more benign are removed first. Glial tumor resection with resultant postoperative edema may lead to grave results if undertaken prior to surgery of tumors with more benign pathological type due to decreased brain compliance from the coexistent lesion. Several authors report deciding on which tumor to remove based upon clinical findings alone. Tumors causing more clinical signs are removed first. This is especially important when dealing with superficial and deep simultaneous tumors that may not necessarily require resection if resection of the symptomatic more superficial lesion is successful. If computer-assisted neuronavigation is used, it must be appropriately adjusted to take into account some of the shifts that may have occurred. In our patient, we chose to perform a staged resection. This sequential staged resection was chosen for several reasons, including the reasons discussed previously and surgeon preference as well as our ability to repeat imaging studies after each resection for more accurate localization, increasing our precision in the context of any shifts that might have occurred.

Choroid plexus tumor management would be greatly
Simultaneous carcinoma and astrocytoma in a pediatric patient

facilitated by an accurate, noninvasive, preoperative diagnosis. Current imaging modalities have been inadequate in differentiating these tumors.\textsuperscript{23,28} Although the diagnosis of choroid plexus tumor was considered preoperatively in our case, no confirmatory tissue diagnosis had been made at that point. Confirmation of pathological type aids in preoperative planning, as these tumors are usually hypervascular. Preoperative embolization of hypervascular tumors has been described for decades as an adjunctive technique purported to decrease operative blood loss and operating times and facilitate larger and more complete resections.\textsuperscript{5,17} Supraselective embolization of tumoral feeding arteries has now become standard at some institutions. However, in the pediatric population, preoperative embolization of these feeding arteries has rarely been reported due to the small size and tortuosity of the blood vessels in these patients.\textsuperscript{30} Given our patient’s declining neurological status, a delay in treatment might have been disastrous. Moreover, it is difficult to ascertain if the overall risk associated with this procedure alone would have been outweighed by its benefit, as no formal risk analysis of preoperative tumor embolization in the pediatric population has been performed. Overall, mortality rates from complications related to surgery have ranged from 0 to 25% and mortality rates attributed to blood loss are reported to be as high as 12%.\textsuperscript{10,32,37} Attempts to use preoperative embolization in pediatric patients have yielded mixed results, with many institutions choosing to forego endovascular treatments in this population. As advancements in microcatheter and microguidewire technology evolve, these patients may have more successful outcomes with these techniques.\textsuperscript{35} Additionally, endovascular techniques may also be used as a salvage measure for operative or perioperative control of head and neck vascular injuries in the proper setting.\textsuperscript{37} Sensitive, noninvasive diagnostic tools may assist with perioperative surgical planning; specifically, surgical approaches and adjuvant therapy, such as preoperative embolization, properly planned to address the observed hypervascularity of choroid plexus tumors.

Multiple familial syndromes and phacomatoses have been described, which may predispose patients to having multiple tumors. Neurofibromatosis and tuberous sclerosis are 2 of the most common syndromes associated with an increased incidence of multiple tumors, and they have been described extensively in the literature.\textsuperscript{26,42} Briefly, multiple café au lait spots, axillary and inguinal freckling, multiple discrete dermal neurofibromas, and pigmentated iris hamartomas (Lisch nodules) characterize neurofibromatosis Type 1 (NF1). Learning disabilities are present in approximately 50% of individuals with NF1. Scoliosis, vertebral dysplasia, pseudarthrosis, and overgrowth are the most serious osseous complications. Less common but potentially more serious manifestations include plexiform neurofibromas, optic and other central nervous system gliomas, malignant peripheral nerve sheath tumors, osseous lesions, and vasculopathy. Neurofibromatosis Type 2 (NF2) is characterized by bilateral vestibular schwannomas with associated symptoms of tinnitus, hearing loss, and balance dysfunction. Age of onset is usually 18–24 years, with nearly all affected individuals developing bilateral vestibular schwannomas by the age of 30 years. Affected individuals may also develop schwannomas of other cranial and peripheral nerves, meningiomas, and rarely, ependymomas and astrocytomas. Diagnosis of NF is based on clinical criteria; \textit{NF2} is the only gene known to be associated with NF2 and is currently being used as a confirmatory test once a clinical diagnosis is made. Tuberous sclerosis is an autosomal dominant genetic disorder affecting cellular differentiation and proliferation, which results in the formation of hamartomas in several organs including the skin, brain, eyes, kidneys, and heart. The frequency in the US is 1 case in 5,800–30,000 persons. The condition is usually diagnosed in childhood, with cardiac and cortical tuber development; skin lesions are seen in more than 90% of patients at all ages. Multiple major and minor features are considered and used in the diagnoses described elsewhere.\textsuperscript{14,39,45} Of interest with respect to our patient, a major diagnostic criterion is the development of astrocytomas. Other syndromes to consider include basal cell nevus syndrome (Gorlin-Goltz syndrome) and Turcot syndrome.\textsuperscript{2,18} It is critical that the most common syndromes be considered in evaluation of the patient who presents with multiple neurological pathological conditions.

