Published in final edited form as:

Neuropathology. 2019 October ; 39(5): 394–397. doi:10.1111/neup.12587.

Co-existent pilocytic astrocytoma with acute B-cell leukemia within the cerebellum

Richard Hickman¹, Rebecca Leeman-Neill¹, Marc Rosenblum², Richard Anderson³, James Goldman¹

¹Department of Pathology and Cell Biology, Columbia University Irving Medical Center, Columbia University, New York, USA

²Department of Pathology, Memorial Sloan Kettering Cancer Center, Columbia University, New York, USA

³Department of Neurological Surgery, Children's Hospital of New York, Columbia University, New York, USA

Abstract

Pilocytic astrocytomas are the commonest childhood brain tumor. They are typically benign and usually are solitary neoplasms. To our knowledge, only one report of a pilocytic astrocytoma with leukemia has been previously issued. We herein describe the first case with documented histopathology of a 2-year-old boy who had a cerebellar pilocytic astrocytoma co-localized with an acute B-lymphoblastic leukemia. We speculate that chemotactic migration of leukemic cells to the pilocytic astrocytoma may be partly mediated through vascular endothelial growth factor (VEGF) and VEGF receptors.

Keywords

angiogenesis; chemotaxis; leukemia; pilocytic astrocytoma

INTRODUCTION

Pilocytic astrocytomas (PA) are typically benign neoplasms that commonly occur in the pediatric age group. The cerebellum is a frequently affected site.¹ In this report, we describe the co-occurrence of a PA and a lymphoblastic leukemia in a cerebellar resection specimen and postulate that chemotaxis between the leukemic cells and the PA may be related to interactions between vascular endothelial growth factors (VEGF) and VEGF-receptors.

Correspondence: Richard Hickman, Department of Pathology and Cell Biology, Columbia University Irving Medical Center, New York, NY 10032, USA. rh2850@cumc.columbia.edu.

DISCLOSURES

The authors do not report conflict of interests related to this article.

CLINICAL SUMMARY

A 2-year-old boy had a witnessed fall at home with head injury. Magnetic resonance imaging (MRI) of the head identified a rim-enhancing, cystic mass with slight thickening of the anterior margin in the right cerebellar hemisphere (Fig. 1A). Gross total resection of the mass was performed.

PATHOLOGIC FINDINGS

Materials and methods

The surgical resection specimen was fixed in 10% formalin and 5- μ m-thick paraffin-embedded sections were produced and stained with either hematoxylin and eosin or specific immunohistochemical stains. For immunohistochemistry, we applied primary antibodies against Ki-67 (rabbit monoclonal, clone 30-9, prediluted; Ventana Medical Systems, Tucson, AZ, USA), glial fibrillary acid protein (GFAP) (rabbit monoclonal, clone EP672Y, prediluted; Ventana), oligodendrocyte transcription factor 2 (Olig-2) (mouse monoclonal, clone 211F1.1, prediluted; Sigma-Aldrich, St. Louis, MO, USA), CD34 (mouse monoclonal, clone QBEnd/10, prediluted; PA0354; Leica, Wetzlar, Germany), CD19 (mouse monoclonal, clone BT51E, prediluted; Leica), CD10 (mouse monoclonal, clone 5656, prediluted; Leica), VEGF-A (mouse monoclonal, clone JH121, diluted 1:25; Invitrogen, Waltham, MA, USA), and VEGF receptor 2 (VEGFR-2) (goat polyclonal, AF357, diluted 1:100; Bio-Techne, Minneapolis, MN, USA).

Pathological findings

Hematoxylin and eosin (HE)-stained sections of the cerebellar mass revealed a biphasic glial neoplasm comprising hypercellular nests of monomorphic tumor cells with perinuclear clearing alternating with loosely textured areas with ovoid nuclei and fibrillary processes. The tumor resided both within the cerebellum and the leptomeninges. The nests of tumor cells were separated by vascular septae, around which were clusters of small cells with a high nuclear : cytoplasmic ratio (Fig. 1B, C). The mitotic activity within the glial neoplasm was very low, but an immunostain against Ki-67 highlighted the vast majority of the perivascular cells. Immunohistochemistry against GFAP (Fig. 1D) and Olig-2 (Fig. 1E) labeled the fibrillary glial processes and nuclei of the glial component, respectively. Additional immunostains for CD34 (Fig. 1F), CD19 and CD10 (not shown) labeled the perivascular aggregates, identifying them as B-lymphoblasts. The features seen in this biopsy therefore were consistent with a PA with an admixed B-cell lymphoblastic leukemia.

