

**Supplementary Table 1** Clinical features of 20 patients in current cohort

| No | Age (Y) /Sex | Period of N <sub>2</sub> O abuse | Complaint                                                                      | Motor                                                                                        | Sensory                                                                                           | Ataxia | Other symptoms                  | Vitamin B12 (pg/ml) | Hb (g/L) | MCV (fl) | HCY (μmol/L) | Spinal cord MRI                          | EMG                             |
|----|--------------|----------------------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|--------|---------------------------------|---------------------|----------|----------|--------------|------------------------------------------|---------------------------------|
| 1  | 16/F         | 1M                               | Weakness and numbness of four limbs and unsteady walk for 4 days               | Four limbs (4/5)                                                                             | Decreased pinprick sensation                                                                      | No     | No                              | 147                 | 104      | 104.3    | 3.4          | C2-C6 (SCD)                              | Demyelination                   |
| 2  | 18/F         | 1Y                               | Progressive weakness and numbness of four limbs and unsteady walk for 8 months | Distal parts of four limbs (5-/5)                                                            | Decreased pinprick sensation below the elbows,increased pinprick sensation of dorsum feet         | Yes    | No                              | ↑                   | 151      | 84.0     | /            | /                                        | Demyelination                   |
| 3  | 19/F         | 0.5M                             | Numbness of four limbs for half a month                                        | Distal part of lower limbs (4/5),hyporeflexia                                                | Decreased pinprick sensation below the ankles and wrists, decreased deep sensation of lower limbs | Yes    | No                              | 161                 | 83       | 67.9     | 20.3         | C3-C6 (SCD)                              | Axonal damage and demyelination |
| 4  | 20/F         | 4M                               | Numbness of four limbs for 2 months, weakness of four limbs for 4 days         | Four limbs (4/5),absent tendon reflexes                                                      | N                                                                                                 | No     | No                              | N                   | N        | N        | 43           | C2-C7 (SCD)                              | Axonal damage and demyelination |
| 5  | 22/F         | 4M                               | Weakness of lower limbs and unsteady walk for 1 week                           | Lower limbs (4/5)                                                                            | Abnormal deep sensory                                                                             | Yes    | No                              | /                   | 98       | 112.2    | 24.7         | Abnormal signal in the whole spinal cord | /                               |
| 6  | 22/F         | 3D                               | Numbness and weakness of upper limbs for 10 days                               | Distal parts of four limbs (5-/5),hypomyotonia, hyporeflexia, postural tremor of upper limbs | Decreased pinprick sensation below the elbows,decreased motor sensation of toes                   | Yes    | Irritability, bad sleep quality | /                   | 120      | 92.2     | 127.2        | N                                        | N                               |
| 7  | 22/F         | 1M                               | Weakness and numbness of four limbs for 1 week                                 | Distal parts of lower limbs(4/5),hyporeflexia                                                | Decreased pinprick sensation below the elbows,decreased motor sensation of toes                   | Yes    | No                              | 136                 | 118      | 98.8     | 16.8         | C1-T2                                    | Axonal damage and demyelination |

| No | Age<br>(Y)<br>/Sex | Period | Complaint                                                                 | Motor                                                                             | Sensory                                                                                                                | Ataxia | Other symptoms                                | Vitamin<br>B12<br>(pg/ml) | Hb<br>(g/L) | MCV<br>(fl) | HCY<br>(μmol/L) | Spinal cord<br>MRI | EMG                             |
|----|--------------------|--------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|--------|-----------------------------------------------|---------------------------|-------------|-------------|-----------------|--------------------|---------------------------------|
| 8  | 24/F               | 2M     | Weakness and numbness of four limbs and unsteady walk for 1 week          | Four limbs(upper:5-/5,lower:3/5), hypomyotonia                                    | Decreased pinprick sensation                                                                                           | No     | No                                            | 319                       | 140         | 98.1        | 20.6            | C2-C6 (SCD)        | Axonal damage and demyelination |
| 9  | 24/F               | 1Y     | Weakness of lower limbs for half of year                                  | Weakness of lower limbs(4/5),hyporeflexia                                         | Paroxysmal numbness of distal parts of all limbs, but sensation examination is normal                                  | No     | No                                            | 91                        | 126         | 102.8       | 66.17           | N                  | Axonal damage and demyelination |
| 10 | 17/M               | 3M     | Progressive weakness and numbness of four limbs                           | Weakness of four limbs(4/5), hypomyotonia, hyporeflexia                           | Decreased pinprick sensation below the elbows and knee joints                                                          | Yes    | No                                            | /                         | 149         | 92.8        | 91.3            | C2-C5 (SCD)        | Demyelination                   |
| 11 | 21/M               | 2Y     | Weakness and numbness of lower limbs for 1 week                           | Decreased muscle strength of dorsal stretch of feet                               | Decreased deep sensation                                                                                               | Yes    | No                                            | 92.31                     | 157         | 90.2        | 102             | C3-C6 (SCD)        | /                               |
| 12 | 22/M               | 6M     | Numbness of four limbs for 1 week                                         | Four limbs(5-/5),hypotonia, hyporeflexia of lower limbs                           | Decreased pinprick sensation of distal parts of four limbs,decreased deep sensation of lower limbs                     | Yes    | Hallucination                                 | /                         | 138         | 102.7       | 35.72           | C1-C7 (SCD)        | Axonal damage                   |
| 13 | 23/M               | 6M     | Weakness of lower limbs for 10 days and numbness of four limbs for 2 days | Four limbs(5-/5),decreased muscle strength of dorsal stretch of feet,hyporeflexia | Decreased touch sensation and hyperalgesia of distal parts of four limbs,decreased deep sensation of lower extremities | No     | No                                            | >2000                     | 134         | 103.6       | 7.92            | C2-C6 (SCD)        | Axonal damage and demyelination |
| 14 | 24/M               | 2M     | Weakness of lower limbs for 2 months, worse for 2 days                    | Lower limbs(3/5), bilateral babinski signs (+)                                    | N                                                                                                                      | No     | No                                            | 224                       | 133         | 94.6        | 24.4            | C2-C7 (SCD)        | Demyelination                   |
| 15 | 27/M               | 3M     | Weakness and numbness of four limbs for 3 months                          | Hyperreflexia of lower limbs                                                      | Decreased pinprick sensation of distal parts of four limbs                                                             | No     | Root pain,dyspnea,palpitation,impaired memory | 975                       | 154         | 97.2        | 64.65           | N                  | Axonal damage and demyelination |
| 16 | 28/M               | 1Y     | Parosymal numbness of four limbs for 2 months                             | N                                                                                 | Decreased pinprick sensation                                                                                           | No     | No                                            | /                         | 150         | 90.2        | 33.9            | C2-C6 (SCD)        | Axonal damage and demyelination |

| No | Age<br>(Y)<br>/Sex | Period | Complaint                                           | Motor                                        | Sensory                                                     | Ataxia | Other symptoms                                          | Vitamin<br>B12<br>(pg/ml) | Hb<br>(g/L) | MCV<br>(fl) | HCY<br>(μmol/L) | Spinal cord<br>MRI                          | EMG                             |
|----|--------------------|--------|-----------------------------------------------------|----------------------------------------------|-------------------------------------------------------------|--------|---------------------------------------------------------|---------------------------|-------------|-------------|-----------------|---------------------------------------------|---------------------------------|
| 17 | 29/M               | 6M     | Numbness of four limbs for 1 months                 | Hyporeflexia of upper limbs,left hoffman(+)  | Decreased pinprick sensation from C3-T6                     | No     | No                                                      | 978                       | 148         | 91.8        | /               | C2-C5 (SCD)                                 | N                               |
| 18 | 31/M               | 6M     | Weakness and numbness of the whole body for 2 weeks | Four limbs (5-/5),unsteady walk,hyporeflexia | Decreased pinprick sensory                                  | Yes    | Bowel and bladder dysfunction                           | 1191                      | 139         | 95.8        | /               | Protrusion of cervical intervertebra I disc | Axonal damage and demyelination |
| 19 | 32/M               | 2M     | Numbness of four limbs for 3 days                   | Lower limbs(4/5)                             | Decreased pain sensation below groin and below wrist joints | Yes    | No                                                      | /                         | 141         | 98.2        | 68.2            | C2-C5 (SCD)                                 | Axonal damage                   |
| 20 | 35/M               | 1Y     | Numbness of left leg for 2 days                     | Amyotrophy of dorsum of left foot            | Decreased pinprick and deep sensation                       | Yes    | Artery thrombosis in lower limbs,aorta abdominalis,pain | /                         | 137         | 98.8        | /               | C2-Th7 (SCD)                                | Axonal damage and demyelination |

Muscle strength assessments according to UK Medical Research Council (MRC);Motor: including MBC, muscle tone and tendon reflex;Hb:hemoglobin;MCV:Mean Corpuscular Volume;HCY:homocysteine;;EMG:Electromyography;/:unknown; N:normal; ↑ :increase;Y:years;M;month;D:day;SCD:Subacute combined degeneration of spinal cord;IVIg:intravenous immunoglobulin;Normal range: vitamin B12:197–771 pg/mL; Hb: female >110 g/L; male >120 g/L; MCV:<100 fl; HCY:5–13.9 μmol/L.

