INTRODUCTION

The first to describe a longitudinally spinal cord lesion on post-mortem examination was probably JA Lockhardt Clarke in 1865.1 Later in the second half of the 19th century, the term acute transverse myelitis (ATM) was introduced by Bastian, when he described an infectious or allergic mechanism in autopsies from patients who died of the myelitis.2 A similar mechanism was found to explain the term “post-vaccinal encephalomyelitis,” which was found as a rare complication related to smallpox vaccination.3 Frank Ford, some years later, hypothesized that many ATM cases were post-infectious rather than infectious in relation to measles since the infectious symptoms faded when the myelitis symptoms began.4 In past years, several other infectious agents such as the herpes virus have been found related to ATM5 and described as a direct infection of the central nervous system (CNS) and a post-infectious reaction.6

The term transverse myelopathy (TM) was later introduced to indicate that the clinical symptoms indicating spinal cord injury were not always consistent with spinal cord inflammation. A follow-up study in TM emphasized that temporal progression from weeks to months could distinguish between compressive etiologies, toxic and hereditary disorders.7 In this study and others, it was reported that TM could be the first symptom of multiple sclerosis (MS).8 Magnetic resonance imaging (MRI) showed small, incomplete, and multiple lesions involving individual tracts in MS patients. By contrast, ATM patients showed complete lesions extending over multiple vertebral segments.5 Thus, in spite of its etiology and of its similar clinical findings of sensory loss and motor impairment below a certain level, long spinal lesions which extended over several vertebral segments on the MRI examination were described as longitudinally extensive transverse myelitis (LETM). This finding is often related to antibody-mediated diseases such as neuromyelitis optica spectrum disorders (NMOSD) and myelin oligodendrocyte glycoprotein antibody diseases (MOGAD) and paraneoplastic-mediated diseases.5,9,10

Transverse myelitis has also been described associated with Hepatitis C virus infection.11–14 Using MRI extensive lesions were observed in these studies in all parts of the spinal cord, both in the white and the gray mater. Recurrence was often described, especially in relation to discontinuation of interferon14 and incomplete remission was...
found clinically and on MRI at follow-up one year later. This unique case report describes the location of the MRI lesions before and after gadolinium enhancement in a patient with hepatitis C infection before and after direct-acting antiviral treatment (DAA) for the infection.

2 | CASE REPORT

A 29 years-old man was admitted to our neurological department with five months of progressive disability in walking, paresthesia in the arms when bending the neck, numbness in the hands, and back pain. He had been treated for many years with aerosol salbutamol during exacerbations of asthma. Apart from periodic jaw spasms during the last five years, there were no apparent previous illnesses and no suspicion of infection within the last six months. During the last two years, he had been successfully treated for his injectable drug abuse with daily oral methadone. The patient had had negative hepatitis C virus RNA (HCV) serology two years before presentation. The neurological examination revealed positive Lhermitte’s sign, hypoesthesia in the hands, normal muscle strength in the upper limbs, reduced muscle strength in the legs (4 on a MRC scale), and reduced dorsiflexion of the feet (4 on a MRC scale). In addition, the patient had severe increased spasticity in the extensor muscles of the lower limbs, bilateral-positive Babinski, and a broad-based gait requiring support.

Spinal cord MRI demonstrated extensive longitudinal spinal cord lesions from the cervical vertebral segment C1 to C5 and thoracic vertebral segment T2 to T11 (Figure 1). The cervical lesion was located in the dorsal part and over a short distance in the lateral part on the right side on T2-weighted images. Discrete enhancement was found in the posterior part. Changes in the thoracic part were seen almost over the cord’s entire cross section on the T2-weighted images, but enhancement was only demonstrated in the lateral part on both sides. The brain MRI was normal.

A lumbar puncture was performed with cerebrospinal fluid showing slight pleocytosis with 11 mononuclear cells, a slightly increased protein to 0.64 g/l, normal IgG index and no oligoclonal bands, no antibodies against the varicella-zoster virus, herpes virus, enterovirus, or borrelia. The blood tests showed normal B12 vitamin, rheumatoid factor IgM and ANA, negative HIV serology, negative syphilis RPR, negative TB gamma interferon release assay, negative MOG- and AQP-4 antibodies, and increased ALAT to 200 U/l. Tests for HCV serology and HCV RNA were both positive.

