Balo’s Concentric Sclerosis in a Young Female Patient: Case Report and Review of the Literature

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Balo concentric sclerosis (BCS) is a rare disease considered as a variant of multiple sclerosis (MS) with a clinical presentation similar to tumefactive MS or Marburg disease. Pathologically it is characterized by concentric demyelinating lesions, consisting of layers of preserved and destroyed myelin arranged in a ring-like shape. We present the case of 29 years old female that developed acute neurological deficits consisting of dysesthesia and paresthesias localized in the right half of the face and right limbs for which the magnetic resonance imaging (MRI) using contrast substance revealed multiple lesions with T2 hyper- and isointense concentric whorled lesions, which are better emphasized on the T1 sequences. The patient received acute treatment with corticosteroids, with good clinical remission and was recommended to start disease modifying therapy (DMT) with interferon beta-1a for clinical stability with good evolution.

Keywords: Balo concentric sclerosis, demyelinating disease, tumefactive multiple sclerosis, Marburg disease

INTRODUCTION

Balo concentric sclerosis (BCS) is a rare demyelinating disease regarded as a variant of multiple sclerosis that has a clinical presentation similar to tumefactive MS or Marburg disease. It was first known to have a rapid progressive course and a fatal outcome, but, within the last 15 years, an increasing number of patients diagnosed with Balo concentric sclerosis were reported to have a less fulminate evolution, presenting increased survival and, some cases achieving spontaneous remission. Usually patients suffer from acute or sub acute neurological deficits like hemiparesis, dysesthesia, confusion, aphasia or seizures. It affects young adults between 4 and 59 years of age, has an even sex distribution and is more common in the East Asian population. Pathologically, BCS is characterized by concentric demyelinating lesions that consist of alternating layers of preserved and destroyed myelin, arranged in a ring-like shape. The typical BCS magnetic resonance imaging (MRI) consists of concentric rings or a whorled aspect on T2-weighted and contrast-enhanced T1-weighted images. The etiology of this concentric demyelization is not known, but several mechanisms were suggested; one mechanism is thought to be the consequence of damaging the oligodendrocytes due to oxidative stress. This can be explained by the numerous inducible nitric oxide syntheses macrophages and microglia within demyelinated bands, and, on the other
hand, by high expression of protective proteins like HIF-1 alpha (hypoxia inducible factor-HIF) and heat shock protein-70 (HSP-70), which are found in oligodendrocytes and astrocytes within the preserved regions of myelin next to the active demyelinating lesions. (Stadelmann et al., 2005; Lu et al., 2006). More recent theories concerning the pathological events in BCS propose that there is an initial immune mediated astrocytopathy resulting in loss of aquaporin-4 and connexins (Kira, 2011; Masaki et al., 2012) followed by oligodendrocyte injury mediated by the above inflammatory mechanisms. Disease management includes the following treatment options: in acute phase, corticosteroids were proved to have a positive response in most of the described patients; if lack of response to this therapy plasma exchange was the second option that showed clinical improvements. For long-term clinical stability several treatment schemes were proposed including disease-modifying treatments as in MS, immunosuppressive treatments or combination of both, in the case of an aggressive disease.

**CASE PRESENTATION**

We report the case of a 29 years old female who was admitted in our clinic for right facial dysesthesia and right side limb paresthesia. The symptoms she described appeared for the first time 2 years ago and had an intermittent pattern lasting about 7-10 days, only this time they lasted for 3 weeks. She was investigated in a neurology clinic 2 years ago and diagnosed with a demyelinating disease; the initial cerebral magnetic resonance imaging (MRI) with contrast revealed 2 demyelinating lesions located in the right temporal and parietal lobes with abnormal restricted diffusion but no contrast uptake; after a 5 day course of intravenous corticotherapy the neurological symptoms disappeared. She performed another MRI 6 months later, and it didn’t reveal any changes or additional lesions.

For the current admission in our clinic, the neurological exam revealed brisk deep tendon reflexes (on the right side more than left), right facial hypoesthesia and right superior limb paresthesia with no other neurological deficits.

The new cerebral MRI performed with contrast substance in our clinic, revealed 4 new sub cortical demyelinating lesions, two of them located in the right frontal lobe, measuring 19/11mm and 15/11/7mm, one in the left frontal lobe and one in the left parietal lobe. These lesions had no abnormal diffusion restriction, had a slight contrast uptake, they had a ring-shaped aspect, better emphasized on T1 multiplaner reconstruction (MPR), suggestive for Balo lesions. (Figures 1-8)

The lumbar puncture performed, did not reveal oligoclonal bands and the IgG index was normal.

