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CASE REPORT

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Polyclonal lymphoid tumor of the choroid plexus presenting as an intraventricular mass in a young gorilla

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Abstract An unusual lymphoid lesion with reactive germinal centers, occurring in the choroid plexus of a young gorilla, is reported. It presented as a large mass in the lateral ventricle with hydrocephalus and neurological symptoms. A work-up did not reveal any underlying cause for this lesion. No similar lesion of the choroid plexus has been reported in either human or veterinary literature. Histological work-up, including flow cytometry, gene rearrangement studies and T and B cell markers, favored the lesion being a non-neoplastic lymphoid proliferation of unknown etiology. The prognosis is unknown, although, following complete removal, the animal is well and free of tumor at the time of this report.

Key words Choroid plexus · Gorilla · Pseudotumor · Atypical lymphoid hyperplasia · Magnetic resonance image

Introduction

The common tumors involving the choroid plexus include papilloma carcinoma, nonspecific cysts, cholesterol granuloma, meningioma and metastasis [3]. This is the first report of a tumor with a unique histology in this location in a gorilla. Inflammatory pseudotumors are extremely uncommon in the central nervous system (CNS). Mirra et al. [9] reported two patients with "inflammatory meningeal masses of unexplained origin". The non-neoplastic nature of these lesions was confirmed by immunological marker studies. A histological resemblance to plasma cell granulomas of the lung and sinus histiocytosis with massive lymphadenopathy has been reported in some of the cases of inflammatory pseudotumors of the CNS [8, 9]. Although most of these reported lesions in the CNS are thought to be variants of meningiomas [9], in two cases the lesions were exclusively inflammatory. An extensive search of both human and veterinary literature did not identify any reports of a primary tumor with reactive lymphoid tissue in the choroid plexus [11].

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Case report

A 9-year-old adolescent male Western lowland gorilla named "Chicory" was seen by the Neurology Department at Loyola University Medical Center, (Maywood, Ill.) for recurring attacks of unsteadiness, malaise, and vomiting. The first attack occurred in February 1994, and lasted 1 day, and a second episode in June 1994, which lasted for 2 days. Two subsequent attacks in November and December lasted approximately 5 days each. In between the attacks, the animal behaved normally. Subdued behavior, unsteady walking, heavy drooling out of either side of his mouth, and vomiting with reduced food and water intake also characterized these episodes. While standing he would exhibit a tendency to rock slightly, with fine quivering of his legs. He did not appear to be in any pain during these attacks. During the second attack in June

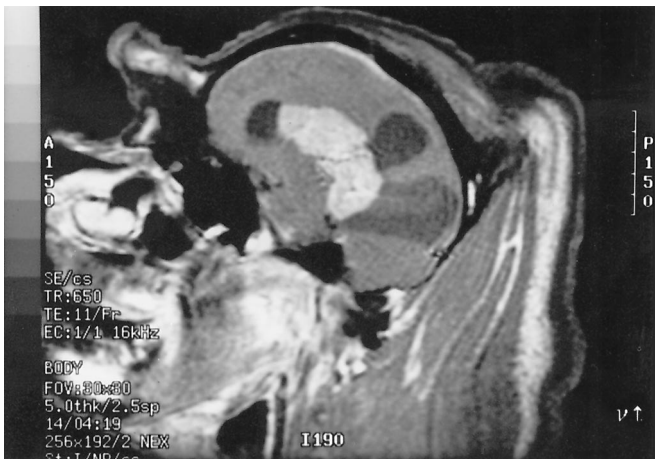

Fig. 1 Magnetic resonance imaging (MRI) scan demonstrating a large intraventricular enhancing lesion

