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Case Report

Chronic inflammatory demyelinating polyneuropathy: A unique case of chronic disease with atypical features^{☆,☆☆}

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ABSTRACT

We present a unique case of diffusely extensive Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). Typically affecting the peripheral nervous system and manifesting with muscle weakness, breakdown or paresthesia, we present a case that additionally demonstrates; cranial nerve involvement, central nervous system parenchymal lesions, and chronic osseous remodeling of the nerve tracts. Cranial nerve involvement to this extent has only been described in one other case report to our knowledge. Central nervous system parenchymal lesions are extremely rare in CIDP and no discrete discussion about osseous remodeling has been presented, thus far, in the literature. The findings illustrated in this case may spur further understanding of imaging characteristics most associated with chronic CIDP disease and care measures that could help stratify patients most at risk for severe symptomologies.

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Introduction

Polyneuropathy is a nervous system disease characterized by symmetric involvement of multiple nerves, typically affected in a length-dependent fashion [1]. Involvement of the nerve roots defines a polyradiculoneuropathy. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an inflammatory

disease that affects nerve roots and peripheral nerves and thus, may present as a polyneuropathy or a polyradiculopathy. Pathologically, inflammatory reactions occur at the Schwann cell-axon junction, and in non-compact regions of myelin to cause demyelination of the nerves [1]. CIDP is the most common demyelinating disease, affecting a wide range of the population, there is no age or gender – specific distribution of this disease [2]. Typically distributed along the somatic nervous

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system, we present a unique case that also demonstrates distribution of disease in the cranial nerves, nerve roots and the nerve fascicles of the cauda equina. Additionally, in the central nervous system, rare multiple sclerosis (MS)-like lesions, were present in this case. The unique case presented is not only extensive in inflammatory nerve involvement but extensive in chronicity resulting in remodeling of the foramina osseous structures in this patient. We have not found another case in the literature, to date, that describes this extent of osseous remodeling.

Case presentation

Our patient is a 46 year old male presenting with decreased sensation in the lower extremities, generalized weakness, worsening ptosis, and slurred speech. Given these symptoms, a neurologic stroke protocol was initiated. A Computed Tomography (CT) Angiogram of the head and neck was performed as part of the stroke code activation, however, no acute intracranial abnormality was found. On hospital day 1, his generalized weakness worsened and he suffered respiratory distress, and subsequent intubation. This patient has had a 20-year history of relapsing and remitting CIDP, thus, this admission was diagnosed as a CIDP exacerbation. In the Neurological Intensive Care Unit (ICU), he was treated with plasmapheresis and prednisone to counteract the neural inflammatory process. He exhibited notable improvement and was weaned off ventilation 8 days later. The following day, he suffered another episode of severe desaturation and had to be intubated for a second time. He failed subsequent spontaneous breathing trials and after two additional weeks of ventilator management, the decision was made to perform a tracheostomy and placement of a feeding tube to maintain nourishment.

Despite initial treatment with Intravenous Immunoglobulin (IVIG), solumedrol, oral prednisone, and rituximab, his clinical status continued to deteriorate to the point of severe bilateral paraplegia in the lower extremities. His clinical management was maintained on combinations of rituximab/prednisone and IVIG with solumedrol, with the addition of pulsed cyclophosphamide. Lab findings were significant for IgM antibodies to Neurofascin-155 and IgG antibodies for Neurofascin-140, paranodal and neuronal proteins known to be involved in CIDP [2]. His electromyography study was abnormal, showing evidence of demyelinating polyneuropathy with signs of chronic and acute denervation, however, no myopathy was identified.