Immediately preoperatively, the patient was found to be anemic (hemoglobin: 2.9 g/dL (10.2–12.7 g/dL); hematocrit: 8.3% (31.0–37.7%); mean cell volume: 78.3 fL, white blood cell count: $6.98 \times 10^3/\mu\text{L}$ ($5.14\text{--}13.38 \times 10^3/\mu\text{L}$)) and thrombocytopenic (platelet count: $25 \times 10^3/\mu\text{L}$). The patient responded to packed red blood cell and platelet transfusion with his hemoglobin level increasing to 5.6 g/dL and his platelet count to $38 \times 10^3/\mu\text{L}$. Blood flow cytometry was performed perioperatively and revealed a population of B lymphoblast cells (approximately 27% of gated events) with an aberrant immunophenotype: CD19⁺, CD20dim⁺/partial, MC7dim⁺/partial, CD79a⁺, HLA-DR⁺, CD10⁺, CD38⁺, CD34⁺, TdTpartial⁺,

CD43⁺, CD25dim⁺/small subset, CD33⁻, CD13⁻, CD117⁻, cIgM⁻ and MPO⁻. A subsequent bone marrow biopsy performed revealed 90% blast cellularity and confirmed the B-lymphoblastic leukemia that was present perivascularly in the PA. Aside from the brain and bone marrow, no other organ involvement was clinically detected.

To explore a possible chemotactic mechanism between the PA and the leukemic component, we applied immunostains against VEGF-A (Fig. 1G) and VEGF-R2 (Fig. 1H). VEGF-A was present within the glial component, while a subset of B-lymphoblasts showed weak cytoplasmic staining for both VEGF-A and VEGF-R2. Additional immunohistochemistry against synaptophysin, isocitric dehydrogenase 1 (IDH1: R132H), BRAF V600E, CD56, CD3, CD20 and CD117 were negative within the specimen.

DISCUSSION

The occurrence of gliomas post-radiotherapy for central nervous system (CNS) hematolymphoid diseases are well-reported, but synchronous cases are rare.^{2,3} To our knowledge, there is only one other report of a patient with a concurrent PA and pre-B-cell lymphoblastic leukemia; this report did not document the neuropathology or describe a physical interaction between the two tumors.⁴

The differential diagnosis for the radiologic appearance of a cystic nodule within the cerebellum includes a PA, hemangioblastoma and potentially an infectious process. The main differential diagnosis for the glial component seen in this case is a PA, a leptomeningeal glioneuronal tumor (LGT) and an oligodendroglioma. LGT are rare tumors seen most often in the pediatric age group and these usually have thick, nodular leptomeningeal enhancements with many small subpial cysts on MRI. In this case, the immunoprofile (negative synaptophysin and diffuse GFAP labeling) and the radiologic appearance are not in favor of a LGT.⁵ Moreover, the negative IDH1, and the biphasic nature of this tumor with oligodendroglial-like cells alternating with tumor cells with ovoid nuclei and fibrillary processes, is more in keeping with a PA than an oligodendroglioma.

PA are well-recognized to have a propensity for angiogenesis and generate vascular hyperplasia. This is partly through the secretion and action of VEGF, the presence of which is seen with immunohistochemistry in this case (Fig. 1G).^{6,7} Furthermore, many B-lymphoblastic leukemias express VEGF-Rs.⁸ Possible expression of both VEGF and VEGF-R2 (Fig. 1G and H) by the leukemic blasts raises the possibility that VEGF signaling, which has been found to play a role in CNS involvement by B-cell acute lymphoblastic leukemia, may be involved in the observed relationship between the PA and lymphoblastic infiltrate in this case.^{8,9}