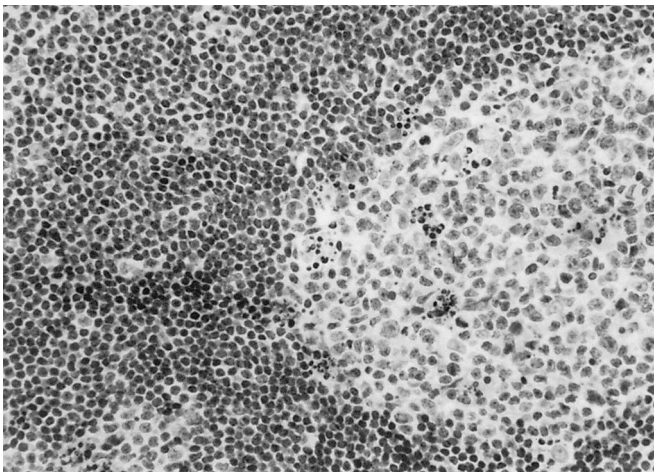

Fig. 2 Hematoxylin-stained section of the tumor showing germinal centers with tingible body macrophages surrounded by a mantle of small lymphocytes. × 200

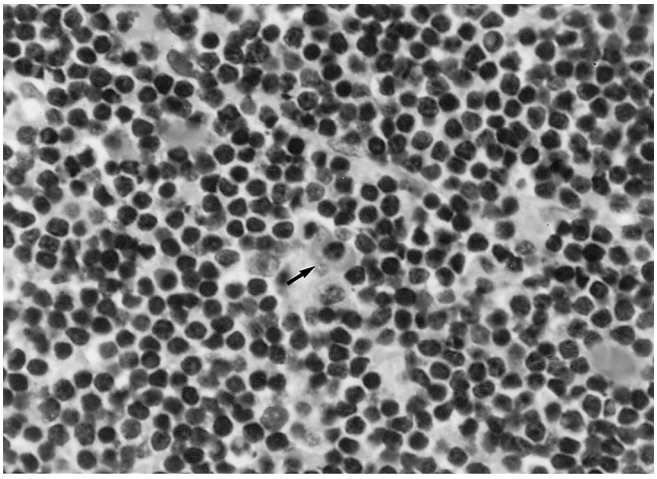

Fig. 3 Hematoxylin and eosin section showing occasional plasma cell and eosinophils. × 400

1994, he had an associated upper respiratory infection which was treated with oral antibiotics. A hematological work-up during one of the attacks was reported to be abnormal with 2–4% peripheral eosinophilia, and mild peripheral leukocytosis. Past medical history include chicken pox in July 1993 and a minor head trauma in January 1994.

Magnetic resonance imaging (MRI) revealed a large enhancing intraventricular mass with the configuration of the choroid plexus on the left side, which extended into the third ventricle (Fig. 1). A craniotomy and total removal of the tumor was achieved by the neurosurgical team at Loyola University Medical Center on 21 December 1994, 10 months after the onset of symptoms.

Pathology

Samples of fresh tumor tissue were sent for flow cytometry and for bacterial, fungal, and viral cultures. Frozen tissue was used for molecular biological studies, and formalin-fixed tissue for routine histology and immunoperoxidase stains.

The hematoxylin and eosin-stained sections revealed a highly vascular lymphoid lesion which formed infrequent germinal centers. The lymphocytes were small, with scanty cytoplasm and without any significant nuclear abnormalities. Nucleoli were inconspicuous and mitoses were not present. In areas, the lymphocytes laminated abnormal blood vessels and/or hyalinized areas (Fig. 2). The germinal centers contained activated lymphocytes (immunoblasts) and tingible body macrophages. Scattered immunoblasts and tingible body macrophages were also present in the interfollicular areas. In some areas, the lymphocytes formed pattern-less sheets around degenerated choroidal epithelium and blood vessels. Occasional plasma cells and eosinophils were also noted within the lymphoid infiltrate (Fig. 3).