**Supplementary Table 2** Treatment and prognosis of 20 patients in current cohort

| No. | In hospital treatment                                                   | Symptoms and physical signs when discharged       | Post-discharge treatment                      | Time of complete remission after discharge | Remarks                     |
|-----|-------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------|--------------------------------------------|-----------------------------|
| 1   | Cobamamide 0.5mg/D*17D, glucocorticoid                                  | Normal muscle strength, improved sensation        | Mecobalamine 1.5mg/D*3M                       | 3M                                         | Relapse of N <sub>2</sub> O |
| 2   | Mecobalamine 2mg/D*16D, IVIG                                            | Improved muscle strength of lower limbs           | Mecobalamine 1.5mg/D*3M                       | 3M                                         |                             |
| 3   | Cobamamide 0.5mg/D*17D, mecobalamine 0.5mg/D*9D                         | Improved sensation                                | Mecobalamine 1.5mg/D                          | Loss to follow-up                          |                             |
| 4   | Mecobalamine 0.5mg/D*10D, glucocorticoid                                | Improved muscle strength of four limbs            | Mecobalamine 0.5mg/D                          | Loss to follow-up                          |                             |
| 5   | Vitamin B12 1.0mg/D*14D                                                 | Improved muscle strength of lower limbs           | Cobamamide 2.25mg/D*1M                        | 0.5M                                       |                             |
| 6   | Mecobalamine 2mg/D*7D                                                   | Improved sensation of upper limbs, normal sleep   | Mecobalamine 1.5mg/D*3M                       | 3M                                         |                             |
| 7   | Mecobalamine 0.5mg/D*16D                                                | Improved muscle strength                          | Mecobalamine 1.5mg/D*1M                       | 1M                                         |                             |
| 8   | Cobamamide 0.5mg/D*14D, glucocorticoid                                  | Improved muscle strength of four limbs            | Mecobalamine 1.5mg/D*2M                       | 2M                                         |                             |
| 9   | Mecobalamine 2mg/D*7D, glucocorticoid                                   | Improved muscle strength of four limbs            | No vitamin                                    | 3M                                         |                             |
| 10  | Mecobalamine 2mg/D*14D, mecobalamine 1mg/D*14D                          | Improved muscle strength of four limbs,normal EMG | Mecobalamine 1.5mg/D*3M                       | 3M                                         |                             |
| 11  | Vitamin B12 1.0mg/D*1M                                                  | Improved muscle strength of lower limbs           | Vitamin B12 1mg/D*10D, cobamamide 2.25mg/D*2M | 2M                                         |                             |
| 12  | Mecobalamine 0.5mg/D*8D, hyperbaric oxygen                              | Improved sensation                                | Mecobalamine 1.5mg/D*2M, hyperbaric oxygen    | 0.5M                                       | Relapse of N <sub>2</sub> O |
| 13  | Mecobalamine 0.5mg/D*7D, cobamamide 1.5mg/D*7D, hyperbaric oxygen, IVIG | Improved muscle strength and sensation            | Mecobalamine 1.5mg/D*3M                       | 3M                                         |                             |
| 14  | Cobamamide 0.5mg/D*8D                                                   | No obvious improvement                            | Mecobalamine 1.5mg/D*2M                       | 2M                                         |                             |
| 15  | Mecobalamine 1mg/D*8D, hyperbaric oxygen                                | Improved muscle strength and sensation            | Mecobalamine 1.5mg/D*5M                       | 5M                                         | Relapse of N <sub>2</sub> O |
| 16  | Cobamamide 0.5mg/D*4D                                                   | No improvement                                    | Mecobalamine 1.5mg/D*1M                       | 1M                                         |                             |
| 17  | Cobamamide 0.5mg/D*15D, glucocorticoid                                  | No obvious improvement                            | Mecobalamine 1.5mg/D*0.5M                     | 0.5M                                       |                             |
| 18  | Cobamamide 0.5mg/D*10D, hyperbaric oxygen                               | Improved muscle strength                          | Mecobalamine 1.5mg/D*3.5M                     | 3.5M                                       |                             |
| 19  | Cobamamide 0.5mg/D*6D, hyperbaric oxygen                                | Exacerbate numbness                               | Mecobalamine 1.5mg/D*6M                       | Walking slowly, numb toes, memory loss*    |                             |
| 20  | Vitamin B12 1.0mg/D*3D, mecobalamine 0.5mg/D*13D                        | Improved sensation                                | Mecobalamine 1.5mg/D                          | Loss to follow-up                          |                             |

Only the dosage of vitamin B12 is listed because vitamin B12 is the most important treatment for the patients ; M:month;D:day;IVIG:intravenous immunoglobulin; \*: the patient still had some symptoms 16 months after discharge