In conclusion, we report for the first time the pathologic features of a synchronous acute B-lymphoblastic leukemia and a PA and, via immunohistochemistry, examine the possibility of VEGF signaling as a mechanism of PA infiltration by the B-lymphoblasts in this case. The patient's chemotherapeutic regimen included induction chemotherapy (intrathecal hydrocortisone, methotrexate and cytarabine) followed by bridging vincristine therapy while awaiting results of his bone marrow pathology, which showed no evidence of disease 1

month after the operation. He was then given four cycles of high-dose methotrexate maintenance therapy and received three cycles of intrathecal methotrexate, cytarabine and hydrocortisone followed by consolidation chemotherapy as per COG AALL0932 clinical trial. The patient is in remission of his leukemia and without recurrence of his PA 18 months post-resection.

ACKNOWLEDGMENTS

Drafting manuscript: RAH and JEG. Critical revision of the manuscript and editing: all authors. This study was exempt from approval by the institutional review board as this is not a research study.

REFERENCES

1. Collins VP, Jones DT, Giannini C. Pilocytic astrocytoma: Pathology, molecular mechanisms and markers. *Acta Neuropathol* 2015; 129: 775–788. [PubMed: 25792358]
2. Vowels MR, Tobias V, Mameghan H. Second intracranial neoplasms following treatment of childhood acute lymphoblastic leukaemia. *J Paediatr Child Health* 1991; 27: 43–46. [PubMed: 2043390]
3. Neglia JP, Robison LL, Stovall M et al. New primary neoplasms of the central nervous system in survivors of childhood cancer: A report from the childhood cancer survivor study. *J Natl Cancer Inst* 2006; 98: 1528–1537. [PubMed: 17077355]
4. Kim AL, Fernandez CV, Greer WL, Hogg D, Lassam NJ, Resch L. Concurrent acute lymphoblastic leukemia and juvenile pilocytic astrocytoma in a pediatric patient. *J Pediatr Hematol Oncol* 2000; 22: 451–453. [PubMed: 11037859]
5. Schniederjan MJ, Alghamdi S, Castellano-Sanchez A et al. Diffuse leptomeningeal neuroepithelial tumor: 9 pediatric cases with chromosome 1p/19q deletion status and IDH1 (R132H) immunohistochemistry. *Am J Surg Pathol* 2013; 37: 763–771. [PubMed: 23588371]
6. Gesundheit B, Klement G, Senger C et al. Differences in vasculature between pilocytic and anaplastic astrocytomas of childhood. *Med Pediatr Oncol* 2003; 41: 516–526. [PubMed: 14595708]
7. Leung SY, Chan AS, Wong MP, Yuen ST, Cheung N, Chung LP. Expression of vascular endothelial growth factor and its receptors in pilocytic astrocytoma. *Am J Surg Pathol* 1997; 21: 941–950. [PubMed: 9255258]
8. Diffner E, Gauffin F, Anagnostaki L et al. Expression of VEGF and VEGF receptors in childhood precursor B-cell acute lymphoblastic leukemia evaluated by immunohistochemistry. *J Pediatr Hematol Oncol* 2009; 31: 696–701. [PubMed: 19707156]
9. Munch V, Trentin L, Herzig J et al. Central nervous system involvement in acute lymphoblastic leukemia is mediated by vascular endothelial growth factor. *Blood* 2017; 130: 643–654. [PubMed: 28550041]

Fig. 1.

MRI (A) and histological (B, C) and immunohistochemical (D–H) findings of the tumor. A post-contrast enhancement T1-weighted image shows a cystic mass rim-enhancement in the right cerebellar hemisphere (A). Microphotographs of HE-stained sections demonstrate nests of tumor cells with ovoid nuclei and clear cytoplasm, and around the vascular septae is a condensation of small cells with a high nuclear:cytoplasm ratio (B, C). Immunohistochemistry for GFAP (D) and Olig2 (E) highlights the neoplastic glial components of the lesion. CD34 immunohistochemistry highlights perivascular lymphoblasts (F). VEGF immunoreactivity is localized in the glial components (G), while

VEGFR-2 immunoreactivity is localized in the endothelial cells and a subset of lymphoblasts (H). Scale bars: 50 μ m (B–H).

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript