



STEREOTACTIC BIOPSY UNMASKING INFECTIVE LESIONS RADIOLOGICALLY MIMICKING GLIOMA: A PROSPECTIVE SERIES OF DEEP-SEATED BRAIN LESIONS

Neurosurgery

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ABSTRACT

Background: Deep-seated intracranial infective lesions can closely mimic glioma on conventional CT and MRI, and this radiological overlap risks inappropriate oncological treatment if histopathological confirmation is omitted. We report a prospective series of infective lesions unmasked by stereotactic biopsy from a cohort of patients undergoing biopsy for suspected deep-seated brain tumors. **Objective:** To describe the clinical, radiological and histopathological features of infective lesions masquerading as glioma or other neoplasms, and to determine the diagnostic contribution of stereotactic biopsy in this subgroup. **Methods:** From a prospective cohort of 30 patients undergoing CT-guided frame-based stereotactic biopsy for radiologically suspected deep-seated brain lesions at a tertiary care centre (January 2024-June 2026), all patients in whom histopathology confirmed an infective or inflammatory aetiology were identified. Clinical presentation, pre-biopsy radiological impression, lesion location and size, biopsy findings, and postoperative outcome were analysed. **Results:** Of 30 patients, 9 (30.0%) had histopathologically confirmed infective lesions: tuberculoma in 7 (77.8%), pyogenic abscess in 1 (11.1%), and fungal granuloma in 1 (11.1%). Mean age was 39.3 years (range 16-68) with a male predominance (7:2). Lesions involved the deep frontal region (n=3), deep parietal region (n=2), fronto-parietal, fronto-temporal, temporal and thalamic locations (n=1 each). In 8 of 9 patients (88.9%), the pre-biopsy radiological impression was non-specifically tumor-suggestive (ring-enhancing, heterogeneously enhancing, or contrast-enhancing mass lesion); only 1 patient (11.1%) had tuberculoma correctly suspected on imaging alone. Stereotactic biopsy achieved a definitive histopathological diagnosis in all 9 patients (100% yield in this subgroup). Postoperative complications occurred in 3 patients (33.3%), all transient (two isolated seizure episodes, one aphasia), with no permanent morbidity or mortality. All patients were subsequently established on appropriate antimicrobial therapy in place of empirical oncological treatment. **Conclusion:** Nearly one in three deep-seated lesions referred for stereotactic biopsy of suspected glioma in this cohort proved to be infective on histopathology, and imaging alone correctly identified the infective aetiology in only one of nine cases. Stereotactic biopsy is indispensable in deep-seated brain lesions with tumor-suggestive imaging, as it reliably distinguishes treatable infective pathology from neoplasia and prevents inappropriate oncological management.

KEYWORDS

Brain abscess; Diagnostic yield; Fungal granuloma; Glioma mimic; Ring-enhancing lesion; Stereotactic biopsy; Tuberculoma

INTRODUCTION

Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) remain the primary tools for evaluating suspected intracranial neoplasms, but a well-recognized and clinically important limitation is that several infective and inflammatory pathologies can closely reproduce the imaging appearance of glioma, particularly high-grade glioma. Ring-enhancing or heterogeneously enhancing deep-seated mass lesions with perilesional oedema and mass effect are frequently interpreted as tumor-suggestive, yet this same appearance is shared by tuberculoma, pyogenic abscess and fungal granuloma^{1,2}. In tuberculosis-endemic regions such as India and much of South and Southeast Asia, intracranial tuberculoma is reported to account for as much as 20-30% of all intracranial mass lesions, in sharp contrast to its rarity in non-endemic Western settings^{3,4}, and misdiagnosis as glioma has repeatedly been described even at experienced tertiary centres^{5,6,7}.

Advanced MRI techniques, including diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping and proton MR spectroscopy (1H-MRS), have been proposed to improve pre-operative discrimination between tumor and infection: restricted diffusion with a bright DWI core and lipid-lactate peaks on spectroscopy are classically described in tuberculoma and pyogenic abscess and are said to be atypical of glioma^{9,10,11,12}. In practice, however, these techniques have imperfect sensitivity and specificity, overlapping metabolite and diffusion profiles have been reported between tubercular, fungal and pyogenic collections and even between tuberculoma and metastasis, and such sequences are not uniformly available or conclusive in routine clinical practice, especially in resource-limited settings^{10,2}. As a result, histopathological examination continues to be regarded as the diagnostic gold standard whenever imaging cannot confidently exclude a neoplastic process⁶.