Imaging findings were most descriptive on magnetic resonance imaging. There was marked enlargement of bilateral cranial nerves, including the facial nerves and branches of the trigeminal nerve (Fig. 1). As a result of long-term polyneuropathy and subsequent nerve enlargement, findings were also significant for enlargement of the anatomic skull base foramina such as the foramen rotundum (Fig. 2C), optic canal (Fig. 2D), foramen ovale (Fig. 3), the pterygopalatine fossa (Fig. 4) as well

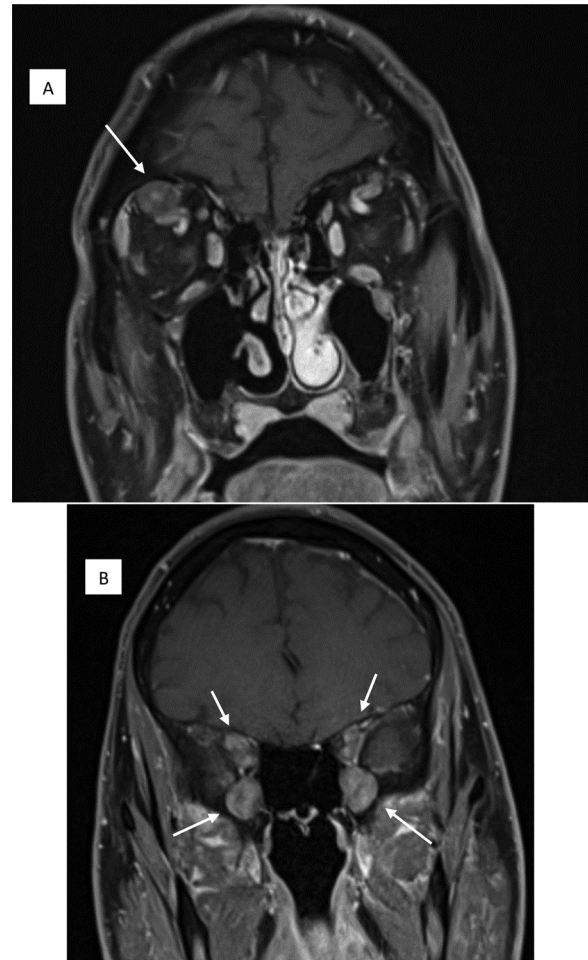


Fig. 1 – Multiple coronal MRI slices through a T1WI G+ sequence showing enlargement of the intraorbital CN IV branch (A, arrow) and bilateral CN V (B, arrows).

as the mandibular canal for the inferior alveolar nerve (Fig. 5). Enlarged superficial nerves were also evident by serpiginous thickening within the scalp. There was diffuse thickening of the bilateral cervical and thoracic nerve roots, most notably at T1-T2, T2-T3, T3-T4, and T8-T9, demonstrated at the cervical level in Fig. 6. On CT abdominal imaging, diffuse bilateral enlargement of the sacral roots as they arose from the neural foramina was identified and depicted in Fig. 7. Additionally, there were cerebral non-enhancing flame-shaped periventricular lesions with T2/FLAIR hyperintensity (Fig. 8), commonly seen in MS. This was unusual in this patient with no prior history of MS.

Improvement in his status occurred after 2-3 total months of treatment. Nearly 70 days after admission, the patient was able to successfully pass a swallow evaluation and begin feeding by mouth again. After approximately 90 days of admission, he was stable and with clinical improvement in his CIDP symptoms. He reported residual weakness in his extremities and was still managed via tracheostomy collar. He was able to

