# The Role of Neurosurgery in the Treatment of Intracranial Tumor–Like Inflammatory Lesions

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■ BACKGROUND: **Different inflammatory diseases can manifest as intracranial lesions. They may be indistinguishable from intracranial neoplasms in the clinical setting, imaging studies, or laboratory studies. The value of surgery in the diagnosis and the treatment of such lesions is still unclear.**

■ METHODS: **A total of 3066 reports of histopathologic examinations over a 10-year period were reviewed. Forty patients with an inflammatory intracranial lesion were identified. Clinical, radiologic, and follow-up data were analyzed and the diagnostic and therapeutic value of surgery was assessed.**

■ RESULTS: **We identified 24 women and 16 men (mean age, 47 years). The diameter of the lesion varied between 1 and 5.5 cm (mean, 2.6 cm). The location of the inflammatory lesion was intracerebral supratentorial ($n = 18$, 45%), intrasellar/suprasellar ($n = 5$, 12.5%), cerebellar ($n = 5$, 12.5%), in the brainstem ($n = 4$, 10%), in the cerebellopontine angle ($n = 3$, 7.5%), meningeal ($n = 3$, 7.5%), and at other locations ($n = 6$, 15%). Seventeen patients underwent surgical removal of the mass lesion, whereas in 23 patients a biopsy was taken. The lesions were classified into 7 groups: specific (infectious) granuloma ($n = 10$, 25%), unspecific granuloma ($n = 7$, 17.5%), idiopathic inflammatory pseudotumor ($n = 5$, 12.5%), demyelinating lesions ($n = 5$, 12.5%) encapsulated hematoma ($n = 4$, 10%), organized cerebral infarction ($n = 3$, 7.5%), and vasculitis ($n = 4$, 10%). Surgery was judged as valuable in 35 patients (87.5%).**

■ CONCLUSIONS: **The differential diagnosis of intracranial inflammatory lesions involves a wide spectrum. Surgery has a diagnostic and/or therapeutic value in most entities and clinical circumstances. However, attention must be taken to avoid surgery without a therapeutic or diagnostic value for the patient.**

## INTRODUCTION

A broad spectrum of inflammatory diseases can manifest as intracranial lesions and simulate neoplasms in the clinical setting and in imaging studies.[1–3] It is of outmost importance to differentiate such lesions from primary cerebral tumors or metastases.[4,5] Although some inflammatory lesions need urgent and specific treatment, others may allow a wait-and-see strategy.[3]

The diagnosis of some inflammatory entities (i.e., intracranial pyogenic abscess) can usually be made by specific imaging studies.[2] However, accurate diagnosis of other intracranial inflammatory entities is often not possible a priori. Clinical examination and diagnostic methods may fail to determine the nature of such lesions, or in other cases, primary treatment may fail to achieve improvement.[6] In such instances, tissue examination of the lesion obtained by surgery is necessary to

**Key words**
- Inflammatory lesion
- Intracranial
- Tumor
- Pseudotumor

**Abbreviations and Acronyms**
ACE: Angiotensin-converting enzyme
CEH: Chronic encapsulated hematoma
CG: Cholesterol granuloma
CNS: Central nervous system
CSF: Cerebrospinal fluid
ECD: Erdheim-Chester disease
HIV: Human immunodeficiency virus
IIP: Idiopathic inflammatory pseudotumor
MR: Magnetic resonance
MS: Multiple sclerosis
PCNSV: Primary central nervous system vasculitis
PCR: Polymerase chain reaction

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establish a definitive diagnosis. In addition, some inflammatory lesions show a significant mass effect and surgery may be useful to decompress neural structures. Nevertheless, the role of surgery in the treatment of various intracranial inflammatory lesions is still unclear or controversial.

Several inflammatory entities simulating intracranial tumors were reported as case reports or small series involving a wide spectrum including demyelinating disease, infections, and vascular disorders.[2,6] We present our experience in the diagnosis and treatment of intracranial inflammatory lesions over 10 years. We review the differential diagnosis of such lesions according to the histologic examination and discuss potential clinical and radiologic features helping to recognize such entities in the preoperative und postoperative setting. We also determine the value of neurosurgical procedures in the management of specific intracranial inflammatory lesions.

## METHODS

### Patient Selection

The reports of 3066 histopathologic examinations from patients who underwent surgery for intracranial lesions over a 10-year period were reviewed. Inclusion criteria for this study were 1) confirmation of an intracranial inflammatory lesion as defined by histopathologic criteria and 2) availability of histopathologic specimens. Exclusion criteria were 1) pyogenic intracranial abscess and 2) foreign body granuloma including tefloma, as reported elsewhere.[7] Clinical, imaging, and histopathologic data of 40 patients who met the inclusion and exclusion criteria were analyzed.

### Preoperative Diagnostic Evaluation

All patients enrolled in this study had standard laboratory tests on admission and magnetic resonance (MR) imaging with gadolinium. Specific blood or cerebrospinal fluid (CSF) analysis or further imaging studies such as angiography were performed in several instances.

### Decision Making: Biopsy versus Resection

The decision to perform surgery and which specific approach to use (biopsy or resection) was reached on discussion in the neurosurgical conference or in the interdisciplinary neuro-oncology board at our institution. Indications for surgery were to obtain tissue to make a final histopathologic diagnosis and/or to decompress neural structures caused by mass lesions. Surgical techniques according to the departmental standards have been outlined elsewhere.[8-10]

### Postoperative Course and Follow-Up

Further treatment was installed or adjusted according to the results of the histopathologic examinations. All patients had follow-up visits to determine clinical and radiologic outcome.

### Retrospective Assessment of the Diagnostic and Therapeutic Value of Surgery

To assess the value of surgery, we retrospectively evaluated each case according to the criteria outlined here. Surgery was considered to have a diagnostic or therapeutic value when $\geq$1 of the following criteria was fulfilled:

1) Patients had progressive symptoms and other noninvasive or less invasive diagnostic methods were inconclusive.
2) Initial medical treatment failed to achieve clinical improvement, and surgery was necessary to obtain tissue to determine a diagnosis.
3) Removal of the inflammatory intracranial lesions proved to be the only or the most effective treatment modality.

## RESULTS

There were 24 women and 16 men. Age ranged between 8 and 85 years (mean age, 47 years). In 39/40 patients (97.5%), a definitive histopathologic diagnosis was made. In only 1 patient (2.5%), the tissue examination showed inflammatory features of the intracranial lesion, but a specific diagnosis could not be established. Patients' clinical, imaging, histopathologic, and other data are summarized in Table 1.

### Signs and Symptoms on Presentation

The signs and symptoms on presentation varied according to the location and the nature of the lesion. They ranged from nonspecific complaints such as headache, nausea, and dizziness to severe neurologic deficits such as hemiparesis or progressive cranial nerve palsy. Signs and symptoms were also suggestive for intracranial neoplasms. A few patients were asymptomatic and the lesions were found incidentally on imaging studies.

### Locations and Characteristics of the Inflammatory Lesions on MR Imaging Studies

In 35 patients (87.5%), a single lesion was identified on MR imaging. In the other 5 patients (12.5%), $\geq$2 lesions were found. The inflammatory lesions affected almost all intracranial structures. Their location was intracerebral supratentorial ($n$ = 18, 45%), intrasellar/suprasellar ($n$ = 5, 12.5%), cerebellar ($n$ = 5, 12.5%), brainstem ($n$ = 4, 10%), cerebellopontine angle ($n$ = 3, 7.5%), meningeal ($n$ = 3, 7.5%), around optic nerve ($n$ = 2, 5%), pineal gland ($n$ = 1, 2.5%), jugular foramen ($n$ = 1, 2.5%), ventricular system ($n$ = 1, 2.5%), and in the infraorbital fissure ($n$ = 1, 2.5%). Some inflammatory entities had preferential locations, for example, all cases with tumefactive vasculitis were found in the supratentorial compartment. The diameter of the mass lesion varied between 1 and 5.5 cm (mean, 2.6 cm). The inflammatory lesions enhanced homogeneously ($n$ = 10, 25%), heterogeneously ($n$ = 9, 22.5%), or ring-shaped ($n$ = 11, 27.5%) or they did not show any enhancement ($n$ = 10, 25%). Although some lesions had some suggestive specific features on MR imaging, most could not be diagnosed definitively according to their MR characteristics (except cholesterol granuloma [CG]).

### Surgery and Related Complications

In 17 patients (42.5%), a total ($n$ = 16, 40%) or subtotal resection ($n$ = 1, 2.5%) of the inflammatory mass lesion was achieved via craniotomy or a transnasal transsphenoidal approach. In the other 23 patients (57.5%), a diagnostic biopsy was obtained via navigated open craniotomy ($n$ = 14, 35%) or frame-based stereotactic surgery ($n$ = 9, 22.5%). Postoperative complications, new deficits, or aggravation of preoperative deficits occurred in 3 patients (7.5%).

**Table 1.** Summary of the Clinical and Radiological Features and the Value of Surgery in a Series of 40 Patients with Intracranial Inflammatory Lesions with Histopathologic Findings, Postoperative Treatmant and Outcome After the Treatment

| Patient Number | Sex | Age (years) | Clinical History, Signs, and Symptoms | Location of Lesion | Lesion Size (Largest Diameter in cm) | MRI Findings | Surgery | Diagnosis | Surgery-Related Complications | Postoperative Treatment | Follow-Up (months) | Value of Surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 24 | Headache, fatigue, amenorrhea | Intrasellar and suprasellar | 2 | Nonenhancing lesion, high signal in T1-weighted and T2-weighted images (Figure 2) | Total resection via transnasal transsphenoidal approach | Cholesterol granuloma | — | None | 12 | Valuable |
| 2 | M | 72 | Headache | Intrasellar and suprasellar | 5.5 | Nonenhancing lesion, high signal in T1-weighted and T2-weighted images | Total resection via transnasal transsphenoidal approach | Cholesterol granuloma | Panhypopituitarism | None | 12 | Valuable |
| 3 | M | 59 | Control MRI after resection of a craniopharyngioma 6 years earlier | Intrasellar and suprasellar | 2 | Nonenhancing lesion, high signal in T1-weighted and T2-weighted images | Total resection via transnasal transsphenoidal approach | Cholesterol granuloma | — | None | 12 | Valuable |
| 4 | M | 33 | Headache, progressive hearing loss, dizziness | Both cerebellopontine angles | 2 | Nonenhancing lesion, high signal in T1-weighted and T2-weighted images | Total resection via craniotomy approach | Cholesterol granuloma | — | None | 12 | Valuable |
| 5 | M | 69 | History of mastoiditis with multiple operations, progressive hearing loss right side | Right cerebellopontine angle | 3 | Nonenhancing lesion, high signal in T1-weighted and T2-weighted images | Total resection via craniotomy approach | Cholesterol granuloma | – | None | 3 | Valuable |
| 6 | F | 26 | Progressive decreasing of the visual acuity on the left side, no history of sarcoidosis | Around optic nerve | 1 | Homogenously enhancing lesion (Figure 3) | Biopsy via craniotomy with navigation | Neurosarcoidosis | — | Corticosteroid+ azathioprine | 24 | Valuable |
| 7 | M | 23 | Seizures, no history of sarcoidosis | Temporal lobe | 2.8 | Heterogeneously enhancing lesion | Biopsy via craniotomy with navigation | Neurosarcoidosis | — | Corticosteroid | 12 | Valuable |
| 8 | F | 48 | Headache, history of kidney transplantation and breast cancer, CSF-PCR positive for toxoplasmosis, initial therapy with trimethoprim+sulfamethoxazole for 2 months without response (progression of the lesion on MRI) | Parietal lobe | 2 | Ring-shaped enhanced lesion | Biopsy via craniotomy with navigation | Cerebral toxoplasmosis | — | Pyrimethamine+ clindamycin | 3 | Valuable |

F, female; M, male; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; HIV, human immunodeficiency virus; FLAIR, fluid-attenuated inversion recovery.

Continues

**Table 1.** Continued

| Patient Number | Sex | Age (years) | Clinical History, Signs, and Symptoms | Location of Lesion | Lesion Size (Largest Diameter in cm) | MRI Findings | Surgery | Diagnosis | Surgery-Related Complications | Postoperative Treatment | Follow-Up (months) | Value of Surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 9 | M | 71 | Headache, nausea, history of HIV was unknown at admission (HIV diagnosis approved after surgery) | Temporal lobe | 4 | Ring-shaped enhanced lesion (Figure 4) | Biopsy via craniotomy with navigation | Cerebral toxoplasmosis | — | Pyrimethamine+ clindamycin + antiretroviral therapy | 3 | Valuable |
| 10 | M | 18 | Progressive visual deterioration, history of acute lymphocytic leukemia with bone marrow transplantation 3 years previously, CSF-PCR positive for toxoplasmosis, initial therapy with trimethoprim+sulfamethoxazole 3 months without response (progression of the lesion on MRI) | Multiple lesions in thalami | 2.5 | Ring-shaped enhanced lesion | Biopsy via borehole with frame-based stereotaxy | Cerebral toxoplasmosis | — | Pyrimethamine+ clindamycin | 24 | Valuable |
| 11 | F | 45 | Dysarthria, diplopia, HIV-positive, toxoplasmosis IgM negative, CSF studies negative for toxoplasmosis, initial therapy with sulfasalazine+trimethoprim+ sulfamethoxazole without response (progressive hemiparesis and progression of the lesion on MRI) | Frontal lobe | 1.4 | Homogenously enhancing lesion | Biopsy via craniotomy with navigation | Cerebral toxoplasmosis | — | Pyrimethamine+ clindamycin | 12 | Valuable |
| 12 | M | 42 | Ataxia, altered mental state, HIV-positive, CSF-PCR, and serologic studies negative for toxoplasmosis, initial therapy with trimethoprim+sulfamethoxazole for 3 months without response (progression of the cerebral lesions on MRI) | Cerebellum | 5 | Ring-shaped enhanced lesion | Biopsy via craniotomy with navigation | Cerebral toxoplasmosis | — | Pyrimethamine+ clindamycin | 3 | Valuable |
| 13 | F | 22 | Seizures, temporary residence in Namibia, tuberculosis negative (chest radiography, sputum studies, Mantoux tuberculin skin test, and CSF-PCR) | Multiple cerebral | 2.5 | Homogenously enhancing lesion | Biopsy via craniotomy with navigation | Intracranial tuberculoma | — | Antituberculosis therapy | 12 | Valuable |
| 14 | F | 39 | Aphasia, hemihypesthesia, tuberculosis negative (chest radiography, sputum studies, Mantoux tuberculin skin test, interferon γ test, and CSF-PCR | Meningeal, frontal | 2.7 | Homogenously enhancing lesion | Biopsy via craniotomy with navigation | Intracranial tuberculoma | — | Antituberculosis therapy | 12 | Valuable |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | F | 60 | Seizures, history of kidney transplantation, immunosuppressant drugs, CSF studies are normal | Two lesions in parietal lobe | 1 | Ring-shaped enhanced lesion | Biopsy via craniotomy with navigation | Intracranial nocardiosis | — | Linezolid+ meropenem | 2 | Valuable |
| 16 | M | 25 | Seizures, history of working in army as cook with a temporary residency in Malawi 6 months previously, CSF studies showed few eosinophils | Temporal lobe | 1.5 | Heterogeneously enhancing lesion | Total resection via craniotomy approach | Neurocysticercosis | — | Praziquantel+ albendazole | 3 | Valuable |
| 17 | F | 41 | Seizures, history of kidney transplantation, immunosuppressant drugs | Attached to cerebral falx | 2.7 | Heterogeneously enhancing lesion | Total resection via craniotomy approach | Cerebral aspergilloma | — | Voriconazole+ caspofungin | 3 | Valuable |
| 18 | F | 85 | Headache, ataxia | Attached to tentorium | 4 | Heterogeneously enhancing lesion | Total resection via craniotomy approach | Chronic encapsulated hematoma | — | None | 12 | Valuable |
| 19 | F | 85 | Headache, hearing loss, dizziness | Medial surface of petrous part of the temporal bone | 3 | Ring-shaped enhanced lesion | Total resection via craniotomy approach | Chronic encapsulated hematoma | — | None | 12 | Valuable |
| 20 | F | 75 | Ataxia | Cerebellum | 2.7 | Ring-shaped enhanced lesion | Total resection via craniotomy approach | Chronic encapsulated hematoma | — | None | 12 | Valuable |
| 21 | F | 68 | Headache, dizziness | Intrasellar and suprasellar | 2 | Ring-shaped enhanced lesion (**Figure 5**) | Total resection via craniotomy approach | Chronic encapsulated hematoma | — | None | 12 | Valuable |
| 22 | M | 68 | Acute paresis of the right upper extremity, history of lung cancer | Frontal lobe | 2 | Nonenhancing lesion | Biopsy via craniotomy with navigation | Cerebral infarction | — | None | X | Without value |
| 23 | M | 17 | Headache | Frontal lobe | 3 | Nonenhancing lesion | Biopsy via craniotomy with navigation | Cerebral infarction | — | None | X | Without value |
| 24 | M | 77 | Visual hallucination, history of bladder cancer | Occipital lobe | 1 | Homogenously enhancing lesion | Subtotal resection via craniotomy | Cerebral infarction | — | None | X | Without value |
| 25 | M | 74 | Focal seizures | Frontal lobe | 1.2 | Heterogeneously enhancing lesion | Biopsy via craniotomy with navigation | Primary central nervous system vasculitis | — | Corticosteroid | 12 | Valuable |
| 26 | M | 46 | Progressive hemiparesis | Temporal lobe | 3.8 | Heterogeneously enhancing lesion (**Figure 6**) | Biopsy via craniotomy with navigation | Primary central nervous system vasculitis | — | Corticosteroid | 18 | Valuable |
| 27 | F | 32 | Seizures | Parietal lobe | 1 | Nonenhancing lesion, high signal in T2- and FLAIR images | Biopsy via borehole with frame-based stereotaxy | Primary central nervous system vasculitis | — | Corticosteroid | 12 | Valuable |

F, female; M, male; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; HIV, human immunodeficiency virus; FLAIR, fluid-attenuated inversion recovery.