The clinical stakes of this diagnostic overlap are considerable: an

infective lesion mistakenly treated as a tumor may be subjected to unnecessary craniotomy, radiotherapy or chemotherapy while the true infective process remains untreated and potentially progresses, whereas prompt histopathological identification allows appropriate antitubercular, antibacterial or antifungal therapy to be instituted without delay^{14,15,16}. Stereotactic biopsy, by providing a minimally invasive route to tissue diagnosis in deep-seated or eloquently located lesions that are otherwise difficult to access safely, is particularly well suited to resolving this diagnostic dilemma⁸. This report describes a prospective series of patients drawn from a larger cohort undergoing stereotactic biopsy for suspected deep-seated brain tumors, in whom histopathology unexpectedly established an infective diagnosis, and examines the extent to which pre-biopsy imaging alone would have correctly identified these lesions.

MATERIALS AND METHODS

This report is derived from a prospective observational cohort of 30 consecutive adult patients who underwent CT-guided frame-based stereotactic biopsy for radiologically suspected deep-seated brain lesions in the Department of Neurosurgery of a tertiary care teaching hospital between January 2024 and June 2026, following Institutional Ethics Committee approval and written informed consent. Full methodological details of the parent cohort, including inclusion and exclusion criteria, sample size estimation, and the stereotactic biopsy technique, have been reported separately.

For the present analysis, all patients from the parent cohort in whom histopathological examination established an infective or inflammatory aetiology (tuberculoma, pyogenic abscess, or fungal granuloma) were identified. For each patient, we recorded age, sex, presenting symptoms and duration, pre-biopsy radiological impression on CT/MRI, lesion location, side and largest dimension, number of biopsy passes, intra- and post-operative complications, final histopathological diagnosis, and clinical outcome at discharge. The

pre-biopsy radiological impression for each patient was classified as either specifically suggestive of an infective/tubercular aetiology or non-specifically tumor-suggestive (i.e., reported as glioma, high-grade glioma, or a heterogeneously/ring/contrast-enhancing mass lesion without a stated infective differential), based on the impression documented in the case record at the time of biopsy planning. Histopathological examination of formalin-fixed, paraffin-embedded tissue, with special stains and microbiological correlation where clinically indicated, served as the reference standard for final diagnosis. Descriptive statistics (frequencies, percentages, mean, range) were used to summarize the findings of this subgroup.

RESULTS

Of the 30 patients in the parent cohort, histopathological examination established an infective or inflammatory aetiology in 9 patients (30.0%), while the remainder had neoplastic or other diagnoses. The infective lesions comprised tuberculoma in 7 patients (77.8%), pyogenic abscess (long-chain streptococcus) in 1 patient (11.1%), and fungal granuloma in 1 patient (11.1%). Mean age in this subgroup was 39.3 years (range 16-68 years), and there was a male predominance (7 men, 2 women).

The commonest presenting features were headache, focal motor weakness, fever and seizures, with symptom duration ranging from one week to six months. Lesions were located in the deep frontal region in 3 patients, the deep parietal region in 2, and one each in the fronto-parietal, fronto-temporal, temporal, and thalamic regions; laterality was right-sided in 6, left-sided in 2, and midline in 1. Lesion size ranged from 24 to 48 mm in maximal dimension. Individual patient characteristics are summarized in Table 1.

The pre-biopsy radiological impression was non-specifically tumor-suggestive — reported as a heterogeneously enhancing deep-seated lesion, a ring-enhancing lesion with mass effect, or a contrast-enhancing mass lesion, without a stated infective differential — in 8 of the 9 patients (88.9%). Only 1 patient (11.1%), who presented with headache and fever with a fronto-parietal lesion, had tuberculoma correctly suspected on the basis of imaging alone. Notably, none of the 9 patients had imaging appearances specific enough to suggest fungal granuloma or pyogenic abscess prior to biopsy, and the single high-grade-glioma-labelled lesion in the parent cohort's radiological diagnosis list (Materials and Methods of the parent study) corresponded to a tuberculoma on histopathology.

Stereotactic biopsy achieved a definitive histopathological diagnosis in all 9 patients, a diagnostic yield of 100% in this subgroup, with three to five tissue samples obtained per patient. Intraoperative complications were minimal, limited to minor tract bleeding in one patient. Postoperative complications occurred in 3 of 9 patients (33.3%): two isolated, self-limiting seizure episodes and one case of transient aphasia; all were managed conservatively without permanent neurological deficit. There was no mortality in this subgroup. At discharge, 4 patients (44.4%) had improved and 5 (55.6%) were clinically stable; all were subsequently transitioned to appropriate antitubercular, antibacterial or antifungal therapy rather than empirical oncological treatment.

Table 1. Clinical, radiological and histopathological features of the 9 patients with infective lesions

Pt	Age /Sex	Size (mm)	Radiological impression	Location/side	Radiology suggested infection?	Complication	HPE diagnosis	Outcome
1	25/ M	26	Tuberculoma (correctly suspected)	Fronto-parietal, R	Yes	None	Tuberculoma	Improved
2	30/ F	32	Ring-enhancing lesion, mass effect	Deep frontal, R	No	None	Tuberculoma	Improved
3	33/ M	28	Heterogeneously enhancing lesion	Fronto-temporal, R	No	Seizure (2 episodes)	Fungal granuloma	Stable
4	35/ M	26	Ring-enhancing lesion, mass effect	Temporal, R	No	None	Pyogenic abscess (streptococcus)	Improved

5	68/ M	24	Ring-enhancing lesion, mass effect	Deep parietal, L	No	Aphasia (transient)	Tuberculoma	Stable
6	45/ M	48	Ring-enhancing lesion, mass effect	Deep frontal, R	No	Seizure	Tuberculoma	Improved
7	52/ M	32	Contrast-enhancing mass lesion	Deep frontal, R	No	None	Tuberculoma	Improved
8	50/ M	40	Heterogeneously enhancing lesion	Thalamus, R	No	None	Tuberculoma	Improved
9	16/ F	26	Contrast-enhancing mass lesion	Deep parietal, midline	No	None	Tuberculoma	Stable

Pt = patient serial number (study-specific, non-identifying); HPE = histopathological examination; R = right; L = left. No patient in this subgroup died.

Table 2. Age and gender distribution of patients with infective lesions (n=9)

Variable	Frequency	Percentage (%)
Age group		
<30 years	2	22.2
30–50 years	5	55.6
>50 years	2	22.2
Gender		
Male	7	77.8
Female	2	22.2

Mean age 39.3 years (range 16–68 years).

Table 3. Histopathological spectrum of the infective lesion subgroup (n=9)

Histopathological diagnosis	Number of cases	Percentage (%)
Tuberculoma	7	77.8
Pyogenic abscess	1	11.1
Fungal granuloma	1	11.1
Total	9	100.0

Table 4. Pre-biopsy radiological impression versus final histopathological diagnosis (n=9)

Radiological impression	n	Final HPE diagnosis (n)
Tuberculoma (correctly suspected)	1	Tuberculoma (1)
Ring-enhancing lesion with mass effect	4	Tuberculoma (3), Pyogenic abscess (1)
Heterogeneously enhancing deep-seated lesion	2	Tuberculoma (1), Fungal granuloma (1)
Contrast-enhancing mass lesion	2	Tuberculoma (2)
Total	9	—

Only 1 of 9 radiological impressions (11.1%) specifically suggested an infective aetiology; the remaining 8 (88.9%) were non-specifically tumor-suggestive.

Table 5. Anatomical location of infective lesions (n=9)

Location	Number of cases	Percentage (%)
Deep frontal	3	33.3
Deep parietal	2	22.2
Fronto-parietal	1	11.1
Fronto-temporal	1	11.1
Temporal	1	11.1
Thalamus	1	11.1
Total	9	100.0

Table 6. Postoperative complications and clinical outcome (n=9)

Outcome measure	Frequency	Percentage (%)
Complications		
None	6	66.7
Transient seizure	2	22.2
Transient aphasia	1	11.1
Clinical status at discharge		
Improved	4	44.4
Stable	5	55.6
Death	0	0.0

All complications were transient and resolved with conservative management; there was no permanent neurological deficit or mortality in this subgroup.