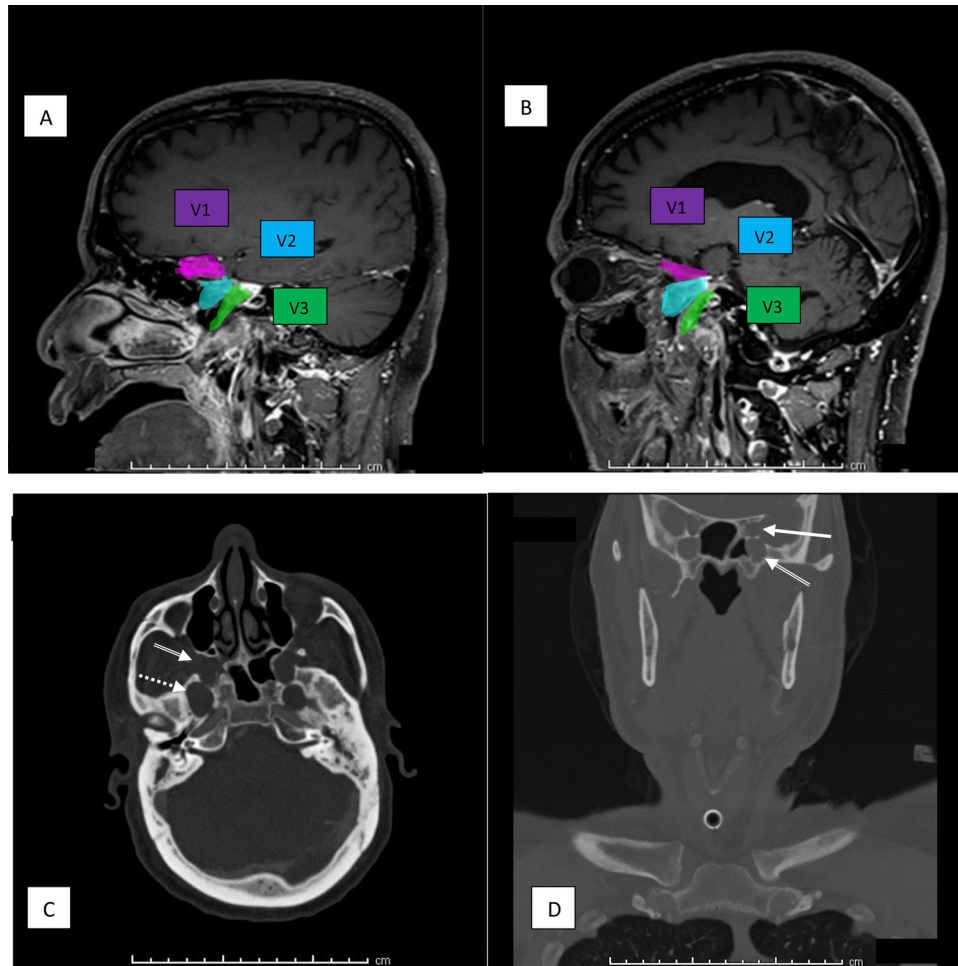


Fig. 2 – Trigeminal nerve branching. (A and B) are sagittal representative MRI images from T1WI G+ sequences showing the enlarged branches of the trigeminal nerve (V1, magenta; V2, blue; V3, green). (C) Axial CT in bone algorithm sequence demonstrating enlargement of the foramen rotundum (white striped arrow) and foramen ovale (white dashed arrow) bilaterally. (D) Coronal CT in bone window, demonstrating enlarged skull base foramina; foramen rotundum (white striped arrow) and the optic canal (solid white arrow).

tolerate a soft diet on his way to regaining baseline function. His acute exacerbation had resolved and he was discharged to a continued care facility with scheduled neurological follow-up.

Discussion

CIDP is characterized by sensory and motor deficit symptoms, progressive weakness and, classically, appropriate response to corticosteroid therapy. Symptoms are typically present for 2 or more months and can relapse and remit for years, causing increased morbidity and decreased quality of life. Clinical evaluation, deficits in electromyography testing, and, definitively, positive nerve biopsy are the criteria that confirm the diagnosis. Although, not diagnostic, radiologic findings can heighten clinical sensitivity for this disease. Magnetic Resonance Imaging (MRI) is the imaging modality of choice, although contrast-enhanced computed tomography (CT) and ultrasonography

can also be used to evaluate CIDP. The best diagnostic finding on MRI is enlargement and T2 hyperintensity of nerve roots, nerve plexi, or peripheral nerves. Involved nerves have also been shown to exhibit enhancement on gadolinium contrast studies (Figs. 3B and C). The enlargement seen on imaging is the result of excessive recurrent demyelination and remyelination of Schwann cells. Schwann cells proliferate and create multiple layers of axonal covering, causing an *onion bulb* appearance histologically and an enlargement of the nerve pathologically and radiologically [3].