Continues

**Table 1.** Continued

| Patient Number | Sex | Age (years) | Clinical History, Signs, and Symptoms | Location of Lesion | Lesion Size (Largest Diameter in cm) | MRI Findings | Surgery | Diagnosis | Surgery-Related Complications | Postoperative Treatment | Follow-Up (months) | Value of Surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 28 | F | 30 | Seizures, history of systemic lupus erythematosus | Temporal lobe | 2 | Homogenously enhancing lesion | Biopsy via borehole with frame-based stereotaxy | Secondary central nervous system vasculitis | — | Corticosteroid+ methotrexate | 12 | Without value |
| 29 | F | 16 | Acute hydrocephalus, history of juvenile idiopathic arthritis and hemolytic anemia, no abnormalities in CSF and serologic studies | Cerebellum | 4 | Heterogeneously enhancing lesion | Total resection via craniotomy approach | Idiopathic inflammatory pseudotumor | — | Corticosteroid | 36 | Valuable |
| 30 | F | 67 | Ataxia, dizziness, history of kidney cancer 3 years previously | Pineal gland | 1.1 | Homogenously enhancing lesion | Total resection via craniotomy approach | Idiopathic inflammatory pseudotumor | — | None | X | Valuable |
| 31 | F | 45 | Headache, memory difficulties | Suprasellar | 2 | Homogenously enhancing lesion | Total resection via craniotomy approach | Idiopathic inflammatory pseudotumor | Temporary hypopituitarism | Corticosteroid | 36 | Valuable |
| 32 | F | 42 | Hypoglossal nerve palsy | Jugular foramen | 2 | Nonenhancing lesion | Total resection via craniotomy approach | Idiopathic inflammatory pseudotumor | Wound infection | None | 36 | Valuable |
| 33 | M | 66 | Swelling of the lower eyelid with pain | Infraorbital canal | 3 | Homogenously enhancing lesion | Total resection via craniotomy approach | Idiopathic inflammatory pseudotumor | — | None | 6 | Valuable |
| 34 | F | 44 | Acute hemiparesis, delirium, history of depression, no oligoclonal bands in CSF analysis | Multiple cerebral lesions | 5 | Heterogeneously enhancing lesion | Biopsy via borehole with frame-based stereotaxy | Demyelinating lesions | — | Corticosteroid | X | Valuable |
| 35 | F | 43 | Ataxia, dizziness, facial paresis, hemiparesis, hearing loss, no oligoclonal bands in CSF analysis | Brainstem with extension in middle cerebellar peduncle | 3 | Heterogeneously enhancing lesion, high signal in T2-weighted and FLAIR-weighted images with severe edema (Figure 7) | Biopsy via borehole with frame-based stereotaxy | Demyelinating lesions | — | Azathioprine | 24 | Valuable |
| 36 | F | 28 | Hemiparesis, history of type 1 diabetes mellitus and autoimmune thyroiditis, oligoclonal bands in CSF analysis, progression of the hemiparesis despite treatment with corticosteroids | Frontal lobe | 4 | Open ring-enhancing lesion | Biopsy via craniotomy with navigation | Demyelinating lesions | — | Corticosteroids+ plasma electrophoresis | 6 | Valuable |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 37 | F | 64 | Headache, memory difficulties, acute temporary aphasia, history of depression, electroencephalography showed epileptic potentials in the temporal lobe | Temporal lobe | 3 | Nonenhancing lesion, high signal in T2-weighted and FLAIR-weighted images | Biopsy via borehole with frame-based stereotaxy | Demyelinating lesions | — | Corticosteroid | 12 | Valuable |
| 38 | M | 46 | Hemiparesis, ataxia, dysmetria, no oligoclonal bands in CSF analysis | Brainstem | 2 | Ring-shaped enhancing lesion | Biopsy via borehole with frame-based stereotaxy | Demyelinating lesions | — | Corticosteroid | 3 | Valuable |
| 39 | F | 51 | Ataxia, mild hemiparesis, deterioration of the visual acuity, normal CSF analysis, whole-body positron emission tomography showed hypermetabolism of the cerebral lesions and 2 retinal tumors | Multiple lesions in ventricles, in hypothalamus, in optic nerve, in cerebellum, and in brainstem | 2 | Homogenously enhancing lesion | Biopsy via borehole with frame-based stereotaxy | Erdheim-Chester disease | — | Corticosteroid+ methotrexate | 24 | Valuable |
| 40 | F | 8 | Progressive tetraparesis, cranial nerves palsies, CSF and serologic studies failed to establish a diagnosis | Brainstem | 2 | Ring-shaped enhancing lesion | Biopsy via borehole with frame-based stereotaxy | Unspecified | | Corticosteroid+ azathioprine | 3 | Without value |

F, female; M, male; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; HIV, human immunodeficiency virus; FLAIR, fluid-attenuated inversion recovery.

They regressed completely in 2 patients (wound infection and temporary hypopituitarism). One patient (2.5%) had permanent panhypopituitarism after total resection of a large intrasellar and suprasellar CG requiring hormonal substitution.

### Results of Tissue Examination

Histopathologic examination showed a wide spectrum of causes. Despite the variety of entities of inflammatory lesions, most lesions could be stratified into 7 groups (see Figure 1). Specific (infectious) granulomas were the largest group (10 patients, 25%) followed by unspecific granulomas (7 patients, 17.5%). Specific infectious granulomas involved toxoplasmosis, isolated cerebral tuberculoma, nocardiosis, granuloma with *Taenia solium*, and aspergilloma. Nonspecific granulomatous lesions included CG (5 patients), and isolated intracranial neurosarcoidosis (2 patients). Idiopathic inflammatory pseudotumor (IIP) was found in 5 patients (12.5%) located in the infraorbital fissure ($n = 1$), the intrasellar and suprasellar region ($n = 1$), the cerebellum ($n = 1$), the pineal gland ($n = 1$), and in the jugular foramen ($n = 1$).

Chronic encapsulated hematoma (CEH) was diagnosed in 4 patients (10%), and in 3 patients (7.5%), an organized cerebral infarction was confirmed in the tissue examination. Tumefactive cerebral vasculitis was found in 4 patients (10%), which manifested in 2 instances as a granulomatous inflammation and in the other 2 as lymphatic vasculitis. The vasculitis lesions were isolated in 3 patients without any systemic manifestation and thus were considered as primary central nervous system vasculitis (PCNSV), whereas in 1 patient, cerebral vasculitis was a manifestation of a systemic disorder (lupus erythematosus). Tumefactive demyelinating mass lesions were diagnosed in 5 patients (12.5%). One patient had isolated intracranial Erdheim-Chester disease. Examples of the different entities are shown in Figures 2–7.

### Postoperative Adjuvant Treatment and Follow-Up

Details on adjuvant treatment and clinical and radiologic follow-up are given in Table 1. Thirty-five patients (87.5%) were followed up at our institution, whereas 5 patients (12.5%) were treated elsewhere and were lost to follow-up. Three of these patients had a diagnosis of an organized cerebral infarction. Postoperative follow-up ranged between 2 and 36 months (mean, 13 months; standard deviation, ±9.6). Thirty-nine patients (97.5%) showed disappearance or regression of the lesions on the last available MR study parallel to clinical improvement. The patient in whom a definitive diagnosis could not be established had a progression of the lesion on MR follow-up. She refrained from having a second biopsy and died 3 months later.

### Value of the Surgery

According to the criteria to assess the value of surgery as outlined earlier, the surgery was considered valuable in 35 patients (87.5%). However, it did not yield valuable diagnostic or therapeutic benefits in the remaining 5 patients. The value of surgery (therapeutic or diagnostic) is also indicated for every patient in Table 1.

## DISCUSSION

The present series extends the knowledge on intracranial tumor–like inflammatory lesions obtained from previous and smaller

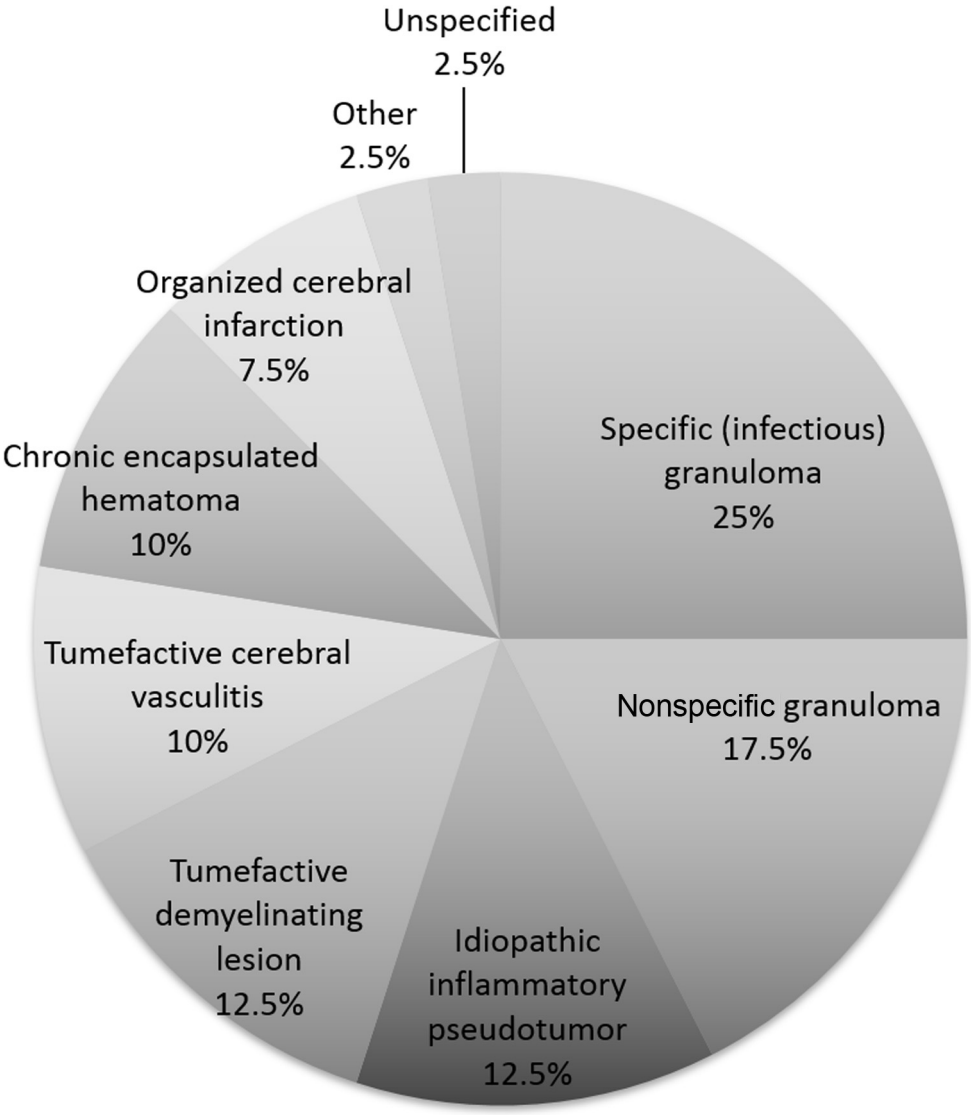


**Figure 1.** Stratification of inflammatory cerebral mass lesions in 40 patients into 7 groups.

series. It also shows that in most patients removal of the lesion or biopsy to obtain tissue specimen provided diagnostic or therapeutic benefit. In the following sections, the 7 groups categorized earlier are discussed separately, focusing on clinical and radiologic features that may be relevant in their differential diagnosis.

## Nonspecific Granuloma

Granuloma formation is the result of a chronic inflammation process accompanied by repair mechanisms involving neovascularization and fibrosis appearing as a mass lesion.[11] Granulomas usually enhance with gadolinium on MR imaging, mimicking a neoplasm. According to the nature of the trigger antigen, there are 2 forms of granulomatous inflammation: nonspecific and specific granulomas. A nonspecific granuloma is initiated and maintained by a nonpathogenic antigen. In our study, 2 entities of nonspecific granulomas were identified: CG and neurosarcoidosis.

***Cholesterol Granuloma.*** CG has been well documented in the otolaryngologic literature, with the typical location in the middle ear.[12] Intracranial CGs are more rare and reported mostly at the skull base close to air-filled spaces such as the petrous apex.[13] Intracranial CGs were also reported in the orbitofrontal region,[14,15] the mastoid,[16] or the middle cranial fossa.[12] In our series, CGs were located in the intrasellar/suprasellar region in 3 patients and in the petrous apex in 2 patients. Intrasellar/suprasellar CGs may arise from the sphenoidal sinus and extend into the intrasellar space.[17] The

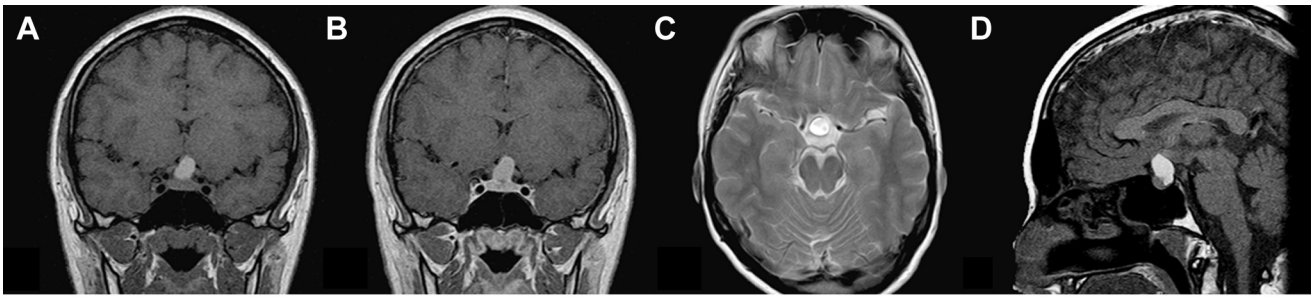


**Figure 2.** Cholesterol granuloma. A 72-year-old woman who presented with headache. (**A**) Coronal T1-weighted magnetic resonance imaging showing hyperintense tumor in the intrasellar and suprasellar region. (**B**) There is no enhancement of the lesion or of the pituitary after administration of gadolinium. (**C**) Axial T2-weighted image showing high signal intensity of the lesion as well. (**D**) A sagittal T1-weighted magnetic resonance image showing the proximity of cholesterol granuloma to the sphenoidal sinus.

pathogenesis of CG is unknown. One hypothesis states that mucosal bleeding into air-filled cavities after trauma or surgery may lead to precipitation of cholesterol crystals, which then stimulate a nonspecific granulomatous reaction.[18] In our series, 1 patient with CG had undergone resection of a craniopharyngioma 6 years earlier.

Presentation of the CG on MR imaging is pathognomonic.[19] CGs are hyperintense both on T1-weighted and T2-weighted images. They are nonenhancing lesions with the exception of a faint peripheral enhancement, which may be difficult to appreciate because of the intrinsic high T1 signal of the lesion. Surgical resection of CG is the treatment of choice.[20] In our series, all patients improved after total surgical removal and there was no recurrence of CG during follow-up.

***Neurosarcoidosis.*** Sarcoidosis is a systemic granulomatous disorder characterized by bilateral hilar adenopathy and pulmonal infiltration. Neurologic involvement occurs in only 5% of patients with sarcoidosis.[21] Isolated neurosarcoidosis is rare and the diagnosis is challenging.[22] The presentation on MR imaging is unspecific and may mimic glioma, metastasis, meningioma, or central nervous system (CNS) lymphoma.[23] Laboratory studies such as angiotensin-converting enzyme in serum and CSF are neither sensitive nor specific.[24-26] Therefore, surgery to obtain tissue samples is recommended in the diagnostic workup in suspected isolated neurosarcodosis.[27] In the 2 patients in our series, thoracic and abdominal computed tomography showed no extracranial manifestation of sarcoidosis. Biopsy of the lesions was necessary to establish the diagnosis. Both patients improved after treatment with corticosteroids, and MR imaging 1 year after surgery documented regression of the lesions.

## Specific (Infectious) Granuloma

***Cerebral Toxoplasmosis.*** *Toxoplasma gondii* is the most common cause for cerebral mass lesions diagnosed in human immunodeficiency virus (HIV)-positive patients.[28] Imaging patterns of cerebral lesions in toxoplasmosis are variable and may show multiple or isolated expanding lesions, with intense enhancement and necrotic areas that may mimic primary or

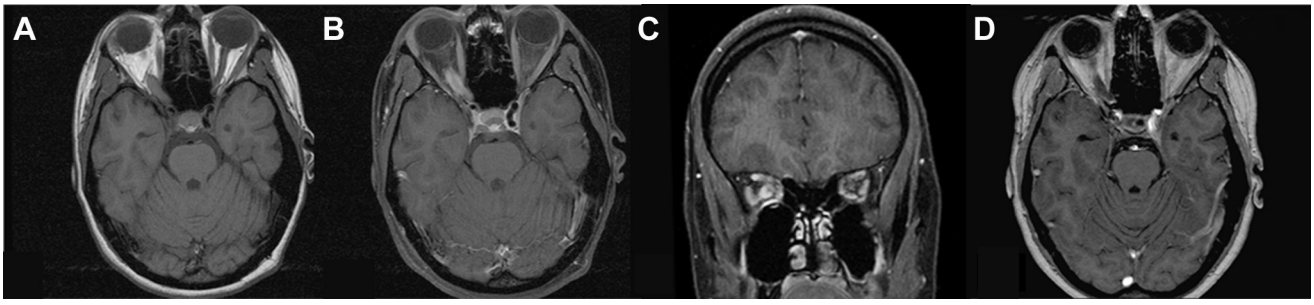


**Figure 3.** Neurosarcoidosis. A 26-year-old woman who presented with progressive decrease of visual activity in the left eye. (**A**) Axial T1-weighted magnetic resonance (MR) image showing thickening of the right optic nerve compared with the left. (**B**) The enlarged optic nerve enhances inhomogenously with gadolinium. (**C**) A coronal T1-weighted MR image showing the enhancement of the right optic nerve with contrast. (**D**) Axial T1-weighted MR image 2 years after biopsy and treatment with corticosteroids and azathioprine showing no more enhancement.

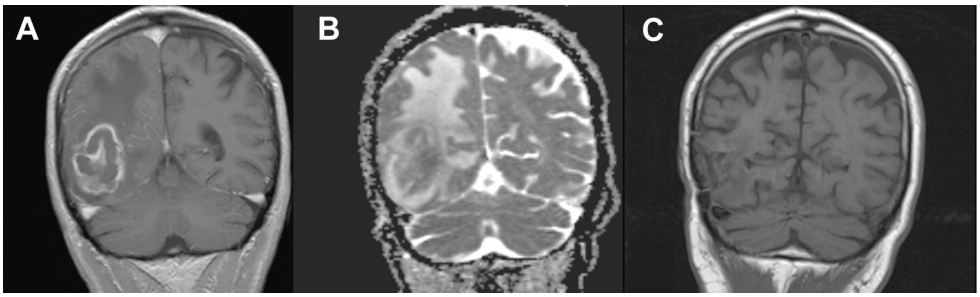


**Figure 4.** Specific granuloma in cerebral toxoplasmosis. A 71-year-old man who presented with headaches and nausea. (**A**) A coronal T1-weighted magnetic resonance image showing a large solitary annularly enhancing lesion with an eccentric nodule along an irregular wall (eccentric target sign). (**B**) Diffusion-weighted imaging does not show changes in apparent diffusion component, which is more suggestive for a tumor than for an abscess. (**C**) Axial T1-weighted magnetic resonance image with contrast 12 months after biopsy and antibiotic treatment showing complete regression of the lesion.

metastatic CNS neoplasms.[29] Several MR imaging features have been proposed to distinguish toxoplasmosis from other conditions such as lymphoma (e.g., eccentric target sign). However, this sign has been found in <30% of patients with neurotoxoplasmosis.[30,31] Both toxoplasmosis and lymphoma need urgent and specific treatment. However, a definitive differentiation between both entities is not always possible. Laboratory studies are usually diagnostic but they may not always provide a definitive diagnosis.[32,33] In addition, there is also a chance of concomitant manifestation of toxoplasmosis and lymphoma in patients with HIV.[34] Therefore, brain biopsy is indicated when a specific treatment for toxoplasmosis shows neither a clinical nor a radiologic response.[3,28,33] In our study, all patients with toxoplasmosis were immunocompromised. In 4, the initial treatment for toxoplasmosis showed no response and therefore biopsies were obtained. In only 1 patient, infection with HIV was unknown at the first presentation and a high-grade glioma was suspected. All patients improved after adjustment of the treatment regimen with specific antibiotics.

***Intracranial Tuberculoma.*** Ten percent of patients with systemic tuberculosis may have CNS involvement.[35,36] Isolated intracranial tuberculomas are rare and may occur in patients without a history of tuberculosis. Only 30% of patients with intracranial tuberculoma undergo pathologic chest radiography.[37,38] Some features of cerebral tuberculoma on imaging studies such as the target sign (central calcification surrounded by a hypointense area with ring-shaped enhancement) are characteristic but unspecific.[39,40] It has been proposed that a combination of MR imaging and CSF–polymerase chain reaction (PCR) would enable a definitive diagnosis of neurotuberculosis to be made.[38,41] However, although CSF cultures and CSF-PCR are specific, they are not absolutely sensitive.[3] In our 2 patients, both serum and CSF serology was negative for tuberculosis. Although the histologic features of the biopsies were highly suggestive for tuberculoma, no bacilli were detected directly in the tissue cultures and only tissue PCR confirmed the diagnosis. Tissue PCR is a reliable tool for bacilli-negative biopsy when histologic features are consistent with a cerebral tuberculoma.[42]

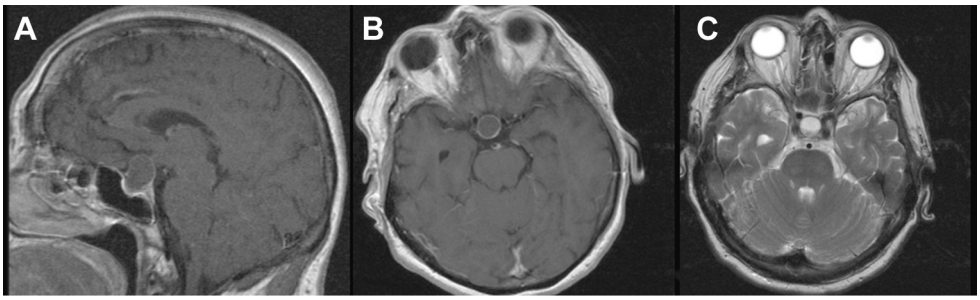


**Figure 5.** Chronic encapsulated hematoma. A 68-year-old man who presented with headaches and dizziness. (**A**) A sagittal T1-weighted magnetic resonance image showing an isointense mass lesion in the intrasellar and suprasellar region with a faint ringlike enhancement. (**B**) Axial T1-weighted image showing more succinctly the faint ringlike enhancement of the encapsulated hematoma. (**C**) An axial T2-weighted magnetic resonance image showing a hyperintense lesion.

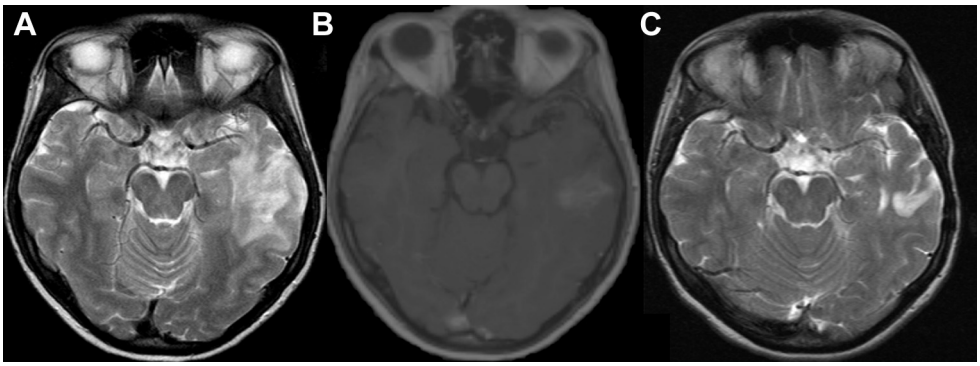


**Figure 6.** Primary vasculitis of the central nervous system. A 46-year-old man who presented with progressive hemiparesis. (**A**) Axial T2-weighted magnetic resonance (MR) image showing a diffuse hyperintense signal alteration in the left temporal lobe. (**B**) Axial T1-weighted MR image showing a faint enhancement of the lesion. (**C**) An axial T2-weighted MR image 1.5 years after biopsy and treatment with corticosteroids showing marked regression of the lesion.

***Intracranial Fungal Infections.*** Aspergillosis, histoplasmosis, and cryptococcosis are the typical fungal infections mimicking brain tumors.[28,43] Isolated intracranial aspergilloma occurs both in immunocompromised and in immunocompetent patients, typically close to the skull base, the orbit, or the paranasal sinuses.[44] Immunosuppressive drugs or immunodeficiency disorders are the most frequent causes for intracranial aspergilloma.[28] The mortality of patients with cerebral aspergillosis without treatment approaches 100% in immunocompromised patients.[45] It has been suggested repeatedly that surgical resection of intracranial aspergilloma is superior to a diagnostic biopsy.[46,47]

***Intracranial Nocardiosis.*** Cerebral nocardiosis is a rare bacterial infection, which may occur in both immunocompromised and immunocompetent patients.[48] A few patients have isolated cerebral nocardiosis and show no other organ involvement.[28,48] Patients with isolated cerebral nocardiosis usually have no systemic signs or symptoms such as fever or leukocytosis.[28] Cerebral nocardiosis is often undistinguishable from brain tumors on MR imaging.[49,50] A definite diagnosis is possible only after histopathologic examination of the resected tissue.[51]

***Neurocysticercosis.*** Cerebral cysticercosis is the most common parasitic infection of the CNS[52,53] and the most common cause of epilepsy in some developing countries.[54] However, the incidence in nonendemic countries is low, which makes diagnosis challenging. In a comprehensive literature review,[55] 77 cases were identified with cysticerci-related single cerebral lesions in nonendemic countries from 1991 until 2011. Cysts can be located close to the meninges, in the brain parenchyma, or in the ventricles.[56] Various specific imaging findings were described on MR imaging. Although the presence of a cystic lesion with a scolex is

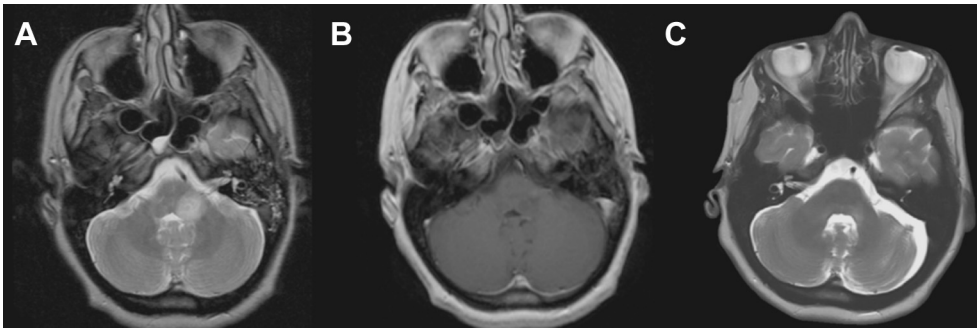


**Figure 7.** Tumefactive demyelinating lesion. A 43-year-old man who presented with ataxia, dizziness, facial paresis, hemiparesis, and hearing loss. (**A**) Axial T2-weighted magnetic resonance image showing a hyperintense lesion in the left middle cerebellar peduncle extending into the pons. (**B**) Axial T1-weighted image showing minimal enhancement with gadolinium. (**C**) Axial T2-weighted magnetic resonance image 6 months after treatment with corticosteroids showing regression of the lesion.

pathognomonic, most cases do not show this finding, especially those with solitary lesions.[57] Although serologic studies are both specific and sensitive, solitary cysts may escape diagnosis.[58] Tissue examination can easily establish the diagnosis and surgical treatment is recommended when the cyst shows tumorlike behavior.[59,60]

### Chronic Encapsulated Hematoma

CEH is characterized by a fibrous capsule with neovascularization surrounding a hematoma in resorption. Cerebral CEH is an unusual manifestation of a cerebral hematoma and was first described 1981 by Hirsh et al.[61] About 57 cases of cerebral CEH were described.[62] The cause for the hematoma is often unclear. In 1 study, about 50% of patients with cerebral CEH showed a vascular malformation.[63] Other causes for its development include trauma or stereotactic radiosurgery.[64] In our series, a cavernoma was confirmed histologically in 1 patient with CEH in the cerebellum. CEHs occurred also in the intrasellar and suprasellar region and in the cerebellopontine angle in 1 patient in our study. In contrast to the acute presentation of a typical intracerebral bleeding, the symptoms of CEH develop gradually and progressively. CEH presents as a ring-enhancing lesion in MR imaging studies and it may show a fluid level. A final diagnosis can be established only by tissue examination. All symptoms improved after removal of CEH in our series and recurrences were not observed. These beneficial results of surgery are in accordance with previous reports.[62]

### Organized Cerebral Infarction

A cerebral infarction is usually distinguishable from brain tumors by its acute clinical onset and its typical presentation and location on imaging studies. However, some cerebral infarctions may have atypical or subtle clinical presentations.[65] In such cases, imaging studies may be performed only with a delay and the infarction will be seen only in subacute or chronic stages when an inflammatory reaction subsequent to tissue necrosis is ongoing. Organized cerebral infarctions may enhance with gadolinium on MR imaging and mimic high-grade glioma.[66] Diffusion-weighted MR imaging is sensitive in outlining early cerebral infarctions, but it is less reliable in subacute infarctions, making it difficult to differentiate between a small subacute cortical infarct and a cortical metastasis.[65,67] Therefore, the frequency of infarcts in retrospective reviews of brain biopsies may range between 1% and 3%.[68] Surgery does not provide diagnostic or therapeutic benefit. A wait-and-see strategy with repeat MR imaging is recommended in patients with suspected infarctions and with stable clinical setting to avoid unnecessary surgery.

