A 52-year-old man developed back pain 4 months ago and the prick-like pain spread to the entire back. One month later, left foot numbness and foot drop appeared. The same symptoms extended to the right foot, and constipation and nocturia additionally developed. Twenty days before admission to the hospital, right hand numbness and pain in the back and both feet worsened, causing sleeplessness. The administration of analgesics (clonazepam: 2 mg, tramadol: 250 mg, amitriptyline: 10 mg, alprazolam: 0.4 mg, pentazocine injection at 15 mg per day) and a rescue dose of morphine did not improve his pain. He had a few years’ history of diabetes mellitus, which was well-controlled by dietary therapy, and had drunk approximately 55 g of alcohol per day over the past 30 years; he stopped drinking at the onset of symptoms.

A neurological examination at admittance revealed distal dominant muscle weakness of both lower extremities, especially of the tibialis anterior (0 in MMT), hypoesthesia below both knees, allodynia in both planta, and loss of lower limb reflexes. He was unable to stand or walk due to painful paraplegia. His blood count was normal. Blood chemistry revealed mild liver damage. Hemoglobin A1c was 6.5% (ref-
Table. The Results of Nerve Conduction Studies.

| MOTOR NERVE | CMAP(mV) | Latency(msec) | MCV(m/sec) | F-latency (msec) |
|-------------|----------|---------------|------------|-----------------|
|             | Distal Proximal | Distal Proximal |            |                 |
| rt. Median  | 5.4 (>5.0) | 4.4 | 3.9 (<4.0) | 7.7 | 58.7 (>55.0) | 27.2 |
| rt. Ulnar   | 9.0 (>5.0) | 3.2 | 2.6 (<3.2) | 7.6 | 49.5 (>55.0) | 26.5 |
| rt. Tibial  | not evoked |             |            |                 |
| lt. Median  | 8.1 (>5.0) | 7.6 | 3.5 (<4.0) | 7.3 | 55.3 (>55.0) | 27.4 |
| lt. Ulnar   | 8.9 (>5.0) | 6.1 | 2.7 (<3.2) | 6.9 | 55.4 (>55.0) | 26.1 |
| lt. Tibial  | 0.06 (>7.0) | 0.05 | 8.4 (<5.7) | 17.9 | 40.6 (>40.0) | not evoked |

| SENSORY NERVE | SNAP(μV) | Latency(msec) | SCV(m/sec) |
|---------------|----------|---------------|------------|
|               | Distal Proximal | Distal Proximal | Distal Proximal |
| rt. Median    | 10.4 (>14.0) | 5.5 | 2.9 (<2.9) | 6.7 | 52.4 (>55.0) | 60.5 |
| rt. Ulnar     | 12.3 (>10.0) | 6.5 | 2.5 (<2.4) | 6.4 | 55.6 (>55.0) | 59.3 |
| rt. Sural     | 8.1 (>8.0) | 1.9 (<3.6) | 1.9 (<3.6) | 53.8 (>40.0) |
| lt. Median    | 5.5 (>14.0) | 2.3 | 2.9 (<2.9) | 6.5 | 55.4 (>55.0) | 54.9 |
| lt. Ulnar     | 24.1 (>10.0) | 8.7 | 2.1 (<2.4) | 5.9 | 65.4 (>55.0) | 61.2 |
| lt. Sural     | 4.7 (>14.0) | 2.6 (<3.6) | 2.6 (<3.6) | 46.9 (>40.0) |

Figure 1. Hematoxylin and Eosin staining (A) and Klüver-Barrera stained (B) images of the sural nerve. Inflammatory cells were distributed in the circumference of the nerve bundle with swelling of the perineurium. Inflammatory cell infiltration in the nerve bundle and loss of myelinated nerve fibers were mild.

