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Baló Concentric Sclerosis Mimicking Encephalitis with Seizures and Progressive Aphasia in a 26-Year-Old Woman: A Challenging Diagnostic Dilemma

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Keywords
Baló concentric sclerosis · Seizures · Aphasia · Encephalitis · Diagnostic dilemma

Abstract
Introduction: Baló's concentric sclerosis (BCS) is a rare subtype of multiple sclerosis characterized by inflammatory demyelination within the central nervous system. ***Case Presentation:*** This case report presents a challenging diagnostic scenario involving a 26-year-old woman diagnosed with BCS. Despite treatment, her condition did not ameliorate, and magnetic resonance imaging (MRI) findings remained unchanged. A subsequent stereotactic biopsy revealed tumefactive Balo disease, highlighting the intricate diagnostic and therapeutic issues surrounding BCS. ***Conclusion:*** The juxtacortical location of the BCS lesion, as observed in our case, suggests an unfavourable prognosis due to treatment-resistant seizures.

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Introduction

Baló's concentric sclerosis (BCS) is an uncommon inflammatory and demyelinating variant of multiple sclerosis (MS) predominantly affecting the central nervous system (CNS) [1]. The classification of BCS as a separate disease entity or a variant of MS is a subject of debate [2, 3]. Initially described by Dr. Jozsef Balo in 1906, it is characterized by demyelinating lesions exceeding 2 cm in size, visible on magnetic resonance imaging (MRI), often causing mass effects and oedema [4]. Although rare, BCS cases have been reported, with only two identified within a cohort of 644 MS cases in Kosovo [5]. The disease primarily targets females and presents at various ages, usually emerging around 34 years [6]. Lesions associated with BCS primarily manifest in the brain's white matter and less commonly in the cerebellum, optic chiasm, or brainstem [7, 8]. While corticosteroids serve as first-line therapy, the debate about maintenance therapy persists [8]. Outcomes vary, ranging from complete recovery to substantial morbidity or even fatal outcomes in aggressive cases [8, 9]. This report details a fatal instance of BCS.

Case Presentation

We present the case of a previously healthy 26-year-old woman who experienced a 5-min generalized seizure. The patient was admitted for the first time on February 8, 2022. Upon admission, she displayed bilateral nystagmus, right facial palsy, and expressive motor aphasia during neurological examination. Initial native computed tomography brain scan and subsequent MRI 1 day later revealed lesions in the left frontal, occipital, and uncal cerebellar regions, prompting a radiological diagnosis of encephalitis (Fig. 1).

Laboratory investigations indicated low levels of red blood cells, haemoglobin, haematocrit, cholesterol, iron, albumins, total proteins, and vitamin D, alongside elevated D-dimer levels. Autoimmune disease panel results showed elevated cardiolipin antibody IgM levels and reduced C3 and C4 complement levels. However, panels for paraneoplastic diseases, limbic encephalitis, and gangliosides (both serum and cerebrospinal fluid [CSF]) yielded negative results. Additionally, the endocrine panel revealed hormonal abnormalities, including low levels of ACTH, FSH, cortisol, FT3, and FT4, and elevated levels of anti-Tg and anti-TPO. The TORCH panel revealed intermediate levels of HSV2 IgM and positive CMV IgG. The CSF examination was unremarkable. The multiplex PCR test for neuroviruses panel returned negative results. Extensive radiological assessments, including ultrasound studies and MRI scans of various regions, yielded normal results, except for an enlarged thyroid gland detected on ultrasound. EEG findings exhibited non-specific slow activity in the parietal and temporal regions. Despite treatment with intravenous corticosteroids, parenterally administered acyclovir, antiepileptics, anticoagulants, human albumins, thyroid hormone replacement therapy, and supportive measures, the patient's condition failed to significantly improve. During the second hospitalization in late April to early May 2022, a follow-up MRI indicated an increase in the size of the left frontal lesion, while other lesions disappeared (Fig. 2).

A stereotactic biopsy of the left frontal lesion was performed, confirming histopathological features consistent with BCS. The patient was treated as an outpatient with anticonvulsive therapy until the last hospitalization on December 14, 2022, due to severe health deterioration marked by progressive expressive aphasia and refractory generalized tonic-clonic seizures progressing to epileptic status, necessitating transfer to the intensive care unit. Unfortunately, she passed away after 3 days of treatment, approximately 1 year after the emergence of initial symptoms and signs of the disease.