FIGURES

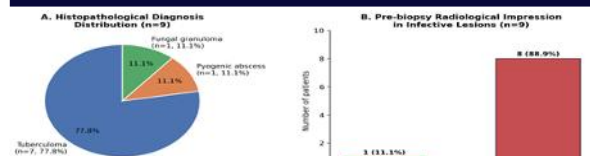


Figure 1. (A) Histopathological diagnosis distribution among the 9 patients with infective lesions. (B) Pre-biopsy radiological impression: only 1 of 9 patients (11.1%) had an infective aetiology correctly suspected on imaging alone; the remaining 8 (88.9%) had a non-specific, tumor-suggestive radiological impression.

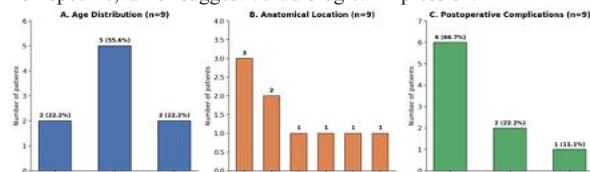


Figure 2. (A) Age distribution, (B) anatomical location, and (C) postoperative complications among the 9 patients with infective lesions, summarizing the data presented in Tables 2, 5 and 6.



Figure 3. Lateral CT scanogram used for stereotactic trajectory planning, showing the stereotactic head frame fixed to the patient prior to CT-guided biopsy.



Figure 4. Axial non-contrast CT of the brain showing a deep-seated, ill-defined hypodense lesion (circled) subsequently confirmed as tuberculoma on histopathology, illustrating the non-specific appearance that prompted a tumor-suggestive radiological impression.



Figure 5. Intraoperative photograph showing the patient's head immobilized in the stereotactic head frame prior to trajectory planning and biopsy.

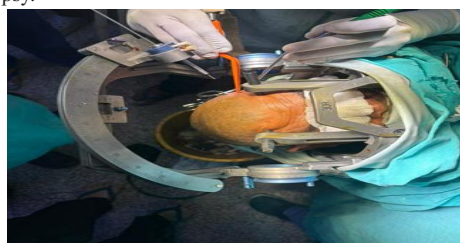


Figure 6. Intraoperative photograph showing the stereotactic arc and trajectory guide mounted on the head frame during CT-guided biopsy.

needle placement.

DISCUSSION

Nearly one in three patients (30.0%) referred to our unit for stereotactic biopsy of a radiologically suspected deep-seated brain tumor in fact had an infective lesion on histopathology, and imaging alone correctly flagged the infective aetiology in only a single patient. This proportion is broadly consistent with previous reports from tuberculosis-endemic settings, where tuberculoma has been described as accounting for a substantial minority of biopsied intracranial mass lesions and is a well-documented mimic of high-grade glioma on both structural imaging and advanced sequences^{4,5}. A recent case report described a large thalamic tuberculoma with an elevated choline peak and reduced N-acetylaspartate on MR spectroscopy — a metabolic profile that, taken in isolation, is classically associated with high-grade glioma — underscoring that even multiparametric MRI cannot always reliably exclude infection⁷. Similar diagnostic pitfalls have been reported for solitary tuberculoma presenting without any systemic features of tuberculosis⁶, and for tuberculoma mimicking neurosarcoidosis on both imaging and initial histology⁷, reinforcing that clinical suspicion alone, even when combined with modern imaging, is an unreliable substitute for tissue diagnosis in this setting.