Table 1 Summary of the results of the flow cytometry analysis of the peripheral blood of the gorilla Chicory

CD45	100%
CD14 monocytes	5%
CD19 B cells	20%
CD20 B cells	19%
CD24 B cells	< 1%
CD19/kappa	11%
CD19/lambda	7%
CD3+/CD2+/CD7+/CD5+ T cells	52%
CD4 T helper cells	21%
CD8 T suppressor/cytotoxic cells	31%
HLA-DR	37%
CD38	70%

Table 2 Summary of the results of the flow cytometry analysis of the tumor specimens

CD45	100%
CD14 monocytes	< 1%
CD19 B cells	43%
CD20 B cells	44%
CD24 B cells	< 1%
CD19/kappa	26%
CD19/lambda	22%
CD3+/CD2+ T cells	62%
CD3+/CD2- T cells	4%
CD4 T helper cells	44%
CD8 T suppressor/cytotoxic cells	15%

Flow cytometry

Peripheral blood from Chicory and another gorilla was tested with three reagents directed to B cells (CD19, CD20, CD24; Becton Dickinson, Mountain View, Calif.), six reagents directed to T cells (CD3, CD4, CD2, CD8, CD5 and CD7; Becton Dickinson), two reagents directed towards myeloid cells (CD13 and CD33; Becton Dickinson), and antibodies to immunoglobulin kappa and lambda light chains and other reagents (CD10, CD38, HLA-DR; Tago Immunological, Burlingame, Calif.). This was done to validate the reactivity and specificity of these anti-human lymphocytes reagents on the lymphocytes of the gorilla.

The results of the study of the peripheral blood and tumor cells are summarized in Tables 1 and 2, respectively. These results showed that all T and B cell reagents tested, except the CD24 antibody, react with both gorilla and human lymphocyte subpopulations in a similar manner. The findings for peripheral blood lymphocytes from Chicory and the control gorilla were identical. The tumor cells were polyclonal and expressed both kappa and lambda light chains.

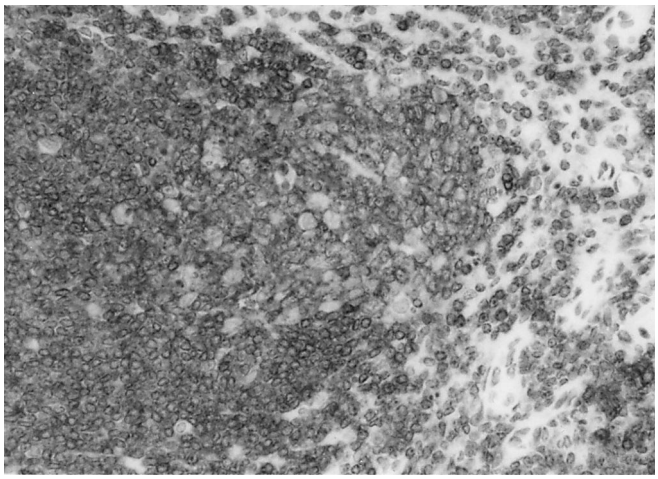

Fig. 4 Immunoperoxidase staining (Pan B) demonstrating the presence of numerous positive cells. × 400

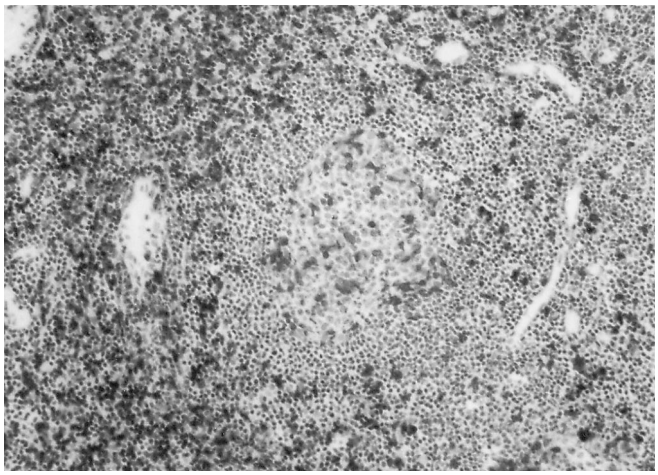

Fig. 5 Immunoperoxidase staining (Pan T) demonstrating the presence of numerous T cells in the perifollicular area. × 200

Immunoperoxidase stains

The formalin-fixed tissue was investigated using for immunoperoxidase stains against Pan B (CD20; Dako, Carpinteria, Calif.) and Pan T (CD45R0; Zymed, San Francisco, Calif.) antigens. The staining pattern revealed the presence of both T and B cells in the lesion (Figs. 4, 5). The monoclonal IgG kappa and lambda chain studies were not optimal in formalin-fixed tissues, but were not performed on fresh tissues.

