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HCV AND GUILLIAN-BARRE SYNDROME- A RARE ASSOCIATION

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ABSTRACT

Case report: We report a case of thirty year old female, not a known case of any chronic illness, recently diagnosed to be having Chronic hepatitis C virus (HCV) infection, presented with acute onset of gradually progressive ascending flaccid paralysis of three days duration. Her HCV viral load was low 2645 I.U./ml and liver function tests were essentially normal. She was non-cirrhotic with normal Fibroscan score of 7 Kpa. At the time of admission, she was conscious, oriented, afebrile but was unable to move all four limbs on her own. Her Nerve conduction studies were suggestive of Guillain-Barré syndrome (GBS). She developed fever and vomiting within six hours of admission, along with features of autonomic dysfunction and involvement of respiratory muscles. Hence was urgently shifted in Intensive care unit (ICU) and was put on ventilatory support. She succumbed to her illness within few hours of stay in ICU, before treatment with Intravenous immunoglobulins or plasmapheresis could be started.

Conclusion: Our case report is an unusual case of GBS in a recently diagnosed young non-cirrhotic HCV patient who had a rapid catastrophic course and died within few days of diagnosis of HCV infection. There is limited case reports of GBS with HCV infection, hence should always be kept in differential diagnosis whenever patient presents with lower limb weakness. Early diagnosis and timely initiation of treatment is crucial to treat GBS.

Keywords: Chronic Hepatitis C, HCV RNA, Guillian- Barre syndrome, Polyneuropathy, Nerve conduction studies.

INTRODUCTION

Guillain–Barré syndrome (GBS) is an inflammatory disease of the Peripheral nervous system and is the most common cause of acute flaccid paralysis, with an annual global incidence of approximately 1–2 per 100,000 person- years (1). GBS occurs more frequently in males than in females and the incidence increases with age, although all age groups can be affected (1). Patients with GBS typically present with weakness and sensory signs in the legs that progress to the arms and cranial muscles, although the clinical presentation of the disease is heterogeneous and several distinct clinical variants exist. Diagnosis of GBS is based on the patient history and neurological, electrophysiological and cerebrospinal fluid (CSF) examinations (2-4). About 20% of patients with GBS develop respiratory failure and require mechanical ventilation. Cardiac arrhythmias and blood pressure instability can occur owing to involvement of the autonomic nervous system (5). This involvement of the autonomic nervous system contributes to

mortality, which is estimated at 3–10% for patients with GBS even with the best medical care available (6–8). GBS is thought to be caused by an aberrant immune response to infections that results in damage to peripheral nerves, although the pathogenesis is not fully understood. In a subgroup of patients with GBS, serum antibodies are found against gangliosides, which reside at high densities in the axolemma and other components of the peripheral nerves (9,10). Complement activation, infiltration of macrophages and oedema are typical characteristics of affected peripheral nerves and nerve roots in patients with GBS (9).

CASE REPORT

A thirty year old female, recently detected to be having Chronic HCV infection, presented with acute onset of gradually progressive ascending flaccid paralysis of three days duration. At the time of admission, she was conscious, oriented, afebrile but was unable to move all four limbs on her own. Initially to begin with, she complained of tingling, numbness, and weakness of his lower limbs for two days. The weakness progressed rapidly over the course of one day so that she was unable to move his lower limbs and ambulate. Over next two days, she also developed weakness, tingling, and numbness in the upper extremities. A neurological examination revealed normal muscle bulk and tone, but power was decreased in the upper extremities as well as in the lower extremities at hips, knees, ankles, and toes bilaterally. His deep tendon reflexes were diminished significantly. A sensory examination also revealed decreased light touch, pinprick, and temperature sensation from the feet to mid-calves as well as hands. Cranial nerve examination was normal and there was history of dysphagia, diplopia or dyspnea. Her General physical examination, Cardiovascular, Chest and per abdomen examination was normal. In view of her presentation and clinical examination, clinical diagnosis of acquired acute inflammatory demyelinating sensorimotor poly-neuropathy was made. The complete haemogram revealed hemoglobin of 10.6 g/dL, white blood cell count 21,300/L, microcytic hypochromic anemia with no malaria parasite. The liver function & renal function tests, International normalized ratio (INR), thyroid profile, blood sugar, autoimmune profile, Serum IgM HAV, Serum IgM HEV antibodies, HbsAg and HIV were all normal. She was non-cirrhotic and her Fibroscan score was also normal i.e. 7 Kpa. The results of a nerve conduction velocity revealed evidence of predominant motor polyneuropathy with prominent demyelinating features, including motor conduction block, low conduction velocity, and prolonged minimum F wave latency in the bilateral ulnar, median, peroneal, and tibial nerves. Lower limbs were involved more than the upper limb. She developed fever and vomiting within six hours of admission, along with features of autonomic dysfunction as evidenced by fluctuating blood pressure and pulse rate and involvement of respiratory muscles. Hence was urgently shifted in Intensive care unit (ICU) and put on ventilatory support. She developed refractory hyponatremia, refractory hypotension and before doing of Cerebrospinal fluid examination and starting on treatment with Intravenous immunoglobulins or plasmapheresis, succumbed to her illness within few hours of stay in ICU.