### Tumefactive Cerebral Vasculitis

CNS vasculitis is categorized as primary and secondary.[69] Secondary vasculitis is associated with a systemic disorder such as systemic lupus erythematosus or polyarteritis nodosa.[70] PCNSV is an isolated vasculitis of the CNS without evidence of systemic disease.[71] The incidence of PCNSV is estimated in Europe at 1–2 cases/million.[71-73] The incidence of secondary CNS vasculitis is markedly higher than that of PCNSV.[69] In our study, 3 patients were diagnosed with PCNSV, whereas only 1 patient had a secondary vasculitis associated with systemic lupus erythematosus. This discrepancy can be explained by the fact that the diagnosis of secondary systemic vasculitis in contrast to PCNSV can usually be achieved without surgery. The cause and pathogenesis of PCNSV remain unclear.[74] Three forms of clinical presentation of PCNSV are known: acute or subacute encephalopathy, atypical multiple sclerosis (MS) picture, und intracranial mass lesion.[73] Our patients with PCNSV all presented with an intracerebral mass lesion accompanied by focal symptoms such as seizures and hemiparesis. According to the histopathologic presentation, 3 forms of PCNSV can be differentiated: granulomatous inflammatory, lymphocytic, or acute necrotizing patterns.[72] The histopathologic analysis in our patients showed a granulomatous inflammatory pattern in 2 instances and a lymphatic pattern in 1 instance. The appearance of PCNSV on MR imaging is variable.[74] Chu et al.[75] reported that the predictive value of brain biopsy (90%–100%) was significantly higher than that of angiography (37%–50%) or MR imaging (43%–72%) in 30 patients with clinical suspicion of PCNSV.

### Idiopathic Inflammatory Pseudotumor

The term IIP is used to describe a condition of unknown pathogenesis. It is characterized by the presence of a benign mass that is composed of spindle cells and variable amounts of collagen, polyclonal lymphocytes, and plasma cells.[76,77] It may affect nearly all human organs but its typical locations are the lungs and the orbita.[78] Many terms are used to describe this condition or its variants according to their anatomic locations and other histologic features, such as orbital pseudotumor or inflammatory myofibroblastic tumor.[76,79] Intracranial manifestations of IIP are rare. Häusler et al.[80] summarized the findings of 57 reported cases with intracranial IIP. Most IIPs arise in contact with meningeal or dural structures and occur more rarely in the brain parenchyma or in the ventricles.[80] The findings on MR imaging studies are not specific. IIPs usually present with homogeneous or heterogeneous enhancement.[81] A histopathologic examination is necessary for a definite diagnosis. Treatment recommendations for intracranial IIP include surgical resection, administration of corticosteroids or immunosuppressants, and radiotherapy.[79] In our series, total resection was achieved in all patients. Postoperatively, 3 patients were treated with corticosteroids in addition. There was no recurrence in any patient regardless of medical treatment. We suggest achieving complete resection of the mass lesion when possible and administering corticosteroids in cases with incomplete surgical resection or for those with recurrence.

### Tumefactive Demyelinating Lesions

The diagnosis of a tumefactive demyelinating lesion is easy to make when associated with a typical history of remitting symptoms and when it presents with typical MR imaging findings.[3] However, such lesions may occur without a previous history and they may show atypical imaging findings such as a tumefactive lesion simulating a brain tumor difficult to distinguish from neoplastic lesions such as glioblastoma or lymphoma.[82,83] Tumorlike demyelinating lesions have often been described as an atypical form of MS, such as Balo concentric sclerosis or Marburg disease.[84] Tumefactive MS is a neuroradiologic term used for a large lesion (diameter >2 cm)

that is usually solitary.[85] Tumefactive demyelinating lesions are estimated to occur at a frequency of 3/million population and they may constitute 1–2/1000 cases of MS.[86,87] Their frequency ranges only between 0.1% and 0.3% in neurosurgical series.[88,89] The clinical manifestation of tumefactive MS is usually acute, including hemiparesis, seizures, or severe cognitive and mental disturbances.[90] In our series, all patients presented with acute symptoms such as hemiparesis or aphasia and none had a previous history of MS. The diagnosis of tumefactive MS is challenging. Some investigators have emphasized that a white matter lesion with open ring enhancement in which a gap faces the cortex in MR imaging is specific for a demyelinating lesion.[91] Another feature on MR imaging is the Dawson sign, which is an oval lesion with its main axis perpendicular to the corpus callosum.[92] Oligoclonal bands in the CSF may help to differentiate these lesions from brain tumors, but they were detected in only 50% of patients with tumefactive lesions in previous series.[93] Thus a biopsy is required in some instances.[84] The histopathologic examination may also be challenging, when a tumefactive demyelinating lesion has not been considered in the preoperative setting. Lucchietti et al.[90] reported that >30% of biopsies were originally misdiagnosed by the referring pathologist mainly as low-grade glioma. We suggest that when a mass lesion shows typical features in imaging studies (open ring) in a typical clinical setting (young women with acute symptoms) a wait-and-see strategy with short-term imaging control and specific treatment can be adopted.

### Erdheim-Chester Disease

Erdheim-Chester disease is a non-Langerhans cell histiocytosis of unknown cause, with about 500 cases having been reported in the literature.[94] Erdheim-Chester disease is characterized by xanthomatous or xanthogranulomatous infiltration of various organs, especially the bones. Isolated CNS presentation mimicking low-grade or high-grade glioma is rare.[95,96] Biopsy is necessary to establish a definite diagnosis with the identification of CD68+/CD1a−/S100− foamy histiocytes.[97]

## CONCLUSIONS

Intracranial inflammatory lesions involve a wide spectrum of entities and they may mimic brain tumors in the clinical setting and imaging studies. Therefore, they should be involved in the differential diagnosis of intracranial tumors. Profound knowledge of their pathogenesis, clinical presentation, and treatment is necessary to optimize treatment algorithms. In many instances, surgical procedures play an important role in their diagnosis or treatment. However, the surgeon must be aware to avoid unnecessary surgery.

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