Treatment of HCV infection with Zepatier (elbasvir 50 mg and grazoprevir 100 mg) one tablet daily was initiated and

FIGURE 1 On the left side, a sagittal T2-weighted MRI illustrates the longitudinally extensive lesions from C1 to C5 and T2 to T11. To the right side, the upper T1-weighted MRI shows enhancement in the dorsal part of the cervical cord and the lower MRI enhancement in the lateral parts of the thoracic cord on both sides.
continued for three months. Follow-up blood tests showed normalization of ALAT, negative HCV serology, and normalization of the spinal cord changes on MRI. The neurological findings were unchanged. There was no clinical suspicion of rheumatic, vascular or skin diseases and normal thyroid, white blood cells and renal function tests. With that condition, we found no indication for steroid treatment also taking into account previous episodes of psychosis in relation to his drug abuse.

Despite a four-week course of inpatient rehabilitation, the physical condition was only slightly improved. Currently (two years later), walking distance is reduced, a stick is required when walking outside, and medication is still necessary for spasticity and neuropathic pain in the legs.

3 | DISCUSSION

This case report reports on the unique normalization of tractopathy lesions of the spinal cord in relation to HCV infection after antiviral treatment. The relation between ATM and HCV has been previously described, where the only possible treatment was steroid, interferon, and IV immunoglobulins.\(^{11–14}\) In one of these case reports, a one-year follow-up MRI showed incomplete remission.\(^{11}\) The same publication reviewed additional 10 cases reporting high-recurrence rate of myelitis between 6 and 16 months.\(^{11}\) In the reports, MRI showed extensive MRI lesions in the white and the gray matter of all spinal cord parts but the location of enhancement to specific areas was not described.\(^{12–14}\) Despite discussion to whether the relationship was causal, inadequate treatment of HCV was specifically linked with relapses.

The pathomechanism of myelitis associated with HCV could be a direct virus infection. This is supported by autopsy studies of brain tissue showing infection of microglia and macrophages.\(^{15}\) However, pathogenesis could also be an indirect immune response. HCV can lead to several autoimmune disorders of the central and peripheral nervous system.\(^{16}\) In this case, a direct infection seems more plausible as we describe a complete normalization on MRI after eliminating the virus.

The description of localization in the dorsal and lateral parts of the spinal cord on MRI found in our patient has previously been reported in relation to vitamin B12 deficiency, HIV infection, and paraneoplastic antibodies.\(^ {10,17}\) In an HIV patient, acute demyelinating encephalomyelitis was described as the presenting symptom. In this patient, steroid pulse treatment resulted in changes on MRI and amelioration of the symptoms, not by antiviral treatment.\(^{18}\)

Other characteristic MRI findings on the transverse sequences with contrast help to discriminate different etiologies for LETM. A trident sign is seen in neurosarcoidosis due to dorsal-subpial and central canal enhancement.\(^{19}\) Other signs include a pancake-like pattern in compressive conditions,\(^ {20}\) shaggy- and ring-like enhancement in NMOSD,\(^ {21}\) and a flame-like pattern in intramedullary metastasis.\(^ {22}\) Other secondary etiologies involved in ATM should be considered especially inflammatory/autoimmune diseases, vascular, nutritional, and toxic causes.\(^ {23–25}\) A diagnostic algorithm has been suggested by the Transverse Myelitis Consortium Working Group,\(^ {26}\) to ensure a rapid and precise diagnosis and treatment of the increasing number of patients with conditions no longer considered to be idiopathic.

Despite the normalization according to the MRI and successful treatment of HCV, the physical symptoms only improved to a minor degree. This highlights the importance of testing and treating patients with HCV as suggested by the WHO.\(^ {27}\) In 2016, a majority of member states made a commitment to the elimination of viral hepatitis by 2030. A recent article noted that 80% of high-income countries were not on track to meet the HCV elimination target in 2030, and elimination was even less likely in low-income countries.\(^ {28}\) In Scandinavia, Sweden is the only country that has started a program targeting the more vulnerable parts of the population to address this problem.

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CONFLICTS OF INTERESTS

The authors declare that there are no conflicts of interests regarding the publication of this article.

AUTHOR CONTRIBUTION

All authors drafted and wrote the article and designed figures. SJ-F and TP scientifically reviewed the manuscript.

ETHICAL APPROVAL

Informed consent was obtained from the patient for publication of information.

DATA AVAILABILITY STATEMENT

The datasets generated or analyzed during the current study are available from the corresponding author on request.

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