**Supplementary Table 3 Clinical data of 99 patients reported previously**

| No. | Age/<br>Sex | Clinical manifestation                                                                                   | Laboratory test                      | Spinal cord<br>imaging | EMG   | Treatment             | Prognosis   | Citation               |
|-----|-------------|----------------------------------------------------------------------------------------------------------|--------------------------------------|------------------------|-------|-----------------------|-------------|------------------------|
| 1   | 28/M        | Paresthesia, weakness, decreased deep sensation                                                          | VitB12 ↓, HCY ↑, Hb, MCV: N, MMA ↑   | C4-C6                  | A     | VitB12, IVIG          | Improvement | Algahtani et al.2020   |
| 2   | 22/M        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction                    | VitB12: N, HCY ↑, Hb ↓, MCV ↑, MMA ↑ | C1-C6                  | /     | VitB12                | Improvement | Al-Sadawi et al.2018   |
| 3   | 24/M        | Paresthesia, decreased deep sensation, involuntary movement, impaired cognition, pain                    | VitB12, Hb, MCV: N, HCY ↑, MMA ↑     | /                      | /     | VitB12                | Lost        | Alt et al.2011         |
| 4   | 29/F        | Paresthesia, weakness, decreased deep sensation, ataxia                                                  | VitB12 ↓, Hb ↓, MCV: N, MMA ↑        | Cervical and thoracic  | /     | VitB12                | Lost        | Anderson et al.2018    |
| 5   | 60/M        | Ataxia, psychiatric symptoms                                                                             | VitB12 ↓, HCY ↑, MMA ↑               | C3-C5                  | /     | VitB12                | Improvement | Anderson et al.2015    |
| 6   | 25/M        | Paresthesia, decreased deep sensation, ataxia, lhermitte symptom                                         | VitB12: N, HCY ↑, MMA ↑              | C1-C6                  | /     | VitB12                | Improvement | Antezana et al.2015    |
| 7   | 20/M        | Paresthesia, weakness, decreased deep sensation                                                          | VitB12 ↓, MCV ↑                      | C2-C4                  | /     | VitB12                | Improvement | Antonucci et al.2018   |
| 8   | 21/M        | Paresthesia, decreased deep sensation, ataxia                                                            | VitB12: N, HCY ↑                     | C2-C7                  | /     | VitB12                | Improvement | Arshi et al.2014       |
| 9   | 27/F        | Paresthesia, weakness, decreased deep sensation, ataxia                                                  | VitB12: N, HCY ↑                     | C2-C6                  | /     | VitB12                | Improvement | Brosset et al.2020     |
| 10  | 31/M        | Paresthesia, weakness, decreased deep sensation                                                          | VitB12: N, MMA ↑                     | C1-C6                  | /     | VitB12, steroid       | Improvement | Buizert et al.2017     |
| 11  | 23/M        | Decreased deep sensation, ataxia                                                                         | VitB12, Hb, MCV: N                   | C1-C6                  | N     | VitB12, methionine    | Improvement | Butzkueven et al.2000  |
| 12  | 42/F        | Paresthesia, decreased deep sensation, ataxia, impaired cognition, pain                                  | VitB12 ↓, HCY ↑, Hb, MCV: N, MMA ↑   | C4-C5                  | /     | VitB12                | Improvement | Campdesuner et al.2020 |
| 13  | 20/F        | Weakness, decreased deep sensation, psychiatric symptoms, thrombosis                                     | VitB12 ↓, Hb ↓, MCV: N               | Abnormal               | /     | VitB12, methionine    | Improvement | Cartner et al.2007     |
| 14  | 20/F        | Paresthesia, decreased deep sensation, involuntary movement                                              | Hb: N, MCV: N                        | C1-C6                  | A & D | VitB12                | Improvement | Chen et al.2016        |
| 15  | Na/F        | Paresthesia, weakness, decreased deep sensation, ataxia                                                  | VitB12 ↓                             | C2-C5                  | /     | VitB12                | /           | Cheng et al.2013       |
| 16  | 29/F        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction, hyperpigmentation | VitB12 ↓, HCY ↑, Hb ↓, MCV: N        | /                      | /     | VitB12                | Improvement | Chiang et al.2013      |
| 17  | 24/M        | Paresthesia, decreased deep sensation, ataxia, bowel or bladder dysfunction                              | VitB12, Hb: N, HCY ↑, MCV ↑          | C1-C7                  | D     | VitB12                | Improvement | Choi et al.2019        |
| 18  | 22/F        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction                    | VitB12 ↓, HCY ↑, Hb, MCV: N          | C3-C5                  | A     | VitB12                | Improvement | Choi et al.2019        |
| 19  | 37/M        | Paresthesia, decreased deep sensation, ataxia                                                            | VitB12, Hb: N, HCY ↑, MCV ↑, MMA ↑   | C3-C5                  | /     | VitB12                | Remain      | Chomin et al.2018      |