Typical distribution of disease

The typical distribution of CIDP has been determined using MR Neurography in multiple studies, found to frequently involve the bilateral extracranial vagus, trigeminal, and intercostal nerves. The distribution of hypertrophy is typically uniform and bilateral [4,5]. The nerve roots, diffusely, are also

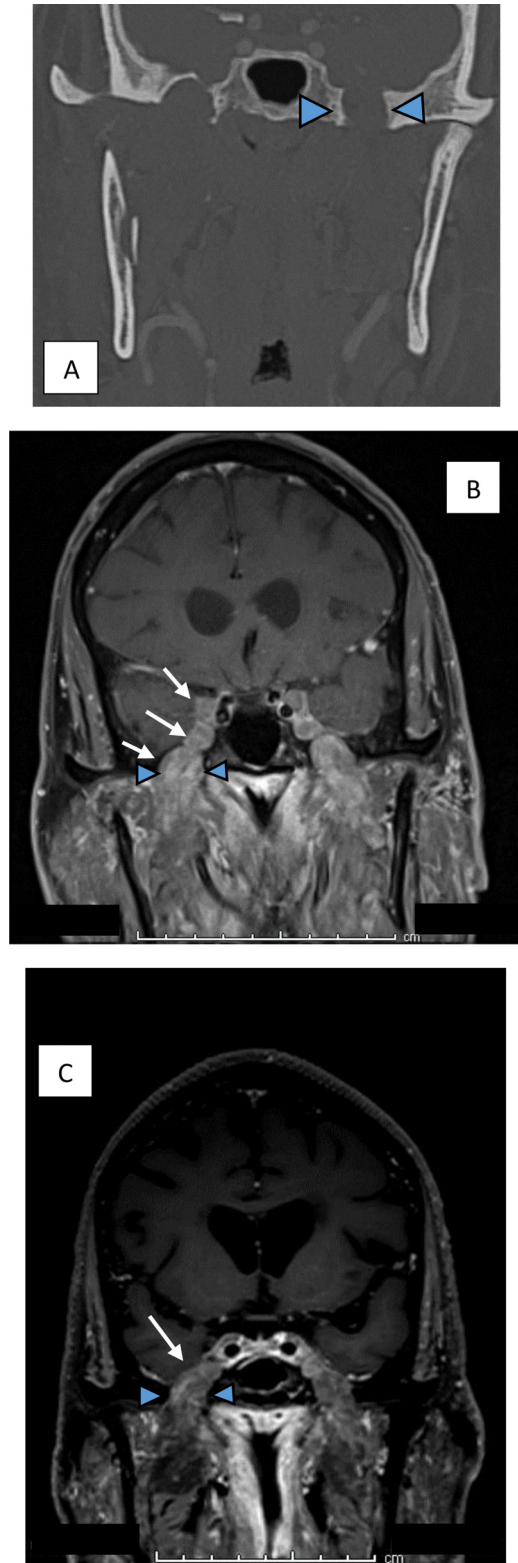


Fig. 3 – Enlarged foramen ovale. (A) is a coronal slice of a CT in bone window, demonstrating the enlargement of the foramen ovale bilaterally (between the blue arrowheads). (B and C) Coronal T1WI G+ MRI depicting the enlarged CNV (solid white arrows) and its branches traversing the foramen ovale (between the blue arrowheads).

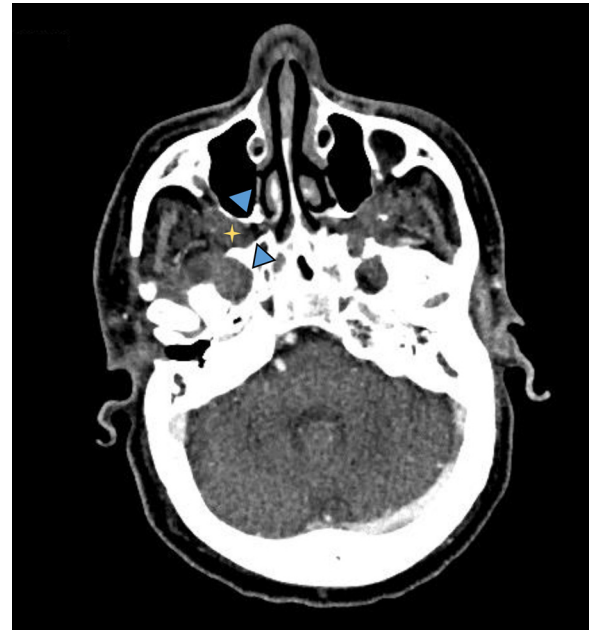


Fig. 4 – Enlarged pterygopalatine fossa. Axial CT in soft tissue window, depicting the enlarged pterygopalatine fossa (between the blue arrowheads). The soft tissue density occupying the fossa is the enlarged zygomatic branch of the maxillary nerve (CN V2), yellow four-point star.