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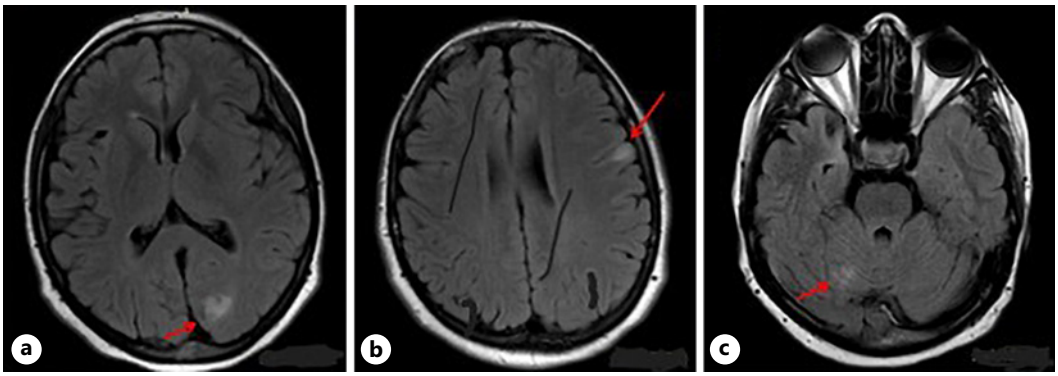

Fig. 1. Brain MRI showing: axial FLAIR hyperintense lesion on the left side subcortical occipital lobe (**a**); axial FLAIR hyperintense lesion on the cortical/juxtacortical left precentral frontal lobe (**b**); axial FLAIR hyperintense lesion on the right cerebellar hemisphere (**c**). FLAIR, fluid-attenuated inversion recovery.

Discussion

BCS represents an uncommon syndrome characterized by acute inflammation and demyelination within the CNS. The diagnosis relies on clinical presentation, imaging findings, and histopathological analysis [1, 8]. The term "concentric" pertains to the distinctive appearance of lesions, resembling concentric layers akin to an onion, featuring alternating demyelinated and myelinated tissues [10]. The clinical manifestation of BCS is diverse, encompassing symptoms such as headaches, muscle pain or spasms, muscle weakness and paralysis, dysphasia, dysarthria, cognitive impairment, and partial or generalized episodes of altered consciousness, as evident in our case [8, 11].

BCS and pseudo-tumoral MS are both demyelinating disorders, but they exhibit distinct radiological and pathological features. Balo's presents as alternating rings of demyelinated and preserved white matter, often with a more aggressive clinical course compared to classical MS. Pseudo-tumoral MS, on the other hand, manifests as mass-like lesions, mimicking brain tumours on imaging. While Balo's is characterized by its characteristic concentric lesions, pseudo-tumoral MS exhibits space-occupying lesions with oedema and mass effect. On the histopathological aspect, pseudo-tumoral MS, also known as Marburg-type MS, is characterised by pronounced plaque demyelination with increased cellularity, a robust astroglial response, and the presence of hypertrophic and enlarged astrocytes. Importantly, both conditions can lead to focal cognitive manifestations, albeit through different mechanisms. In Balo's, cognitive deficits may arise from the disruption of neural circuits within the concentric lesions, while pseudo-tumoral MS-induced cognitive impairment may result from a combination of direct tissue compression, inflammation, and secondary effects on surrounding brain regions. The distinguishing radiological and pathological features of these conditions highlight the importance of accurate diagnosis for appropriate clinical management and treatment strategies [6–8, 12–15]. The differential between Balós aphasia with other types of aphasia, like vascular aphasia with typically a sudden onset, and tumoral aphasia which tends to develop gradually and progress over time, is made by characteristic unique concentric ring lesion pattern in the brain and occurs in the context of this rare demyelinating disorder [10, 16–18].

Typically, BCS manifests around age 34, with onset ranging from 3 to 62 years [6]. Research indicates a higher prevalence of BCS in females, with a ratio of approximately 2 to 1 [13, 17]. Often, BCS exhibits clinical features resembling MS [17]. Nonetheless, BCS differs from MS histopathologically concerning lesion patterns and sizes [10, 19]. Unlike the small

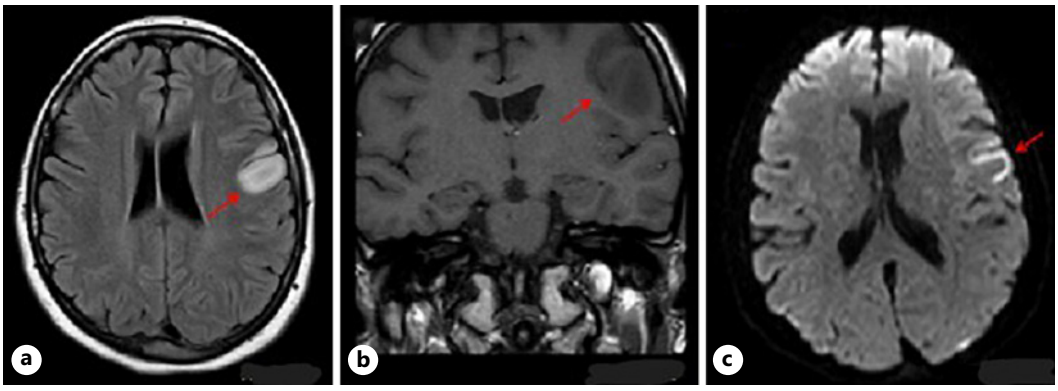

Fig. 2. Brain MRI showing: axial FLAIR hyperintense lesion on the left precentral gyrus (**a**); the same lesion on coronal hypointense on T1 sequence (**b**); DWI with hyperintense cortical ribbon (**c**). FLAIR, fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging.

ovoid lesions usually associated with MS, BCS lesions are generally larger and display a concentric pattern [19]. BCS usually features a single lesion, mainly in the white matter of both cerebral hemispheres, with lesions occasionally appearing in other regions like the optic chiasm, cerebellum, brainstem, and spinal cord, albeit less frequently [18, 19]. In our case, the patient exhibited multiple lesions, including two in the cerebral hemisphere and one in the cerebellum.