The finding of simultaneously occurring tumors during infancy within members of the same family is rare and suggests the presence of a germline mutation with a predisposition to malignancy.\textsuperscript{54} Choroid plexus carcinomas and other multiple primary brain tumors have been associated with several familial neoplastic syndromes including Li-Fraumeni, Aicardi, and Turcot. Data are sparse regarding the precise mechanisms involved due to the infrequent nature of these syndromes as well as multifactorial etiologies. A variety of somatic and germ cell line mutations have been implicated, including the \textit{TP53} and \textit{hSNF5/INI-1} genes as well as X-linked chromosomal abnormalities. The \textit{TP53} gene is located on 17p13.1 and expresses the protein product p53, which influences tumor suppression via a variety of mechanisms, including DNA repair, apoptosis, cellular differentiation, and angiogenesis.\textsuperscript{31} Mutations of the \textit{TP53} gene may produce loss of p53 function as well as prolongation of the half-life of the protein, both implicated in the oncological effects seen. Choroid plexus carcinomas are among the tumors found in Li-Fraumeni families with \textit{TP53} germline mutations.\textsuperscript{12,20,28} The \textit{hSNF5/INI-1} gene is located on 22q11.2 and encodes a unit of the SWI/SNF adenosine triphosphate–dependent chromatin-remodeling complex.\textsuperscript{50} Genetic studies of families with this mutation have identified the development of both renal and extrarenal malignant rhabdoid tumors, choroid plexus carcinomas, atypical teratoid rhabdoid tumors, and medulloblastomas.\textsuperscript{54}

In our patient, no stigmata of phacomatoses were identified. External examination did not reveal any skin lesion, nor was there any history of masses or other lesions. Fundoscopic examination revealed papilledema but no evidence of Lisch nodules or other intraocular pathological condition. There was a family history of sporadic age-related neoplasm, but no familial tumors were identified. Radiographic studies did not reveal any masses in the cerebellopontine angle or evidence of intraparenchymal tubers suggestive of neurofibromatosis or tuberous
sclerosis, respectively. An echocardiogram did not reveal any cardiac abnormality or lesions. Analysis of DNA was negative for TP53 or NF2 mutations. Results of testing for the hSNF5/INI-1 gene were positive, indicating a normal genotype pattern. The hSNF5/INI-1 gene is involved in several atypical teratoid and rhabdoid tumors and helps to distinguish these tumors (which are negative for immunoochemical staining with INI-1 antigen) from choroid plexus carcinoma (which is positive). In this case, a positive staining for INI-1 helps to confirm the pathological diagnosis of choroid plexus carcinoma. Chromosomal analysis failed to show any mutations. Microarray analysis of the oligodendrogial tumor component failed to show 1p or 19q deletions or duplications. Although studies showing the association between TP53 mutations and choroid plexus carcinoma have predominantly been seen in adults, it is not entirely clear if children with this same mutation will phenotypically express the neoplasms as well. Unlike astrocytomas in adults, pediatric astrocytomas are characterized by a low incidence of TP53 mutations. Genetic studies in patients with secondary neoplasms due to familial neoplastic syndromes have concluded that the incidence of TP53 mutations among pediatric patients with astrocytic tumors is low and, unlike in adult patients, TP53 mutations do not play an important role in the development of these tumors in the pediatric population. Further genetic testing performed on all pediatric brain tumors will allow more detailed understanding of the pathogenesis of these uncommon and often deleterious cancers.

The optimal treatment for pediatric choroid plexus tumors is currently unknown, and the precise role that adjunctive chemotherapy and/or radiotherapy has in their treatment is currently being investigated. The ongoing SIOP 2000 protocol for patients with choroid plexus tumors is a prospective registry and randomized study for children and adults with choroid plexus tumors. Treatment consists of maximal resection, and for those with choroid plexus carcinoma, postoperative chemotherapy, and—for patients > 3 years old—delayed radiation therapy. Goals of the study are to compare response rates, survival, and tumor resectability after chemotherapy randomized to carboplatin or cyclophosphamide backbones. This protocol is currently being used at a number of international cancer centers in both Europe and the US and results are forthcoming.