Discussion

Perineuritis was first reported by Asbury in 1972 as distally dominant recurrent painful neuropathy characterized by
oral or intravenous prednisolone, intravenous immunoglobulin administration, and plasmapheresis in 12 (58 percent) patients with perineuritis were reported as having improved by immunosuppressive therapy including prednisolone, intravenous immunoglobulin administration, and plasmapheresis. Eric reported on the efficacy of immunosuppressive therapy for the treatment of perineuritis with diabetes mellitus. In this case, single oral prednisolone administration was included because the symptoms were aggravated after temperance in our patient. Some cases of diabetic neuropathy can lead to the subacute onset of painful neuropathy, such as treatment-induced neuropathy of diabetes due to the rapid correction of hyperglycemia (12), acute painful diabetic neuropathy due to the continuation of hyperglycemia (13) or radiculoplexus neuropathy caused by microvasculitis (14) mimicking perineuritis symptoms. Perineuritis is difficult to diagnose by electrophysiological examinations because both axonopathy and demyelination may be observed (7). High levels of protein in the cerebrospinal fluid are not specific among these diseases (7). Perineuritis complicated by diabetes mellitus develops irrespective of blood sugar control (7). Although perineuritis was suggested to be related to diabetes mellitus in previous reports (7), its pathogenesis due to diabetes complications has not been clarified because of the lack of pathologically specific findings. Therefore, a nerve biopsy examination should be performed for diabetes mellitus patients who develop painful neuropathy with no history of rapid correction of hyperglycemia or continuation of hyperglycemia because the treatment approach for perineuritis with diabetes mellitus differs from that for diabetic neuropathy.

Although there is no standard treatment, Asbury first empirically reported on the efficacy of immunosuppressive therapy for the treatment of perineuritis. Eric reported that 7 out of 12 (58 percent) patients with perineuritis saw their condition improved by immunosuppressive therapy including oral or intravenous prednisolone, intravenous immunoglobulin, plasmapheresis, immunosuppressant and total lymphoid irradiation (7). In our case, single oral prednisolone administration was not sufficient for relief. Although there was no exacerbation of blood glucose control, no improvement was observed. Therefore, we conducted plasmapheresis and intravenous immunoglobulin administration simultaneously with oral prednisolone. These combined treatments were effective, and the patient had almost no pain or muscle weakness when low doses of analgesics were administered (pregabalin: 150 mg per day and clonazepam: 1 mg per day).

At present, the patient is receiving oral prednisolone according to the standard treatment for vasculitis syndrome. We intend to taper oral prednisolone as much as possible. If recurrence or side effects of prednisolone appear, we will consider the addition of an immunosuppressant. A trial for combined immunotherapy may be useful for establishing a standard therapy for perineuritis with diabetic mellitus.

The authors state that they have no Conflict of Interest (COI).

References

1. Asbury AK, Picard EH, Baringer JR. Sensory perineuritis. Arch Neurol 26: 302-312, 1972.
2. Koike H, Hashimoto R, Tomita M, et al. The wide range of clinical manifestations in leprous neuropathy. Intern Med 50: 2223-2226, 2011.
3. Konishi T, Saida K, Ohnishi A, Nishitani H. Perineuritis in mononeuritis multiplex with cryoglobulinemia. Muscle Nerve 5: 173-177, 1982.
4. Tomita M, Koike H, Kawagashira Y, et al. Clinicopathological features of neuropathy associated with lymphoma. Brain 136: 2563-2578, 2013.
5. Yamada M, Owada K, Eishi Y, Kato A, Yokota T, Furukawa T. Sensory perineuritis and non-Hodgkin’s T-cell lymphoma. Eur Neurol 34: 298-299, 1994.
6. Furusho K, Watanabe M, Ohkoshi N, Tamaoka A, Shojo S. A case of sensory perineuritis with Bowen disease. Rinsho Shinkeigaku 42: 527-529, 2002 (in Japanese, Abstract in English).
7. Sorenson EJ, Sima AA, Blaivas M, Sawchuk K, Wald JJ. Clinical features of perineuritis. Muscle Nerve 20: 1153-1157, 1997.
8. Chad DA, Smith TW, DeGirolami U, Hammer K. Perineuritis and ulcerative colitis. Neurology 36: 1377-1379, 1986.
9. Bourque CN, Anderson BA, del Campo CM, Sima AA. Sensorimotor perineuritis-an autoimmune disease? Can J Neurol Sci 12: 129-133, 1985.
10. Lee SS, Yoon TY. Sensory perineuritis presented as a mononeuritis multiplex associated with livedo vasculitis. Clin Neurol Neurosurg 103: 56-58, 2001.
11. Koike H, Iijima M, Sugiura M, et al. Alcoholic neuropathy is clinicopathologically distinct from thiamine-deficiency neuropathy. Ann Neurol 54: 19-29, 2003.
12. Gibbons CH, Freeman R. Treatment-induced neuropathy of diabetes: an acute, iatrogenic complication of diabetes. Brain 138: 43-52, 2015.
13. Thomas PK. Classification, differential diagnosis, and staging of diabetic peripheral neuropathy. Diabetes 46: S54-S57, 1997.
14. Dyck PJ, Norell JE, Dyck PJ. Microvasculitis and ischemia in diabetic lumbosacral radiculoplexus neuropathy. Neurology 53: 2113-2121, 1999.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).