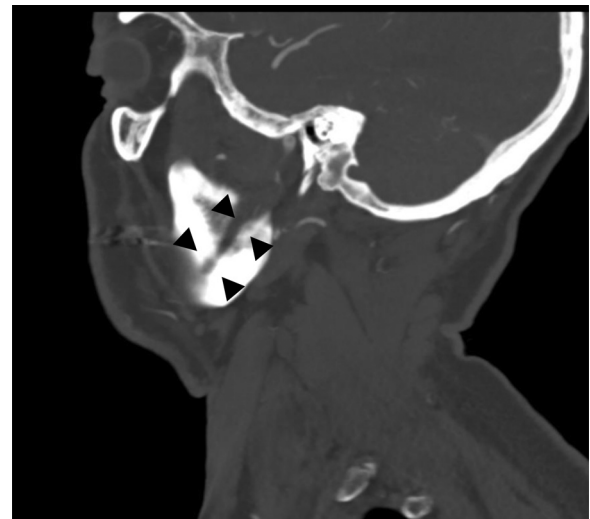


Fig. 5 – Sagittal CT in the bone window, demonstrating an enlarged mandibular canal for the inferior alveolar nerve (between the arrowheads).

known to hypertrophy in this disease. Other distributions, such as multifocal fusiform hypertrophy or unilateral involvement of the nerves may be seen in variant cases and atypical demonstrations of CIDP [4,5]. A 2003 case study presented a patient enduring a 10-year history of CIDP, with intercostal nerve enlargement in addition to brachial plexus and nerve root involvement illustrating the typical, expected distribution of disease [6]. Nerve involvement has been shown to in-

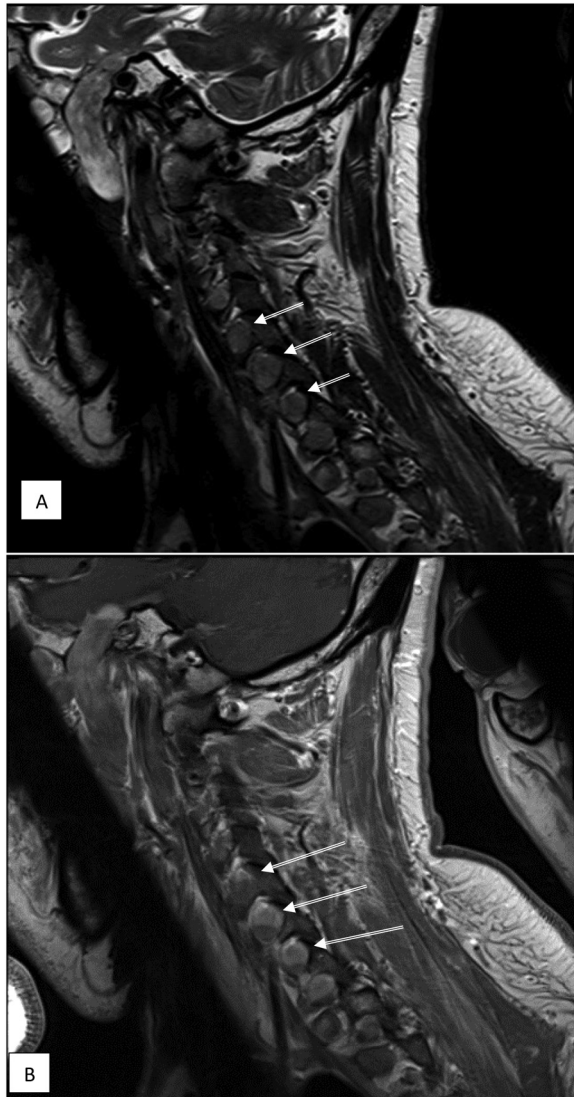


Fig. 6 – Sagittal T2WI (A) and T1WI (B) MRI images depicting the diffusely enlarged nerve roots at every level of the cervical spine (striped arrows at C4-5, C5-6, and C6-7 neuroforamina). These findings were bilateral in this patient and extended through the thoracic, lumbar, and sacral spine as well.

clude the cranial nerves in only 11% of cases, and when severe, were manifested as facial and bulbar nerve palsies [7].

Unique distribution of disease

Our patient demonstrates extensive involvement of the cranial nerves and nerve roots in his chronic 20-year journey with CIDP. Typical involvement of the nerve roots was demonstrated throughout the spine and into the sacrum. He also demonstrated hypertrophy of the proximal and distal branches of the trigeminal and facial nerves. In addition, our patient demonstrated hypertrophy of bilateral optic nerves,

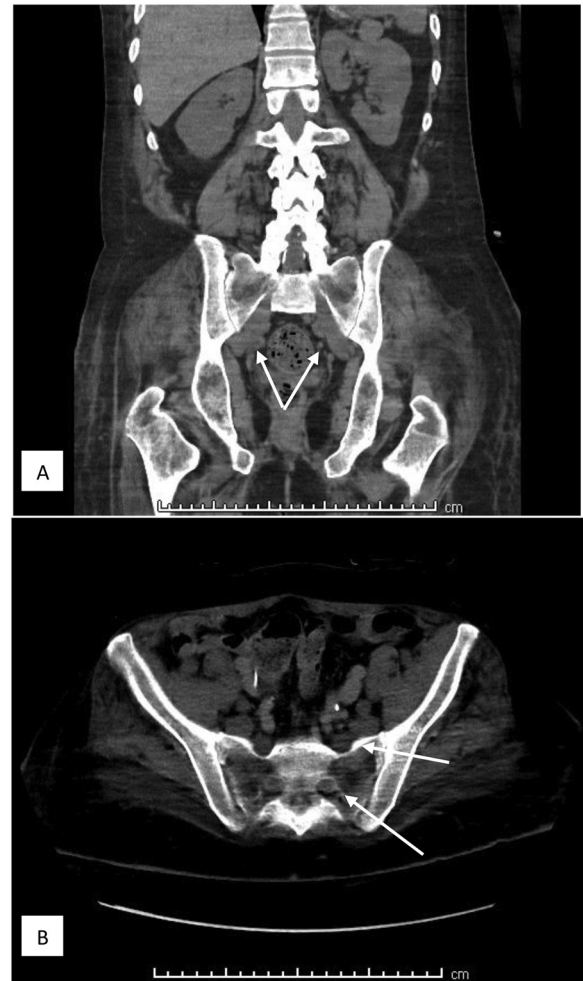


Fig. 7 – Coronal (A) and Axial (B) CT of the abdomen exhibiting enlarged sacral nerve roots filling the exiting canals bilaterally (solid white arrows).

intraorbital trochlear nerves, the vagus nerves, glossopharyngeal nerves and even the inferior alveolar nerves. His extent of involvement of the cranial nerves and proximal neural structures is unlike that seen previously. Clinically, nerve involvement manifested with respiratory distress, likely secondary to the vagus nerve, however facial palsies were not part of this patient's course. Chronicity of CIDP has been suggested to correlate with worsened symptomology, namely papilledema and proptosis, in a 2013 case review article describing the ophthalmologic manifestations of CIDP [3]. Our patient presented with ptosis, suggesting early oculomotor nerve involvement, however, this nerve was normal on imaging. His hospital course and difficulty with swallowing may correlate with vagus and glossopharyngeal nerve involvement. A case review article by Fong et al. displays a similar, extensive distribution of nerve hypertrophy in a patient who exhibited mild symptoms, discordant with the diffuse nerve involvement found on imaging [8]. This patient, however, reported a 5-year intermittent history of bifacial and bilateral upper extremity paresthesia. Correlation between nerve hypertrophy and severity of disease or duration of disease has not been