Microbiological and serological studies

Fresh tissue specimens were also sent for routine bacterial, microbacterial, viral and fungal cultures. All were reported as negative. The serum samples from Chicory were analyzed at the Virus Reference Laboratory in San Antonio, Texas. The results for a 1:5 serum dilution are given in Table 3.

In addition, the formalin-fixed tissue from the tumor immunostained for herpes simplex virus types 1 and 2, cytomegalovirus and toxoplasmosis; all these stains were negative.

Table 3 Summary of the microbiological and serological analysis [*SA8* Simian antigen 8, *Para* parainfluenza, *HSV-1(2)* herpes simplex virus type 1(2), *FluA(B)* influenza virus A(B), *Chm-CMV* Chimpanzee cytomegalovirus, *RSV* respiratory syncytial virus]

SA8	HSV-1	HSV-2	Chm-CMV	EBV	FluA	FluB
–	+	–	+	+	–	–
Para 1	Para 2	Para 3	Measles	RSV		
+	–	+	+	+		

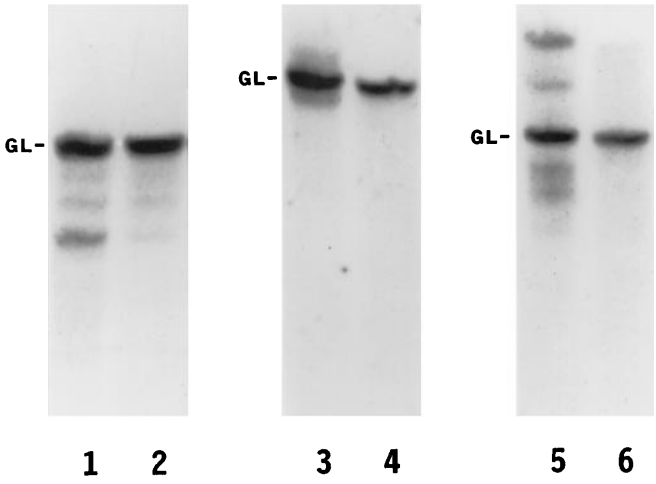

Fig. 6 Southern blot analysis of tumor DNA indicating oligoclonal rearrangement of the immunoglobulin heavy chain and kappa light chains

Molecular biology and gene rearrangement studies

High molecular weight DNA was prepared from total, homogenized tissue for Southern blot analysis. The genes for the immunoglobulin heavy chain, kappa light chain, and beta subunit of the T cell antigen receptor were probed using previously described methods [5]. No detectable clonal rearrangements or deletions of these genes were found on the autoradiograms. However, as shown in Fig. 6, the patterns exhibited for the immunoglobulin genes suggested that a number of small, separate populations of B lymphocytes were present in the tumor (i.e., oligoclonal). This is not indicative of a distinct, clonal expansion process.

Southern blot and polymerase chain reaction (PCR) analyses did not detect translocations of the *bcl*-1 or *bcl*-2 proto-oncogenes. Amplification of Epstein-Barr nuclear antigen sequences by PCR failed to detect the presence of Epstein-Barr virus DNA in the tumor.

Discussion

The present case closely resembles that of an “intracranial lesion resembling giant lymph node hyperplasia” reported by Lacombe et al. [6], although the plasma cell component is minimal. The origin of this lesion is unknown. No cause for an inflammatory reaction was found. It might represent a hyperimmune reaction, probably virally driven; however, no Epstein-Barr or herpes viruses were found in the tumor cells.