| 20  | 24/M        | Paresthesia, ataxia                                                                                      | VitB12, Hb, MCV: N, HCY ↑            | C2-C6                  | /     | VitB12                | Improvement | Demas et al.2020       |
| 21  | 31/M        | Paresthesia, weakness, decreased deep sensation, ataxia, involuntary movement                            | VitB12 ↓, HCY ↑, Hb, MCV: N          | Cervical and thoracic  | /     | VitB12                | Improvement | Diamond et al.2004     |
| 22  | 22/M        | Paresthesia, weakness, decreased deep sensation, bowel or bladder dysfunction                            | VitB12 ↓, HCY ↑, Hb, MCV: N          | C1-C6                  | A & D | VitB12                | Improvement | Dong et al.2019        |
| 23  | 20/F        | Paresthesia, weakness, decreased deep sensation, pain                                                    | VitB12 ↓, Hb, MCV: N, MMA ↑          | Abnormal               | D     | VitB12, steroid, IVIG | Improvement | Duque et al.2015       |
| 24  | 27/F        | Paresthesia, weakness, decreased deep sensation, ataxia                                                  | VitB12 ↓, HCY ↑, Hb ↓, MCV ↑, MMA ↑  | /                      | /     | VitB12                | Improvement | Edigin et al.2019      |

| No. | Age/<br>Sex | Clinical manifestation                                                                                       | Laboratory test                        | Spinal cord<br>imaging   | EMG          | Treatment          | Prognosis   | Citation                |
|-----|-------------|--------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------|--------------|--------------------|-------------|-------------------------|
| 25  | 24/F        | Ataxia,pain,hyperpigmentation                                                                                | VitB12 ↓ ,HCY ↑ ,Hb:N,MCV<br>↑ ,MMA ↑  | C2-C7                    | /            | VitB12             | /           | Egan et<br>al.2018      |
| 26  | 30/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia                                                      | VitB12:N,MMA ↑                         | C1-C6                    | /            | VitB12             | Improvement | Ernst et<br>al.2015     |
| 27  | 17/F        | Paresthesia,weakness,decreased<br>deep senstaion,hyperpigmentation                                           | VitB12 ↓ ,HCY ↑ ,Hb<br>↓ ,MCV:N        | C2-C5                    | A&D          | VitB12             | Improvement | Fang et<br>al.2020      |
| 28  | 19/F        | Paresthesia,weakness,decreased<br>deep senstaion,hyperpigmentation                                           | VitB12 ↓ ,HCY ↑ ,Hb<br>↓ ,MCV:N        | C2-C5                    | A&D          | VitB12             | Improvement | Fang et<br>al.2020      |
| 29  | 23/M        | Paresthesia,weakness,decreased<br>deep senstaion,hyperpigmentation                                           | VitB12 ↓ ,HCY ↑ ,Hb ↓ ,MCV<br>↑        | N                        | A            | VitB12             | Improvement | Fang et<br>al.2020      |
| 30  | 20/F        | Paresthesia,hyperpigmentation                                                                                | VitB12 ↓ ,HCY ↑ Hb,MCV:N               | N                        | D            | VitB12             | Improvement | Fang et<br>al.2020      |
| 31  | 27/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia,pain                                                 | VitB12 ↓ ,HCY ↑ ,Hb,MCV:N              | Cervical and<br>thoracic | /            | VitB12             | Improvement | Fernandez et<br>al.2017 |
| 32  | 22/F        | Paresthesia,decreased deep<br>senstaion,ataxia                                                               | VitB12:N,HCY ↑                         | C2-C6                    | D            | VitB12             | Improvement | Fong et<br>al.2016      |
| 33  | 38/M        | Paresthesia,decreased deep<br>senstaion,ataxia,psychiatric<br>symptoms                                       | VitB12 ↓ ,HCY ↑ ,Hb ↓ ,MCV<br>↑ ,MMA ↑ | /                        | /            | VitB12             | Improvement | Forzani et<br>al.2013   |
| 34  | 24/F        | Paresthesia,weakness                                                                                         | VitB12,Hb,MCV:N,HCY<br>↑ ,MMA ↑        | Abnormal                 | /            | VitB12             | /           | Francis et<br>al.2019   |
| 35  | 19/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia,pain                                                 | VitB12:N                               | C2-C7                    | /            | Steroid            | Improvement | Ghobrial et<br>al.2012  |
| 36  | 23/F        | Paresthesia,weakness,decreased<br>deep senstaion,thrombosis                                                  | VitB12 ↓ ,HCY ↑ ,Hb<br>↓ ,MCV:N,MMA ↑  | N                        | A&D          | VitB12             | Improvement | Glijn et<br>al.2017     |
| 37  | 45/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia,psychiatric<br>symptoms ,<br>impaired cognition,pain | VitB12 ↓ ,HCY ↑ ,Hb,MCV:N              | /                        | A            | VitB12             | Improvement | Hew et<br>al.2018       |
| 38  | 23/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia                                                      | VitB12 ↓ ,HCY ↑                        | N                        | A&D          | VitB12             | Death       | Hirvioja et<br>al.2016  |
| 39  | 19/M        | Paresthesia,weakness,ataxia,involu<br>ntary movement                                                         | VitB12 ↓ ,Hb:N,MCV ↑                   | C1-C5                    | D            | VitB12             | Improvement | Hsu et<br>al.2012       |