DISCUSSION

The common etiologies of demyelinating polyneuropathy include infections, drugs, toxins, and immune-mediated (11). About two- thirds of patients who develop GBS report symptoms of an infection in the 6 weeks preceding the onset of the condition

(12). These infections are thought to trigger the immune response that causes GBS. Six pathogens have been temporally associated with GBS in case–control studies: Campylobacter jejuni, cytomegalovirus, hepatitis E virus, Mycoplasma pneumoniae, Epstein–Barr virus and Zika virus (13,14,15). It has been suggested that other pathogens are linked to GBS on the basis of evidence from case series or studies, but their role in the pathogenesis of GBS is uncertain (16-21). To our best knowledge, till date, only seven cases of GBS associated with HCV infection have been reported so far (22-25). Peripheral neuropathy, the most common neurologic complication of HCV (26), is more prominent with HCV associated Mixed cryoglobulinemia (MC) where the most frequently described form is a symmetrical sensory-motor polyneuropathy with predominant sensory features (27). However, the presence of MC doesn't increase overall risk of developing a neuropathy (28) and the pathophysiology of neuropathy associated with HCV is not definitively known (27). It is worth to mention that GBS has also been reported in association with non-A, non-B hepatitis (29-31); perhaps these cases were due to HCV infection. In our patient, HCV viral load in low amount was present but rest viral screen including HIV, HbsAg, Serum IgM HAV and Serum IgM HEV were negative. Our patient had no exposure to any of the known toxins, drugs reported to cause immune-mediated chronic inflammatory demyelinating polyneuropathy when used for chronic hepatitis C treatment (32). Uremic neuropathy has a symmetric pattern and affects upper and lower limbs at the same time. The weakness in our patient was started first in lower limbs and then moved to involve upper limbs with respiratory muscle involvement which is not the pattern seen in uremic neuropathy. In our case, patient had a very rapid downhill course of four days only and succumbed to illness before initiation of plasmapheresis and intravenous immunoglobulins. We report an unusual case of GBS with a multiple association where we could not find any traditional predisposing factors associated with GBS. The limitation in our case was that we didn't got the time for CSF sample to prove albumino- cytologic dissociation. However, according to the recently proposed new diagnostic classification, GBS could be diagnosed by clinical characteristics and electrophysiological examinations, without the need of CSF examinations, and whether or not they disclose existing diagnostic criteria (33). Our Department is Model treatment centre under National Viral Hepatitis Control Program (NVHCP) and in last Eleven Years have treated more than twenty five thousand patients of Chronic Hepatitis C. This is the first case where GBS syndrome has been seen with HCV infection. Whether there is association between HCV infection and GBS or it is mere co-incidence, is matter of future research. It should be pondered that whether GBS could be added to the list of Extrahepatic manifestations of hepatitis C as well as HCV as an additional cause of GBS.

CONCLUSION

GBS is associated with both infective and non infective etiologies. It is usually preceded by acute gastrointestinal or respiratory infections. Our case report is an unusual case of GBS in a recently diagnosed young non-cirrhotic HCV patient who had a rapid catastrophic course and died within few days of diagnosis of HCV infection. There is limited case reports of GBS with HCV infection, hence should always be kept in differential diagnosis whenever patient presents with lower limb weakness.