Biologically she presented no signs of inflammation and C3 and C4 were within normal ranges. A wider immunological profile was obtained in which the anti-nuclear antibodies, anti DNA antibodies, pANCA, cANCA,
Figure 2. MRI 1.5T - T2WI showing the sub cortical right frontal lesion with alternating hyper intense and isointense concentric oval shaped rings.

Figure 4,5. MRI 1.5T - T2WI showing hyper intense demyelinating lesion located adjacent to the right ventricle anterior horn (left picture) and another hyperintense image in the left frontal lobe (right picture)
anti-cardiolipin antibodies, rheumatoid factor, HIV, TPHA, Lyme antibodies and HCV-Ab were negative.

At this stage, based on the clinical, paraclinical and imagistic studies, the diagnosis was suggestive for Balo concentric sclerosis and intravenous (iv) corticotherapy was recommended for this patient as acute therapy. After a 5 day course of treatment with metilprednisolone iv (500mg/day) a favorable outcome was obtained with remission of the presenting neurological symptoms. A treatment with disease modifying therapy (DMT) (interferon beta-1a) was recommended.

A good clinical control was achieved since the introduction of interferon beta-1a, no side effects were reported, and a new MRI was scheduled within 3 months.
DISCUSSION
Balo concentric sclerosis is an atypical inflammatory demyelinating disease within the multiple sclerosis spectrum, that has a similar pathological substrate except for the fact that the lesions are organized in a whorled way.

Initial studies have suggested that the pathological mechanisms implies a preconditioning of the oligodendrocytes to react to oxidative stress (Stadelmann et al., 2005), while other authors completed this theory by demonstrating that, in fact, intracellular mitochondrial injury may be involved in the pathogenesis of such lesions (Mahad et al., 2008) and explained the hypoxia-like tissue injury seen in this subtype of multiple sclerosis lesions. Recent studies offered different view to the initial mechanism triggering these lesions. This new studies suggest that an immune response caused by infiltrating T cell factors such as proinflammatory cytokines and chemokines might act on astrocytes causing aquaporin-4 and connexins loss which lead to astrocryopathy that would later affect neighboring oligodendrocytes causing the demyelinating process. (Kira, 2011; Masaki et al., 2012). Adding to these mechanisms is a new case report that proved vascular involvement in Balo concentric sclerosis pathology using a 7 Tesla MRI (Berghoff et al., 2013) where microhaemorrhages and ectatic veins were visible in T2 hyper intense regions.

MRI imaging studies of patients with BCS confirm there is a pathognomonic aspect due to presence of alternating layers of demyelinated and myelinated white matter, visible in the T1WI with contrast enhancement (Caracchio et al., 2001; Wiendl, 2005). As with the currently presented case, it is frequently seen that these lesions are associated with other MS specific demyelinating lesions. Clinical presentation of patients with BCS translates into acute or sub acute neurological deficits, consisting of motor deficits – hemiparesis (Moore et al., 2001), sensory deficits – hypesthesia, dysesthesia, cognitive and behavioral impairment, aphasia, dysarthria, ataxia and seizures (Purohit et al., 2015).

Several cases of BCS were described in association with different other pathologies besides MS which include progressive multifocal leukoencephalopathy (Markiewicz et al., 1977), encephalitis with human herpes virus 6 (Pohl et al., 2005), atypical neuromyelitis optica (NMO), NMO spectrum (Grabber et al., 2009) and a case with Notch 3 mutation associating CADASIL (Chitnis et al., 2012).

The treatment option for acute symptoms consists of oral or intravenous corticotherapy, with most cases presenting a positive response. However there were cases reported in which corticotherapy was insufficient and additional plasma exchange therapy was necessary showing possible benefits (Sekijima et al., 1997). For clinical stability, several treatment options were reported: DMT’s, natalizumab, alemtuzumab, immunosuppressive treatment with azathioprine, cyclophosphamide, mitoxantrone, the latest being used to achieve control of a very active disease (Hardy et al., 2014). Even though BCS was largely considered as a fulminating disease, current reports conclude that it has a rather benign course, and a review of the reported cases till this date indicate that just 14% of the patients died, and 26% of them did not develop any clinical activity for up to 2 years. (Kepes, 1993; Lucchinetti et al., 2008).

CONCLUSION
The case report suggests that BCS my not be a rapidly progressive or a fatal dymielinating disease.

A precise mechanism of action is not yet known, but recent reports suggest that astrocytes loss of aquaporin-4 channels and connexis due to immune mediated response triggers the inflammatory mechanisms that lead to destruction of susceptible oligodendrocytes.

Long-term studies are necessary to determine the pathological mechanisms and to develop efficient treatment options for patients with this rare type of demyelinating disease.

REFERENCES
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