Even though there is no defined treatment for multiple tumors, we chose to tailor treatment toward the pathologic entity with the more aggressive natural history: choroid plexus carcinoma. Our patient was treated with a well-established chemotherapy protocol that is being used internationally. Based upon his having undergone gross-total resection at the time of initial diagnosis, and the fact that during the 8 months of chemotherapy, no evidence of recurrence was observed (either clinically or on MR images), it was elected to withhold planned radiation treatments. It is well documented that radiotherapy may cause significant neurocognitive delays, and its precise role in the pediatric population is currently under review. In the setting of this patient’s renal condition and in light of potential adverse effects of radiation therapy, significant issues regarding his quality of life were viewed as greater risk than benefit. An important result of the SIOP 2000 study thus far is that international collaboration on treatment for these rare tumors is possible; this may serve as a future model for collaboration in other rare pathological conditions. Ultimately, the optimal treatment will depend on multiple factors, including pathological characteristics of the lesion, extent of resection, comorbidities, and quality of life, and must be tailored to each patient on an individual basis.

Reports of multicentric or multiple tumors are not uncommon and have been previously published in the literature. Multiple hypotheses have been proposed, but all remain unproven. Currently, no plausible pathophysiology exists to explain simultaneously occurring primary brain tumors of varying histological types. In a retrospective review of cases compiled from over 2 decades, 57 cases involving patients with diagnoses of meningiomas and glial tumors were examined. Spallone et al. found many of the cases to have conflicting results, including improper or missing diagnoses and varying treatments, as was often seen in the pre-CT, pre-MR imaging, and pre-microsurgical era of neurosurgery. Further, many cases involved patients who had recently undergone radiation therapy or chemotherapy. Only 4 of 24 cases were reported in the CT era as having preoperative verification of both tumor types. This further confounds the little data that we have available to study as well as adding to the uniqueness of the case presented here. Studies of the pathogenesis of multiple tumors have looked at CSF channels for answers. Ependymomas have a known disposition to spread and seed at other distant sites through these channels. Given their predominant location, these tumors usually have ample access to CSF, and it is possible that certain tumors will grow in areas with substrates that are advantageous for their growth and proliferation. More recently, other authors have proposed that local mechanisms may be partly responsible for simultaneous tumor formation, proposing that astroglial irritation may cause local cellular transformation leading to adjacent gliotic changes and tumor formation. As many as 32% of tumors in cases of multiple tumors have been reported to be located adjacent to another tumor. This juxtaposition increases the possibility that one tumor may act as an irritating agent inducing local proliferation of the other. This can be partially explored when looking at brain tumors that have been found to be composed of 2 separate distinct histopathological diagnoses within the same lesion. If local “crosstalk” does exist between simultaneously occurring tumors, one might expect the incidence of multicentric tumors to be higher than is currently observed. In our case, histological examination of the tumor specimens did not reveal any characteristics that would make these lesions unique if occurring independently. Histological examination identified 2 tumors that had no variations greater than those observed in different regions of single tumors. It is feasible that further genetic testing or microscopy not yet clinically used might be able to discern features of these tumors suggesting “crosstalk” communication or a propensity for multicentricity. Russell and Rubinstein suggested the possibility of coincidental multiple primary brain tumors and Kuroiwa et al. reached the same conclusion after analyzing 116 cases of multiple intracranial tumors not associated with NF1. They found
that the most frequent combinations were meningiomas and gliomas, meningiomas and pituitary adenomas, and meningioma and neuromas. Since these represent relatively common tumors, it is possible that several multiple tumors incidentally coexist. It appears plausible that our patient may have had a de novo mutation of a yet unknown tumor suppressor gene(s) or may just have fallen victim to coincidence.

Based upon the Cohnheim theory of embryonic rests, Ostertag in 1941 proposed that tumors grew from primitive cells that were displaced during embryogenesis and the development of the central nervous system. These cells, which in the presence of multipotent cells, had a propensity to multiply with blastomatous potential, phenotypically presenting in later life to develop into coordinated “blastomas” throughout the nervous system. His theory was blasted down at that time as he could not explain the delay in the development of the brain and clinical manifestations, nor could he find evidence of such multipotent cells with the technology then available to him. However, we now know that stem cells are ubiquitously found throughout the central nervous system and are likely to play an active role in tumor formation and control. Stem cells, when in the presence of cells with germ line mutations, are at increased predisposition for uncontrolled “blastomatous” cellular growth ideal for tumor formation, thereby providing some theoretical support to Ostertag’s early theory.

In this report, we describe the first published case of a pediatric patient with both choroid plexus carcinoma and pilocytic astrocytoma with oligodendrogial features. Initial radiographic interpretation led to an impression of multicentric glioma or multicentric choroid plexus carcinoma, but histopathological examination revealed the distinct tumors. This has important implications for clinicians in regard to diagnosis and treatment planning. The origin, growth, and genetics of multicentric and multiple tumors in the pediatric population are not very well understood, and further study is needed to optimize patient treatment and outcome.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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References

24. Litofsky NS, Hinton D, Raffel C: The lack of a role for p53