REFERENCES

1. Sejvar, J. J., Baughman, A. L., Wise, M.

W. Population incidenc of
Guillain- Barré syndrome: a systematic rev analysis. Neuroepidemiology 36,
123–133 (2011).
2. Asbury, A. K., Arnason, B. G. W., Karp, H. R. & McFarlin, D. E. Criteria for diagnosis of Guillain- Barré syndrome. Ann. Neurol. 3, 565–566 (1978).
3. Asbury, A. K. & Cornblath, D. R. Assessment of current diagnostic criteria for Guillain- Barré syndrome. Ann. Neurol. 27, S21–S24 (1990).
4. Sejvar, J. J. et al. Guillain- Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 29, 599–612 (2011).
5. Willison, H. J., Jacobs, B. C. & van Doorn, P. A. Guillain- Barré syndrome. Lancet 388, 717–727 (2016).
6. Van den Berg, B., Bunschoten, C., van Doorn, P. A. & Jacobs, B. C. Mortality in Guillain- Barré syndrome. Neurology 80, 1650–1654 (2013).
7. Dominguez- Moreno, R. et al. Mortalidad asociada al diagnostico de sindrome de Guillain- Barré en adultos ingresados en instituciones del sistema sanitario Mexicano [mortality associated with a diagnosis of Guillain- Barré syndrome in adults of Mexican health institutions]. Rev. Neurol. 58, 4–10 (2014).
8. Dourado, M. E., Felix, R. H., da Silva, W. K., Queiroz, J. W. & Jeronimo, S. M. Clinical characteristics of Guillain- Barré syndrome in a tropical country: a Brazilian experience. Acta Neurol. Scand. 125, 47–53 (2012).
9. Yuki, N. Infectious origins of, and molecular mimicry in, Guillain- Barre and Fisher syndromes. Lancet Infect. Dis. 1, 29–37 (2001).
10. Yoshikawa, K. et al. Varied antibody reactivities and clinical relevance in anti-GQ1b antibody- related diseases. Neurol. Neuroimmunol. Neuroinflamm. 5, e501 (2018).
11. Stübgen JP. Interferon alpha and neuromuscular disorders. J Neuroimmunol 2009; 207:3-17.
12. Doets, A. Y. et al. Regional variation of Guillain- Barré syndrome. Brain 141, 2866–2877 (2018).
13. Jacobs, B. C. et al. The spectrum of antecedent infections in Guillain- Barré syndrome: a case- control study. Neurology 51, 1110–1115 (1998).
14. Cao- Lormeau, V. M. et al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case- control study. Lancet 387, 1531–1539 (2016).
15. Van den Berg, B. et al. Guillain- Barré syndrome associated with preceding hepatitis E virus infection. Neurology 82, 491–497 (2014).
16. Vellozzi, C., Iqbal, S. & Broder, K. Guillain- Barré syndrome, influenza, and influenza vaccination: the epidemiologic evidence. Clin. Infect. Dis. 58, 1149–1155 (2014).
17. Thornton, C. A., Latif, A. S. & Emmanuel, J. C. Guillain- Barré syndrome associated with human immunodeficiency virus infection in Zimbabwe. Neurology 41, 812–815 (1991).
18. Islam, B. et al. Guillain- Barré syndrome following varicella- zoster virus infection. Eur. J. Clin. Microbiol. Infect. Dis. 37, 511–518 (2018).
19. Carod- Artal, F. J., Wichmann, O., Farrar, J. & Gascon, J. Neurological complications of dengue virus infection. Lancet Neurol. 12, 906–919 (2013).
20. Wielanek, A. C., Monredon, J. D., Amrani, M. E., Roger, J. C. & Serveaux, J. P. Guillain- Barré syndrome complicating a Chikungunya virus infection. Neurology 69, 2105–2107 (2007).
21. Cornblath, D. R., McArthur, J. C., Kennedy, P. G., Witte, A. S. & Griffin, J. W. Inflammatory

22. De Klippel N, Hautekeete ML, De Keyser J, Ebinger G. Guillain-Barré syndrome as the presenting manifestation of hepatitis C infection. Neurology. 1993;43(10):2143.
23. Zylberberg H, Hagège H, Roualdes B, Meyrignac C, Chousterman M. Guillain-Barré syndrome in a patient with chronic active hepatitis C. Gastroenterol Clin Biol. 1995;19(5):551.
24. Lacaille F, Zylberberg H, Hagège H, Roualdès B, Meyrignac C, Chousterman M, et al. Hepatitis C associated with Guillain-Barré syndrome. Liver. 1998; 18(1):49–51.
25. Massengo SA, Furby A, Stanescu C, Charasse C, Madigand M. Hepatitis C with cryoglobulinemia associated with Guillain-Barre syndromePresse Med. 2001;30(15):739.
26. Mathew S, Faheem M, Ibrahim SM, Iqbal W, Rauff B, Fatima K, et al. Hepatitis C virus and neurological damage. World J Hepatol. 2016;8(12):545–56.
27. Benstead TJ, Chalk CH, Parks NE. Treatment for cryoglobulinemic and noncryoglobulinemic peripheral neuropathy associated with hepatitis C virus infection. Cochrane Database Syst Rev. 2014;(12):CD010404.
28. Santoro L, Manganelli F, Briani C, Giannini F, Benedetti L, Vitelli E, et al. Prevalence and characteristics of peripheral neuropathy in hepatitis C virus population. J Neurol Neurosurg Psychiatry. 2006;77(5):626–9.
29. Macleod WN. Sporadic non-a, non-B hepatitis and Epstein-Barr hepatitis associated with the Guillain-Barré syndrome. Arch Neurol. 1987;44(4):438–42.
30. Tabor E. Guillain-Barré syndrome and other neurologic syndromes in hepatitis A, B, and non-A, non-B. J Med Virol. 1987;21(3):207–16.
31. Gutzler F, Andrassy K, Kommerell B, Krieger D. Guillain-Barré polyneuropathy in Wegener's granulomatosis with pulmonary-renal syndrome. Dtsch Med Wochenschr. 1990;115(10):372–7.
32. Marzo ME, Tintoré M, Fabregues O, Montalbán X, Codina A. Chronic inflammatory demyelinating polyneuropathy during treatment with interferon alpha. J Neurol Neurosurg Psychiatry1998;65:604.
33. Wakerley BR, Uncini A, Yuki N. GBS classification group, GBS classification group. Guillain-Barré and miller fisher syndromes--new diagnostic classification. Nat Rev Neurol. 2014;10(9):537–44.