When employing contrast-enhanced MRI, T1-weighted lesions may exhibit peripheral enhancement, indicating active demyelination or disease progression [14, 18, 19]. MRI stands as a valuable diagnostic tool for both BCS and MS, offering more insight than computed tomography scans [5, 11, 16]. Lesions resembling tumefaction or pseudo-tumours in MS demonstrate hyperintensity on T2-weighted and fluid-attenuated inversion recovery images [1, 11, 16]. Acute BCS lesions may also display restricted diffusion on diffusion-weighted imaging and apparent diffusion coefficient images. While magnetic resonance spectroscopy plays a pivotal role in BCS diagnosis, it was not available in our case [20]. EEG finding of "non-specific slow activity in the parietal and temporal region" is probably linked to the effect of the treatment with anticonvulsive therapy. The atypical MRI findings in our patient and the lack of definitive diagnosis necessitated histopathological confirmation through a stereotactic biopsy.

As of now, no specific, highly effective therapy exists for BCS due to its rarity. Treatment centres on supportive and symptomatic measures, often involving high-dose intravenous steroids during the acute phase, followed by gradual oral steroid tapering. Commonly, methylprednisolone is administered intravenously at doses ranging from 500 to 2,000 mg/day for 3–10 days, with most patients showing excellent recovery post-steroid treatment [14, 21]. For patients with inadequate steroid response, alternate treatments such as plasma exchange, intravenous immunoglobulin, cyclophosphamide, and immunosuppressive agents may be considered [10]. Some patients may require long-term immunotherapy to prevent relapse, which can be combined with steroid therapy for enhanced effectiveness [10, 19]. Oligoclonal IgG in CSF has been identified as a predictor of relapse in Baló-like lesions [10]. Symptomatic treatment plays a crucial role in managing symptoms in most BCS cases [13].

It's imperative to note that BCS lesions can be aggressive and life-threatening, especially when the diagnosis is delayed or treatment response is inadequate, significantly affecting clinical outcomes. A review of published cases reveals that 14% of BCS patients succumb to the disease. Another study analysing 17 deceased patients with BCS reported time frames varying from 5 days to 8 months post-diagnosis, averaging 2.38 months [6]. Secondary infections such as pneumonia were the most prevalent cause of death, with brain herniation

also reported in some instances [10]. In our presented case, brain herniation or secondary infection was not evident; however, the cause of death was attributed to recurrent seizures unresponsive to standard anticonvulsant medication, eventually escalating to epileptic status 11 months after the patient's initial hospitalization. The CARE Checklist has been completed for this case report and it is attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534358) [22].

Conclusion

BCS has the potential to mimic various neurological conditions, including CNS tumours. In settings with limited resources, when clinical presentation, laboratory findings, and MRI results are inconclusive, a stereotactic brain biopsy becomes indispensable. Delayed diagnosis and suboptimal treatment substantially impact disease outcomes. Although MRI provides valuable information for diagnosing BCS, uncertainty in diagnosis may necessitate histopathological confirmation. This case underscores the successful clinical and diagnostic journey to identify BCS as the underlying condition. However, the juxtacortical location of the BCS lesion, as observed in our case, suggests an unfavourable prognosis due to treatment-resistant seizures.

Statement of Ethics

This case report was reviewed and approved by the Committee of Ethics of the Kosovo Medical Association, approval number 7327. Written informed consent was obtained from the patient's next of kin for publication of the details of their medical care and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Nexhmedin Shala, conception of the work, drafting the work, interpretation of the data for the work, and final approval of the version to be published; Ilir Tolaj, critically reviewing the work for intellectual content and final approval of the version to be published; Fisnik Jashari, design of the work, acquisition, analysis, and interpretation of data for the work, and final approval of the version to be published; Edita Malazogu, Argjend Shala, and Gentian Bajraktari, acquisition and analysis of the data for the work, and final approval of the version to be published; Ilir Ahmetgjekaj, interpretation of the data for the work, and final approval of the version to be published; and Shemsedin Dreshaj, substantial contribution to the conception of the work, and final approval of the version to be published.

Data Availability Statement

All data generated or analysed during this study are included in this article and its online supplementary material. Further enquiries can be directed to the corresponding author.

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