| 40  | 16/F        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia                                                      | VitB12,HCY,Hb,MCV:N                    | C1-C6,T7-T8              | Abnor<br>mal | VitB12             | Improvement | Hu et al.2014           |
| 41  | 19/F        | Weakness,ataxia                                                                                              | /                                      | Cervical and<br>thoracic | D            | /                  | /           | Huang et<br>al.2009     |
| 42  | 55/M        | Decreased deep<br>senstaion,psychiatric symptoms                                                             | VitB12 ↓ ,Hb:N,MCV ↑                   | Abnormal                 | /            | /                  | Improvement | Iwata et<br>al.2001     |
| 43  | 19/F        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia                                                      | VitB12:N,HCY ↑ ,MCV ↑                  | C2-C6                    | A & D        | VitB12,<br>steroid | Improvement | Ji et al.2018           |
| 44  | 24/M        | Paresthesia,weakness,decreased<br>deep senstaion,ataxia,lhermitte<br>symptom                                 | VitB12 ↓ ,HCY ↑ ,Hb ↓                  | C2-C6                    | /            | VitB12             | Improvement | Jiang et<br>al.2020     |
| 45  | 21/F        | Weakness,decreased deep<br>senstaion,ataxia,impaired<br>cognition,hyperpigmentation                          | VitB12 ↓ ,Hb ↓                         | C2-C7                    | A & D        | VitB12             | Improvement | Johnson et<br>al.2018   |
| 46  | 18/F        | Paresthesia,weakness,ataxia                                                                                  | VitB12,MMA:N                           | Cervical and<br>thoracic | /            | VitB12             | Improvement | Jones et<br>al.2015     |
| 47  | 19/F        | Paresthesia,decreased deep<br>senstaion,ataxia                                                               | VitB12 ↓ ,HCY ↑ ,Hb ↓ ,MCV<br>↑ ,MMA ↑ | C1-T4                    | /            | VitB12             | Improvement | Kanin et<br>al.2020     |
| 48  | 27/M        | Paresthesia,decreased deep<br>senstaion                                                                      | VitB12,Hb,MCV:N,HCY<br>↑ ,MMA ↑        | N                        | A            | VitB12             | Improvement | Kaski et<br>al.2017     |

| No. | Age/<br>Sex | Clinical manifestation                                                                | Laboratory test                     | Spinal cord<br>imaging | EMG      | Treatment          | Prognosis   | Citation                 |
|-----|-------------|---------------------------------------------------------------------------------------|-------------------------------------|------------------------|----------|--------------------|-------------|--------------------------|
| 49  | 22/F        | Paresthesia, weakness, decreased deep sensation, ataxia, thrombosis                   | VitB12 ↓, MCV ↑                     | C1-C5                  | A        | VitB12             | Improvement | Kwon et al.2019          |
| 50  | 33/M        | Paresthesia, weakness, decreased deep sensation, ataxia                               | VitB12 ↓, MCV ↑                     | C2-C6                  | A        | VitB12             | Improvement | Kwon et al.2019          |
| 51  | 32/F        | Decreased deep sensation, ataxia                                                      | VitB12 ↓, HCY ↑, Hb:N, MCV ↑        | C1-2                   | /        | VitB12             | Improvement | Lee et al.2019           |
| 52  | 41/M        | Paresthesia, weakness, decreased deep sensation, ataxia, lhermitte symptom            | VitB12 ↓, Hb:N, MCV ↑               | C2-C7                  | A        | /                  | /           | Lin et al.2007           |
| 53  | 24/M        | Paresthesia, decreased deep sensation, ataxia, bowel or bladder dysfunction           | VitB12 ↓, Hb:N, MCV ↑               | C2-C6                  | A & D    | VitB12             | Improvement | Lin et al.2011           |
| 54  | 18/F        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction | VitB12, Hb:N, HCY ↑, MCV ↑          | C2-C6                  | A & D    | VitB12             | Lost        | Lin et al.2011           |
| 55  | 20/F        | Paresthesia, weakness, decreased deep sensation                                       | VitB12, Hb:N, MCV ↑                 | C2-C7                  | D        | VitB12             | Lost        | Lin et al.2011           |
| 56  | 21/F        | Weakness, ataxia, psychiatric symptoms                                                | VitB12 ↓, HCY ↑, Hb ↓, MCV:N, MMA ↑ | N                      | /        | VitB12             | Improvement | Lundin et al.2019        |
| 57  | 35/M        | Paresthesia, weakness, decreased deep sensation, ataxia, psychiatric symptoms         | VitB12 ↓, HCY ↑, MMA ↑              | C2-C6                  | N        | VitB12, methionine | Improvement | Mancke et al.2016        |
| 58  | 36/M        | Paresthesia, decreased deep sensation, ataxia, involuntary movement                   | VitB12 ↓, HCY ↑, MCV ↑              | C1-Th11                | A & D    | VitB12             | Improvement | Massey et al.2016        |
| 59  | 24/F        | Paresthesia, weakness, decreased deep sensation, ataxia                               | VitB12 ↓, HCY ↑, Hb, MCV:N          | C1-C5                  | A        | VitB12             | /           | McArdle et al.2020       |