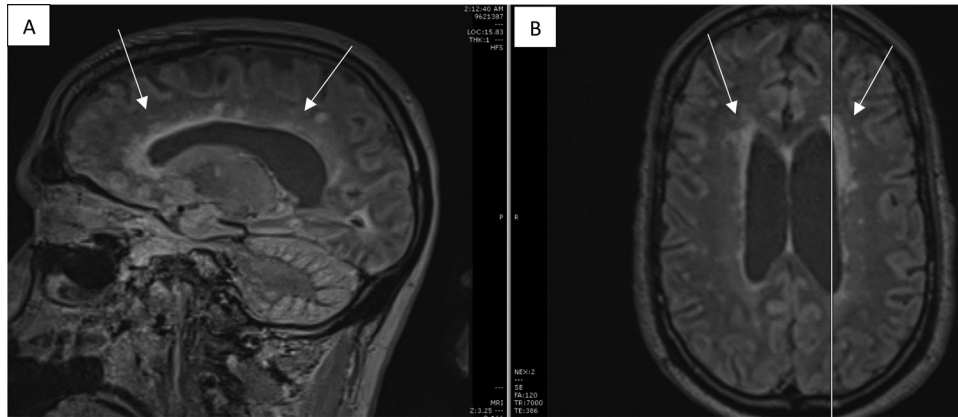


Fig. 8 – Sagittal (A) and Axial (B) T2 FLAIR MRI images with slice localization demonstrating flame-like periventricular white matter lesions. These MS-like lesions were bilateral (solid white arrows). These lesions did not enhance on this examination (not shown). MS, multiple sclerosis.

demonstrated, however, we postulate that osseous remodeling secondary to chronicity of disease may be an indicator to a patient's risk of developing severe disease in the future.

White matter brain lesions mimicking multiple sclerosis (MS)

Disruption of the paranodal and nodal proteins have been found to attribute to a variety of polyneuropathies, albeit by different antibody culprits [9]. Specifically, there is an association with altered Neurofascin-155 paranodal proteins and active demyelination in Multiple Sclerosis (MS) [10]. This protein was identified in our patient and is known to be associated with CIDP, the question of how often imaging findings of both CIDP and MS are present has yet to be completely answered. Although seen in a few cases, MS-like lesions are rare in the literature. In patients with CIDP, under the age of 49, 21% of patients had MRI evidence of irregular periventricular lucencies as well as other lesions within the brain. These findings were non-specific, however, non-distinguishable from the distribution of lesions in MS [11]. Out of 19 patients, Feasby et al. found one patient under the age of 50 demonstrating subcortical lesions that were in the expected distribution of MS [12]. Furthermore, a Grecian study of 12 patients found no abnormal central nervous system white matter lesion in their patient cohort [13]. Recently, Sisak et al. present a case of MS subsequently developing in a patient diagnosed with CIDP [14]. Our patient, without a prior diagnosis of MS, demonstrates non-enhancing flame shaped periventricular lesions with T2/FLAIR hyperintensity, very similar to lesions seen in MS (Fig. 8).

Osseous remodeling

A unique finding that has not been described in the literature to our knowledge, is the extensive remodeling of the skull

base and spinal foramina. It has been suggested that there is limited correlation between extent of nerve hypertrophy and disease severity or duration. We propose that in addition to worsening symptomology, osseous remodeling and the widening of skull base foramina, spine foramina, and nerve tracks such as the mandibular groove of the inferior alveolar nerve, may have a correlation with chronicity of the disease. Chronicity of CIDP has been suggested to correlate with worsened symptomology, namely papilledema and proptosis in a 2013 case review article describing the ophthalmologic manifestations of CIDP [4]. In 1999, Duarte et al. reported a patient with a 26-year history of disease that was ultimately found to be CIDP [15]. This patient demonstrated involvement of the trigeminal nerves, facial nerve, cervical, thoracic, and lumbar spinal nerve roots with diffuse enlargement of the cauda equina. This was one of the first instances of cranial nerve thickening in CIDP. Additional case reviews of patients with a 20-plus year history of CIDP may be of utility for further determination of this correlate. This would enable us to better identify patients with chronic CIDP disease on imaging, regardless of their current symptomology and stratify them into appropriate risk levels of future severe symptomology. These patients can receive a more aggressive follow-up or treatment regimen.

Authors' contribution

All authors contributed to writing the manuscript. All authors read and approved the final manuscript.

Ethics approval

This is a retrospective case report not requiring ethics approval.

Patient consent

Appropriate informed consent has been obtained prior to publication of this manuscript.

Availability of data and materials

Not Applicable.

Code availability

Not Applicable.

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