A Case of Balo's Concentric Sclerosis Confirmed by Stereotactic Intracranial Brain Biopsy and Literature Review

Hang Hang
Affiliated Hospital of Guizhou Medical University
Siying Ren
Affiliated Hospital of Guizhou Medical University
Yuanhong Mao
Affiliated Hospital of Guizhou Medical University
Guofeng Wu
Affiliated Hospital of Guizhou Medical University
Likun Wang (769070308@qq.com)
Affiliated Hospital of Guizhou Medical University

Case Report

Keywords:

Posted Date: November 29th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3657214/v1

Additional Declarations: No competing interests reported.

Abstract

Baló's Concentric Sclerosis (BCS) is an extremely rare central nervous system demyelinating disease, often presenting as acute or subacute neurological damage, with lesions typically occurring in the brain white matter. On MRI, it manifests as one or more concentric circular structures, forming multilayered ring-like patterns. Balo's Concentric Sclerosis, named after the Hungarian neuropathologist József Balo, was first defined in 1928. Traditionally, BCS was identified postmortem, but in recent years, magnetic resonance imaging (MRI) has become a crucial diagnostic method, allowing effective diagnosis and treatment during a patient's lifetime. While brain biopsy remains the gold standard for diagnosing this condition, reports of intracranial biopsy cases are relatively scarce. This article reports a case of BCS diagnosed through stereotactic intracranial brain biopsy and MRI, aiming to further enhance understanding of this disease.

1. Case report

A 58-year-old man, admitted for "memory decline for 7 days." Main symptoms include decreased memory, abnormal behavior, spontaneous laughter, delayed responses, reduced speech, difficulty in speech expression, and partial comprehension impairment. History of herpes zoster on the lower back about 1 + month ago. On admission, vital signs stable, clear consciousness, indifferent facial expression, partial cooperation during physical examination, relevant and coherent responses. Advanced cognitive functions decreased, decreased memory, pupils bilaterally round and equal, approximately 3.0 mm in diameter, reactive to light, full extraocular movements, no diplopia, rough assessment of bilateral hearing normal. Symmetric forehead wrinkles, slightly shallow left nasolabial fold, no facial asymmetry, tongue protrudes centrally, elevated bilateral pharyngeal reflex, normal bilateral gag reflex. Neck is supple. Muscle strength in both upper limbs is approximately grade 4, and in both lower limbs, it is grade 5. Moderate muscle tone in all limbs, limb tendon reflexes (++). Examination of limb pain sensation, tactile sensation, and joint position sensation is uncooperative. Alternating movements, finger-to-nose, and finger-pointing are stable and accurate in both upper limbs. Heel-to-shin test, Romberg sign (+). Babinski sign (+) and Chaddock sign (+) on the left lower limb, Babinski sign (-) and Chaddock sign (-) on the right lower limb. After admission, blood cell analysis, urine examination, routine stool examination + occult blood, renal function, electrolytes, cardiac markers, myocardial enzymes, complete coagulation, three infectious disease screenings (hepatitis B, syphilis, HIV antibodies), highly sensitive C-reactive protein, erythrocyte sedimentation rate, complete liver function, thyroid function, anti-streptolysin O, immunoglobulin, single complement (Ig + C3, C4), and multiple tumor markers all showed no significant abnormalities. Full immunological panel: Anti-neutrophil cytoplasmic antibody (ANCA) testing for cANCA, PR3, MPO, PANCA, anti-cardiolipin antibody IgG, anti-cardiolipin antibody IgA, and ACA (IgM) were all negative. Lymphocyte subset percentages + absolute counts: Total T cells (CD3+) 60.84%, CD4 + T cells (CD3 + CD4+) 29.80%, B cells (CD3-CD19-) 15.77%, CD4/8 0.99, total T cell count 293 cells/μL, CD8 + T cell count 145 cells/μL, CD4 + T cell count 144 cells/μL, NK cell count 113 cells/μL, B cell count 76 cells/μL. Lumbar puncture revealed a cerebrospinal fluid pressure of 130 mmH2O, routine cerebrospinal fluid analysis, Gram stain, acid-fast stain showed no significant abnormalities, India ink stain showed no Cryptococcus growth. Biochemistry of cerebrospinal fluid: Protein 522.00 mg/L, glucose 4.761 mmol/L. Cerebrospinal fluid cultures showed no bacterial or fungal growth. Full set of cerebrospinal fluid virus antibodies (TORCH) (-).

The CT scan of the brain shows large areas of decreased density in the bilateral frontal lobes, parietal lobes, and centrum semiovale. The MRI scan of the brain reveals multiple nodular abnormal signal shadows of varying sizes in the bilateral frontal lobes, parietal lobes, and left temporal lobe, predominantly showing long T1 and long T2 signals, with high signal intensity on FLAIR. The larger lesion measures 1.8×1.9 cm, with unclear boundaries. Surrounding the lesion on FLAIR, there is a patchy edema with high signal intensity. The left lateral ventricle is slightly compressed, and midline structures are slightly shifted to the right. Nodular shadows with slightly long T1 and long T2 signals are observed around the bilateral centrum semiovale, and there is high FLAIR signal intensity around the right lateral ventricle. Strip-like long T2 signal is seen under the right frontal dura. The diagnosis includes: 1. Multiple brain lesions: metastatic tumors? Balo concentric sclerosis? Drug-induced encephalopathy? Contrast-enhanced brain MRI reveals nodular and ring-enhanced lesions in the bilateral frontal and parietal lobes, as well as the left frontal lobe, suggesting consideration of multiple intracranial metastatic

tumors. Diffusion-weighted imaging (DWI) of the head indicates restricted diffusion in lesions in the bilateral frontal and parietal lobes and the left temporal lobe. Magnetic resonance spectroscopy (MRS) of the head suggests tumor-like features in the lesions. Susceptibility-weighted imaging (SWI) shows nodular low signal in the left frontal and temporal lobes, and multiple patchy high signal lesions in the parenchyma of both cerebral hemispheres, cerebellum, and brainstem. The diagnosis includes: 1. Microhemorrhage in the left frontal and temporal lobes. 2. Multiple high signal lesions in the brain. Magnetic resonance angiography (MRA) of the head suggests: 1. The right vertebral artery is not clearly displayed. 2. Arteriosclerosis in the cerebral arteries, with moderate stenosis in the A1 segment of both anterior cerebral arteries(Fig. 1).

To clarify the nature of the intracranial lesion, with the patient's consent, a stereotactic minimally invasive intracranial lesion biopsy was performed. The pathological results indicate(Fig. 2), based on Hematoxylin and Eosin (HE) staining, that most of the brain tissues in the left temporal-parietal lobe, right parietal lobe, and frontal lobe exhibit edema, neuronal degeneration, accompanied by the formation of softening foci and bleeding, as well as infiltration of inflammatory cells and proliferation of glial cells. Immunohistochemical analysis reveals positive staining for Vimentin, GFAP (Glial Fibrillary Acidic Protein), S100, NF (Neurofilament), CD68 (macrophages), CD3 (T cells), CD20 (B cells), and Ki-67 (proliferation marker, approximately 1%), while P53 is negative. Olig-2 shows partial positivity, IDH1 is negative, and PAS (Periodic Acid-Schiff) staining is positive, suggesting a demyelinating lesion in the brain tissues of the left temporal-parietal lobe, right parietal lobe, and right frontal lobe.

The patient was treated with methylprednisolone for anti-inflammatory and immunomodulatory effects, ganglioside for neuroprotection, and symptomatic support. The patient's symptoms improved compared to before. Upon multiple follow-ups, occasional exacerbations were observed, and a 1000mg intravenous pulse of steroids for 3 days proved effective. Follow-ups at 6 months and 12 months post-discharge showed no significant progression of the patient's condition.

2. Discussion

According to reports, Balo's concentric sclerosis (BCS) tends to occur in young individuals, with an average onset age of 34 years. The incidence of BCS in females is reported to be twice that in males, and it is more prevalent among patients in East Asian countries[4]. Depending on the location of the lesions, patients may exhibit acute or subacute symptoms. Generally, BCS presents with more severe cortical dysfunction compared to typical multiple sclerosis, including symptoms such as aphasia, cognitive or behavioral disorders, and seizures[5]. The diagnosis of BCS is typically based on a combination of clinical evaluation, MRI findings, and cerebrospinal fluid analysis.

In summary, the characteristics of the present case are as follows: Clinical Presentation: A middle-aged male patient with an acute onset, presenting primarily with cognitive dysfunction and behavioral abnormalities. Pathological signs were present on admission, and improvement was observed with steroid treatment, with the disappearance of pathological signs, suggesting the effectiveness of steroid therapy. Cerebrospinal Fluid Analysis: Presence of oligoclonal bands, with lymphocyte subset analysis indicating a decreased proportion of lymphocytes, suggesting immune dysfunction and intrathecal synthesis of immunoglobulins. Radiological Features: T2/FLAIR high signals, partially elevated signals on DWI, layered appearance of lesions, significant perilesional edema, nodular enhancement on contrast-enhanced imaging, and MRS indicating elevated Cho and Cr peaks with decreased NAA peak. Pathological Results: Brain tissue showing loose edema, abundant vacuolated foam cells, and proliferation of hypertrophic glial cells indicative of inflammatory reactive proliferation. Increased proliferation of star-shaped glial cells (Creutzfeldt cells) and extensive lymphocytic infiltration were observed, with no evidence of atypical cells. Further immunohistochemistry revealed positivity for Vimentin, indicating glial cell proliferation and foam cell formation, and GFAP positivity, suggesting the presence of nerve fibers. The uniform staining of star-shaped glial cells ruled out tumors, supporting the consideration of a demyelinating disease. Based on these features, the diagnosis for this case is BCS.

BCS is a rare demyelinating disease with unclear etiology and pathogenesis. Its clinical presentation is complex and often misdiagnosed as stroke, brain tumor, or brain abscess. The classic neuroimaging feature of BCS on MRI is concentric ring-

like changes, and the pathological changes in the affected areas indicate primary involvement of the myelin sheath, with relative preservation of axons. This is considered characteristic and serves as the gold standard for diagnosing concentric sclerosis. Given its rarity, to further understand the disease, our research team reviewed 37 cases of typical BCS reported in both Chinese and English literature from 2010 to 2020. Among them, 8 cases underwent brain biopsy, primarily showing glial cell proliferation and demyelinating lesions, as summarized in Table 1. Of these cases, 15 were male, 22 were female, with an average age of 39.7 years. Clinical presentations varied, as did the locations of onset. Cerebrospinal fluid results showed increased cell count in 5 cases, elevated protein in 4 cases, positive oligoclonal bands in 5 cases, and increased IgG index in 2 cases. The main treatment approach was steroid pulse therapy, with some patients receiving a combination of steroids and plasma exchange. One patient was treated with steroids, plasma exchange, and alemtuzumab, while another received steroids, intravenous immunoglobulin, and azathioprine.

Table 1
Basic Information of 8 Typical BCS Patients with Brain Biopsy

Sex	Age	Symptom	Location	Brian biopsy	CSF	Treatment	References
male	23	Numbness on the left side of the face and limb	Right parietal and frontal lobes	Inflammatory changes, gliosis	No	Dexamethasone 4mg, intravenous, Q12h	[6]
male	36	Right limb weakness	• Left frontal lobe	Periaxonal myelin deficiency, reactive glial cell hyperplasia	No	High doses of steroids	[7]
female	52	Speech disorder	Left frontal lobe	The incomplete myelin sheath alternates with the preserved myelin sheath	No oligoclonal tape	Dexamethasone 4 mg, Tid; Methylprednisolone 1000mg, intravenous, Qd	[7]
male	56	Progressive left hand weakness and spasm	Bilateral radiating crown	Lymphohistiocytic inflammation with relative axon preservation and myelin loss	Protein 35 mg/dL, no oligoclonal band	Methylprednisolone 1000mg, intravenous drip, Qd; Antiepileptic medication	[4]
female	24	Dysarthria and double upper limb weakness	Bilateral cerebral hemispheres	A large number of foamy histiocytic infiltrates, a few lymphocytes; Myelin sheath scattered in loss	Slightly increased protein (88.3 mg/dL); No oligoclonal tape	no	[8]
male	55	Left limb weakness	Right anterior central gyrus	demyelinating disease	no	Methylprednisolone 500mg, intravenous drip, Bid, for 3 days	[9]
male	41	Dysarthria and mutism are associated with significant sleepiness and psychomotor disturbances	White matter around the ventricles	Gliosis, swelling of eosinophilic astrocytes, annular around blood vessels. Axon staining shows complete axon length extension.	High albumin level, no oligo-clonal bands, normal IgG index	Take a large dose of methylprednisolone orally for 15 days	[10]
female	49	Slow response, right limb weakness	Bilateral parietal occipital, left frontal lobe	White matter stroma edema, astrocyte reactive hyperplasia, scattered lymphatic cell infiltration, lymphocyte sheath formation around individual small blood vessels, local myelin loss. Proliferating glial cells GFAP(+), CD20(-), CD45RA (+)	Normal, no oligo-clonal band	High dose methylprednisolone shock therapy	[11]

Cerebrospinal fluid analysis showed mononuclear inflammatory response, elevated protein levels, and occasional oligoclonal bands [12]. The MRI features of Balo's concentric sclerosis (BCS) include alternating concentric rings on T1-weighted images, creating a "bull's eye" pattern on T2-weighted images [13]. This case exhibits these characteristic features. However, other complex patterns have been reported, such as mosaic, rosebud, and double-bar patterns [13–14]. The typical MRI presentation of BCS is an "onion-ring" appearance, consisting of alternating demyelinated and myelin-phospholipid preserved regions [14, 15]. Lesions can be solitary or multiple and may infiltrate from small lesions to involve the entire cerebral hemisphere [4, 16]. In the early stages of the disease, the concentric ring pattern may not be evident, and lesions may mimic features of acute disseminated encephalomyelitis, tumors, or abscesses [12].

High signal intensity in diffusion-weighted imaging on MRI suggests cytotoxic edema and ischemia. This phenomenon, occasionally seen in multiple sclerosis but different from ischemia, persists longer in BCS, up to 4 to 5 weeks [5]. Literature reports indicate that BCS exhibits characteristic biochemical changes, including a decrease in the N-acetylaspartate (NAA)/creatine (Cr) ratio, a reduction in choline (Cho)/Cr ratio, and lactate production. The relative NAA values decrease from the periphery to the center, with higher choline values in the center gradually decreasing toward the lesion's edge [3]. Additionally, acute BCS shows characteristic features in magnetic resonance spectroscopy (MRS), with a decrease in NAA peak, an increase in lactate peak, and elevated choline and lipid peaks [17]. This case's MRS demonstrates a similar trend.

BCS is a rare subtype of idiopathic inflammatory demyelinating diseases [12, 18], with lesions ultimately presenting as diffuse demyelinated plaques [19]. In recent years, scholars have reported that, compared to multiple sclerosis, BCS patients show similarities in oligoclonal protein and immunoglobulin G (IgG) index to neuromyelitis optica. In this case, the cerebrospinal fluid (CSF) analysis also indicates the presence of oligoclonal bands. The typical pathological features of BCS include the loss of oligodendrocytes and demyelinating lesions in the brain white matter [4]. Multiple reactive astrocytes with enlarged nuclei and mitotic granules, known as Creutzfeldt cells, are characteristic of BCS demyelinated plaques [13]. This case's brain biopsy confirmed the presence of proliferative astrocytes in the lesion. However, due to various reasons such as patient factors and advancements in hospital technology, the number of collected pathological biopsy samples remains limited, requiring further research.

In summary, the distinctive features of this case include the involvement of multiple sites, with concentric sclerosis distributed in the bilateral frontal, parietal lobes, and left temporal lobe. Moreover, after contrast-enhanced MRI, nodular and ring enhancement was observed in the bilateral frontal, parietal lobes, and left temporal lobe lesions, a phenomenon rarely reported in other cases. The application of the unique stereotactic minimally invasive brain biopsy technique by our research group further provides a solid basis for understanding the pathological changes and diagnosing this disease.

As there is still no unified treatment protocol for Balo's concentric sclerosis (BCS), steroids are currently the first-line treatment. Reviewing the literature, most patients experience symptom relief through steroid treatment, while some patients may undergo plasma exchange therapy. Following steroid treatment, the patient in this case exhibited significant symptom improvement. However, the lack of imaging follow-up materials at present emphasizes the need for ongoing monitoring and follow-up. By sharing this case, our research group aims to contribute to a deeper understanding of BCS and provide insights that may guide future clinical work.

Declarations

Acknowledgements

Not Applicable.

Authors' contributions

H.H drafted the manuscript. YH.M treated the patient at the hospital and followed them up after treatment. LK.W revised the manuscript critically. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Funding

The study is supported by science and Technology Fund project of Guizhou Provincial Health Commission, gzwjk2020-1-016 and Science and Technology Program of Guizhou Province, 2021071.

Availability of data and materials

Data can be available upon request by the corresponding author.

Ethics approval and consent to participate

Written approval has been obtained from the ethics committee of the Affiliated Hospital of Guizhou Medical University.

Consent for publication

Written consent for publication was obtained from the patient of our study.

Competing interests

None.

References

1. JJAoN BALO. Psychiatry Encephalitis periaxialis concentrica. 1928;19(2):242–64.
2. Moore GR, Neumann PE, Suzuki K, Lijtmaer HN, Traugott U, Raine CS. Balo's concentric sclerosis: new observations on lesion development. Ann Neurol. 1985;17(6):604–11.
3. Moore GW, Neumann PE, Suzuki K, Lijtmaer HN, Traugott U, Raine CSJANOJANA, et al. Balo's concentric sclerosis: new observations on lesion development. 1985;17(6):604–11.
4. Hardy TA, Miller DHJTLN. Baló's concentric sclerosis. 2014;13(7):740–6.
5. Nader Kawachi JA, Andrade Magdaleno ML, Peñaherrera CA, De Fernández Y, Lavenant Borja MIJM. Early diagnosis of Balo's concentric sclerosis by diffusion tensor tractography: a case report and literature review. 2016;16(02).
6. Yang YC, Tsai CH. Balo concentric sclerosis in a 23-year-old man. CMAJ: Can Med Association J = J de l'Association medicale canadienne. 2018;190(31):E937.
7. Agarwal M, Ulmer JL, Klein AP, Mark LP. Why Is This Auntminnie a Diagnostic Conundrum? A Knowledge-Based Approach to Balo's Concentric Sclerosis From Reports of 3 Cases and Pooled Data From 68 Other Patients in the Literature. Curr Probl Diagn Radiol. 2019;48(4):415–22.
8. Son YR, Yang H, Lee S, Kim JY, Han SG, Park KS. Balo's Concentric Sclerosis Mimicking Cerebral Tuberculoma. Experimental Neurobiol. 2015;24(2):169–72.
9. Darke M, Bahador FM, Miller DC, Litofsky NS, Ahsan H. Baló's concentric sclerosis: imaging findings and pathological correlation. J Radiol case Rep. 2013;7(6):1–8.
10. Grasso D, Borreggine C, Castorani G, Vergara D, Dimitri LMC, Catapano D, et al. Balò's concentric sclerosis in a case of cocaine-levamisole abuse. SAGE open medical case reports. 2020;8:2050313x20940532.
11. . J Balo . 2013;13(3):394–7.
12. Purohit B, Ganewatte E, Schreiner B, Kollias SJCRN. Balo's concentric sclerosis with acute presentation and co-existing multiple sclerosis-typical lesions on MRI. 2015;7(1):44–50.

13. Harandi AA, Esfandani A, Pakdaman H, Abbasi M, Sahraian MAJRN. Balo's concentric sclerosis: an update and comprehensive literature review. 2018;29(8):873–82.
14. Pelzers E, Van Goethem J, Van den Hauwe L, Degryse H, Geens K, Parizel PJJBR. Baló's concentric sclerosis. 2008;91(3):108.
15. Lassmann HJNcoNA. The pathologic substrate of magnetic resonance alterations in multiple sclerosis. 2008;18(4):563–76.
16. Hickey WFJJon. The pathology of multiple sclerosis: a historical perspective. 1999;98(1):37–44.
17. Darke M, Bahador FM, Miller DC, Litofsky NS, Ahsan HJJ. Baló's concentric sclerosis: imaging findings and pathological correlation. 2013;7(6):1.
18. Rovira Á, Auger C, Rovira A. Other noninfectious inflammatory disorders. Handbook of Clinical Neurology. Volume 135. Elsevier; 2016. pp. 425–46.
19. Capello E, Mancardi GJNS. Marburg type and Balo's concentric sclerosis: rare and acute variants of multiple sclerosis. 2004;25(4):s361–s3.

Figures

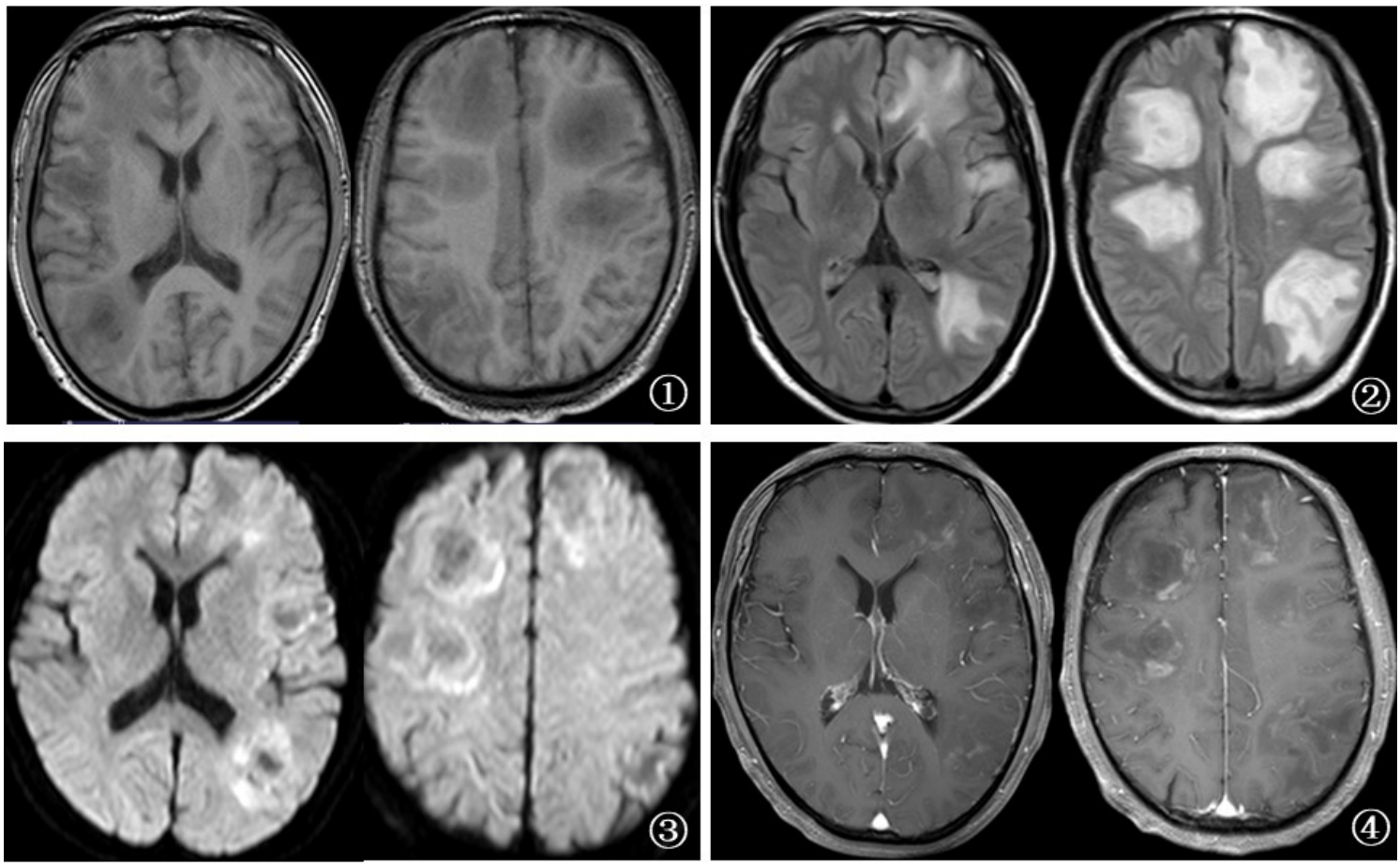

Figure 1

MRI results The image shows multiple nodular abnormal signals of varying sizes in the bilateral frontal lobes, parietal lobes, and left temporal lobe. The predominant signal is long T1, with high signal intensity on FLAIR (T1, FLAIR). The diffusion-weighted imaging (DWI) presents uneven signals (DWI). Contrast-enhanced imaging reveals nodular and ring-enhanced lesions (enhanced imaging).

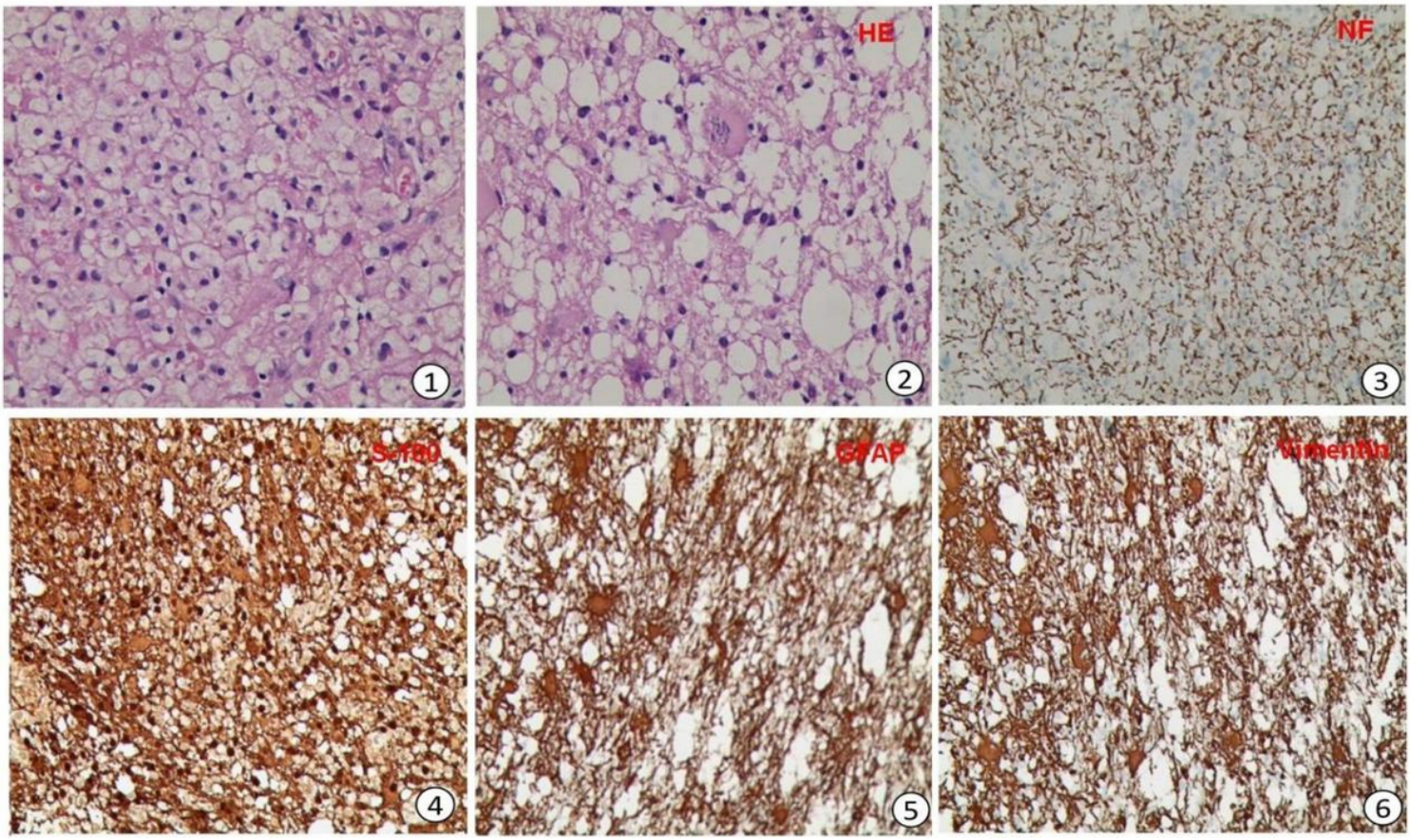

Figure 2

Pathological Biopsy Results and are Hematoxylin and Eosin (HE) staining reveals loose brain tissue, edema, foam cell reaction, and proliferation of reactive astrocytes. Creutzfeldt cells are observed, along with lymphocyte infiltration around blood vessels. Immunohistochemical staining results: shows positive staining for NF (Neurofilament) and Vimentin; for S100; for GFAP (Glial Fibrillary Acidic Protein),;and for Vimentin.