| 60  | 19/F        | Weakness, ataxia, impaired cognition                                                  | VitB12 ↓, Hb ↓, MCV:N               | C3-C6                  | A        | VitB12             | /           | McArdle et al.2020       |
| 61  | 19/F        | Paresthesia, ataxia, psychiatric symptoms, bowel or bladder dysfunction               | VitB12 ↓, MCV ↑                     | C1-C5                  | A        | VitB12             | /           | McArdle et al.2020       |
| 62  | 18/F        | Paresthesia, weakness, ataxia                                                         | VitB12 ↓, Hb, MCV:N                 | C1-thoracic            | A        | VitB12             | /           | McArdle et al.2020       |
| 63  | 22/M        | Paresthesia, weakness, thrombosis                                                     | VitB12:N                            | /                      | D        | VitB12             | Improvement | Middleton et al.2018     |
| 64  | 39/M        | Decreased deep sensation, ataxia                                                      | VitB12:N                            | /                      | /        | VitB12             | Improvement | Miller et al.2004        |
| 65  | 22/M        | Paresthesia, weakness, decreased deep sensation, ataxia, lhermitte symptom            | VitB12 ↓, HCY ↑, Hb:N, MCV ↑        | N                      | Abnormal | VitB12             | Improvement | Morris et al.2015        |
| 66  | 24/M        | Paresthesia, decreased deep sensation, ataxia, involuntary movement                   | HCY ↑, MMA ↑                        | N                      | /        | VitB12             | Lost        | Morrissey et al.2009     |
| 67  | 37/M        | Paresthesia, weakness, ataxia, psychiatric symptoms, bowel or bladder dysfunction     | VitB12 ↓, Hb, MCV:N                 | C1-C7                  | /        | VitB12             | Improvement | Ng et al.2002            |
| 68  | 30/M        | Paresthesia, decreased deep sensation, ataxia, thrombosis                             | VitB12:N, HCY ↑, Hb ↓, MMA ↑        | N                      | /        | VitB12             | Improvement | Olney et al.2019         |
| 69  | 30/F        | Paresthesia, weakness, decreased deep sensation, ataxia, lhermitte symptom            | VitB12 ↓, HCY ↑, Hb, MCV:N, MMA ↑   | C2-C7                  | /        | VitB12             | Improvement | Onrust et al.2019        |
| 70  | Na/M        | Weakness, decreased deep sensation, ataxia                                            | VitB12 ↓                            | Cervical               | /        | VitB12             | /           | Papathanasiou et al.2015 |
| 71  | Na/M        | Weakness, decreased deep sensation, ataxia                                            | VitB12:N                            | Cervical               | /        | VitB12             | /           | Papathanasiou et al.2015 |

| No. | Age/<br>Sex | Clinical manifestation                                                                                         | Laboratory test                      | Spinal cord<br>imaging      | EMG      | Treatment          | Prognosis   | Citation              |
|-----|-------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------|-----------------------------|----------|--------------------|-------------|-----------------------|
| 72  | 31/M        | Paresthesia, weakness, decreased deep sensation, ataxia, Lhermitte symptom                                     | VitB12 ↓, MCV ↑                      | C2-C5                       | /        | VitB12             | Improvement | Pema et al.1998       |
| 73  | 31/F        | Paresthesia, weakness, decreased deep sensation                                                                | /                                    | C1-T8                       | /        | VitB12             | Lost        | Prigge et al.2012     |
| 74  | 27/F        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction, pain                    | VitB12, HCY, MCV: N, Hb ↓, MMA ↑     | C3/C4-T11/T12               | /        | VitB12             | Lost        | Pugliese et al.2015   |
| 75  | 35/M        | Paresthesia, weakness, ataxia, impaired cognition, bowel or bladder dysfunction                                | VitB12, Hb, MCV: N                   | C2-C7                       | /        | VitB12             | Remain      | Rheinboldt et al.2014 |
| 76  | 28/M        | Paresthesia, decreased deep sensation                                                                          | VitB12, Hb, MCV: N, HCY ↑            | /                           | /        | VitB12             | Remain      | Richardson et al.2010 |
| 77  | 25/M        | Paresthesia, ataxia                                                                                            | VitB12, Hb: N                        | Cervical and upper thoracic | /        | VitB12, methionine | Improvement | Sadr et al.2010       |
| 78  | 22/M        | Paresthesia, weakness, decreased deep sensation, ataxia                                                        | VitB12, Hb, MCV: N, HCY ↑, MMA ↑     | C2-C5                       | /        | VitB12             | Improvement | Seed et al.2020       |
| 79  | 45/M        | Paresthesia, weakness, decreased deep sensation, ataxia                                                        | VitB12 ↓, HCY ↑, Hb, MCV: N, MMA ↑   | Cervical and thoracic       | /        | VitB12             | Improvement | Shah et al.2019       |
| 80  | 22/F        | Paresthesia, weakness, decreased deep sensation, impaired cognition, bowel or bladder dysfunction              | VitB12, MCV: N, HCY ↑                | C1-T11                      | Abnormal | VitB12             | Improvement | Shen et al.2019       |