Advanced MRI sequences have been proposed to bridge this diagnostic gap. Diffusion-weighted imaging characteristically shows a bright, restricted-diffusion core in tuberculoma and pyogenic abscess, contrasting with the typically unrestricted diffusion of necrotic glioma, and proton MR spectroscopy of tuberculous and pyogenic collections classically demonstrates lipid-lactate peaks with an absent or minimal choline peak, differing from the elevated choline-to-creatine ratios seen in high-grade glioma^{9,10,12}. However, comparative imaging studies of pyogenic, tubercular and fungal abscesses have shown overlapping wall morphology, apparent diffusion coefficient values and spectroscopic patterns across aetiologies¹⁰, and differentiation between tuberculoma and metastasis on perfusion imaging has similarly been hampered by overlapping apparent diffusion coefficient values despite differences in relative cerebral blood volume². None of these advanced sequences were diagnostic in isolation for any patient in our series, consistent with the broader literature indicating that biopsy remains the only truly reliable means of excluding neoplasia when imaging is equivocal⁶.

The clinical consequence of this diagnostic overlap is substantial. Case reports have documented brain abscesses of pyogenic, fungal and even parasitic origin proceeding to biopsy or resection after being confidently diagnosed as glioblastoma on pre-operative imaging^{14,17}, a systematic review of individual patient data specifically cataloguing brain abscesses misdiagnosed as brain tumors¹⁴, and, conversely, reports of glioblastoma masquerading as a postoperative abscess¹⁸ and of cerebral toxoplasmosis mimicking high-grade glioma sufficiently convincingly that palliative oncological treatment was initiated before histopathology corrected the diagnosis¹⁵. Our single fungal granuloma and single pyogenic abscess, both presenting with imaging appearances essentially indistinguishable from the seven tuberculomas and from tumor, exemplify this same phenomenon and reinforce that the differential for a deep-seated, contrast-enhancing brain lesion in an endemic setting must routinely include infective aetiologies regardless of how tumor-suggestive the imaging appears.

Stereotactic biopsy achieved a 100% diagnostic yield in this infective subgroup, with only minor, self-limiting complications (33.3%) and no permanent morbidity or mortality, comparing favourably with diagnostic yields for non-neoplastic lesions reported in larger contemporary series^{19,22}, in which non-neoplastic pathology has been specifically associated with somewhat lower yield (73.3% versus 91.2% for suspected primary brain tumor) and a higher requirement for repeat biopsy than neoplastic lesions²², underscoring the value of adequate, multi-pass sampling when an infective process is even remotely possible. Complication rates in our subgroup were consistent with the low overall morbidity described in systematic reviews of frame-based stereotactic biopsy²⁰, and with the substantial infective component previously documented in general stereotactic biopsy series from similar settings²¹. Prompt histopathological confirmation in each of our 9 patients allowed timely initiation of antitubercular, antibacterial or antifungal therapy in place of empirical radiotherapy or chemotherapy that a purely radiological diagnosis of glioma might otherwise have prompted — a distinction with direct and immediate implications for patient management, prognosis and avoidance of

unnecessary treatment-related toxicity.

This series has limitations inherent to its design: it is a descriptive subgroup analysis drawn from a single-centre cohort of modest size, radiological impressions were derived from routine clinical reporting rather than a standardized, blinded re-review incorporating advanced sequences in every patient, and microbiological confirmation (culture, PCR) was not uniformly available for all tuberculoma cases. Nonetheless, the consistency of our findings with the wider published literature on tumor-mimicking CNS infection supports the central message: in tuberculosis-endemic and similar resource settings, a substantial proportion of radiologically tumor-suggestive deep-seated brain lesions will prove infective, and stereotactic biopsy should be regarded as a routine, non-negotiable step before committing such patients to oncological therapy.

CONCLUSION

In this prospective series, nearly one-third of patients biopsied for a radiologically suspected deep-seated glioma had an infective lesion — predominantly tuberculoma, but also pyogenic abscess and fungal granuloma — and conventional imaging correctly identified the infective aetiology in only one of nine cases. Stereotactic biopsy provided a definitive diagnosis in all such patients with an acceptable, largely transient complication profile and no mortality, enabling prompt appropriate antimicrobial therapy and averting unnecessary oncological treatment. These findings reinforce that histopathological confirmation by stereotactic biopsy, rather than radiological impression alone, should guide management of deep-seated brain lesions, particularly in tuberculosis-endemic regions.

Conflict Of Interest: None declared.

Funding: None.

Ethical Approval

This study was approved by the Institutional Ethics Committee (approval details to be inserted) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

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