Although the tumor was quite vascular, no hyaline vascular change typical of Castleman's disease was present. A low-grade lymphoid neoplasm was the diagnosis entertained by the veterinary pathologist. However, our laboratory studies did not support the diagnosis of a lymphoma, and we believe that this lesion is an atypical lymphoid hyperplasia of unknown etiology.

A diagnosis of reactive lymphoproliferative lesion versus lymphoma may be extremely difficult based on the histology alone, particularly in extranodal sites. Many extranodal B cell lymphomas produce follicular nodules which may resemble benign germinal centers [12]. In addition, lymphomas may arise from reactive states in which benign germinal centers may be prominent. Demonstration of a mixture of cell types, including lymphocytes in various stages of transformation, indicates a benign process. Immunological features, particularly the demonstration of a monoclonal versus a polyclonal cell population in a given lesion, represent a strong diagnostic tool and should be performed for all CNS lesions with a predominant lymphoid cell population. Flow cytometry and gene rearrangement studies are extremely useful tools for identifying small clonal proliferation of cells. Bone marrow examination may be helpful in some cases for diagnosing lymphoma, particularly the peripheral T cell type which may occasionally involve the CNS. Lymphoid hyperplasia similar to Castleman's disease has been described in patients with HIV infection, syphilis and autoimmune diseases [4, 12].

Pimentel et al. [11] reported a case of inflammatory pseudotumor of the choroid plexus in an 18-year-old man. The pseudotumor was located in the left lateral ventricle and was completely removed. The pathology was described as a lesion consisting of fibrovascular tissue with a dense infiltrate of plasma cells and lymphocytes, with occasional histiocytes, neutrophils and eosinophils. Lymphoid hyperplasia with germinal centers were described. Our case was not fibrotic and had only occasional plasma cells, neutrophils and eosinophils. An additional case of inflammatory pseudotumor involving the choroid plexus of the lateral ventricle was reported by Chang et al. [4], in association with Sjögren's disease; in this case the lymphoid infiltrate did not have germinal centers. Lymphomatoid granulomatosis [2, 12] may involve as much as 23% of the CNS; however, the involvement of the choroid plexus was not recorded in the autopsy cases studied. Their histopathology was quite different from that seen in the present case.

Although inflammatory pseudotumors have been reported in the CNS [4, 9, 11] and in the soft tissues [2, 7], we could not find a similar lesion reported in the choroid plexus with a predominant lymphoid cell population with extensive germinal center formation.

A repeat MRI scan 6 months later showed no residual tumor (Fig. 7). The ventricles were almost back to normal except for the left temporal horn which was slightly dilated. At the time of this report, 1 year following surgery, Chicory is reported by the Zoo officials to be normal.

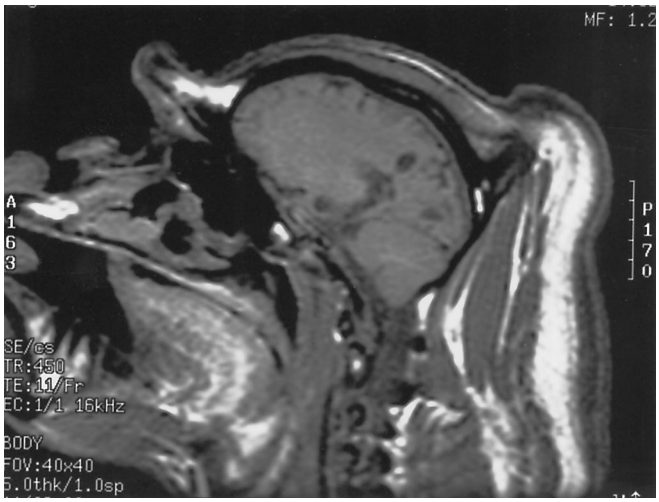

Fig. 7 Repeat MRI scan showing no residual tumor and minimally enlarged ventricles

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