| 81  | 23/F        | Paresthesia, weakness, bowel or bladder dysfunction, thrombosis                                                | Hb ↓, MCV: N                         | C1-T12                      | A        | VitB12             | Improvement | Shulman et al.2007    |
| 82  | 28/M        | Paresthesia, decreased deep sensation                                                                          | VitB12 ↓                             | Cervical                    | /        | VitB12, IVIG       | Improvement | Simpson et al.2019    |
| 83  | 29/F        | Paresthesia, weakness, decreased deep sensation, bowel or bladder dysfunction                                  | VitB12: N                            | C2-T5                       | /        | VitB12             | Improvement | Sleeman et al.2016    |
| 84  | 28/M        | Paresthesia, decreased deep sensation, bowel or bladder dysfunction, Lhermitte symptom                         | VitB12, Hb: N                        | Caudal medulla to C7        | /        | VitB12             | Improvement | Sotirchos et al.2012  |
| 85  | 25/F        | Paresthesia, ataxia                                                                                            | VitB12: N, HCY ↑                     | N                           | Abnormal | VitB12, steroid    | Improvement | Spickler et al.2019   |
| 86  | 22/M        | Paresthesia, weakness, decreased deep sensation, ataxia                                                        | VitB12, MCV: N, HCY ↑, Hb ↓, MMA ↑   | C1-T5                       | /        | VitB12             | Improvement | Stockton et al.2017   |
| 87  | 46/F        | Paresthesia, weakness, decreased deep sensation, impaired cognition                                            | VitB12: N, HCY ↑, Hb ↓, MCV ↑, MMA ↑ | N                           | /        | VitB12             | Improvement | Sutaria et al.2018    |
| 88  | 25/M        | Paresthesia, weakness, decreased deep sensation                                                                | VitB12: N                            | C2-C6                       | A & D    | VitB12, steroid    | Improvement | Tatum et al.2010      |
| 89  | 22/M        | Paresthesia, weakness, decreased deep sensation, ataxia                                                        | VitB12, Hb, MCV, MMA ↑               | N                           | D        | VitB12, IVIG       | Improvement | Thompson et al.2015   |
| 90  | 27/M        | Paresthesia, weakness                                                                                          | VitB12, HCY, Hb, MCV, MMA: N         | N                           | A & D    | VitB12, IVIG       | Worse       | Thompson et al.2015   |
| 91  | 23/F        | Paresthesia, weakness, decreased deep sensation, ataxia, bowel or bladder dysfunction, Lhermitte symptom, pain | VitB12: N, HCY ↑                     | N                           | N        | VitB12             | Improvement | Thompson et al.2015   |
| 92  | 23/M        | Paresthesia, decreased deep sensation                                                                          | VitB12 ↓, HCY ↑, Hb: N, MCV ↑, MMA ↑ | /                           | /        | VitB12             | Improvement | Waclawik et al.2003   |

| No. | Age/<br>Sex | Clinical manifestation                                                                                        | Laboratory test                     | Spinal cord<br>imaging | EMG          | Treatment                          | Prognosis   | Citation                 |
|-----|-------------|---------------------------------------------------------------------------------------------------------------|-------------------------------------|------------------------|--------------|------------------------------------|-------------|--------------------------|
| 93  | 24/M        | Paresthesia, decreased deep<br>sensations, ataxia, impaired<br>cognition                                      | VitB12 ↓, HCY<br>↑, MCV: N, MMA ↑   | C2-C7                  | /            | VitB12                             | Remain      | Waters et<br>al.2005     |
| 94  | 25/M        | Paresthesia, weakness, bowel or<br>bladder dysfunction                                                        | /                                   | C2-T1                  | Abnor<br>mal | VitB12,<br>steroid                 | Improvement | Weng et<br>al.2017       |
| 95  | 17/M        | Paresthesia, weakness, decreased<br>deep sensations, involuntary<br>movement, bowel or bladder<br>dysfunction | VitB12, Hb, MCV: N, HCY<br>↑, MMA ↑ | C1-C6/7                | /            | VitB12,<br>steroid                 | Improvement | Williamson et<br>al.2019 |
| 96  | 26/F        | Paresthesia, weakness, decreased<br>deep sensations                                                           | VitB12 ↓, Hb: N, MCV ↑              | C2-C7                  | D            | VitB12,<br>plasma<br>exchange      | Improvement | Wu et al.2007            |
| 97  | 20/F        | Paresthesia, weakness, decreased<br>deep sensations, ataxia, impaired<br>cognition                            | VitB12, HCY, Hb, MCV: N             | C1-T2                  | D            | VitB12                             | Improvement | Yuan et<br>al.2017       |
| 98  | 21/M        | Paresthesia, weakness, decreased<br>deep sensations, ataxia                                                   | VitB12, Hb, MCV: N, HCY ↑           | C2-C6                  | D            | VitB12                             | Improvement | Zhao et<br>al.2020       |
| 99  | 18/F        | Paresthesia, weakness, decreased<br>deep sensations                                                           | VitB12, MCV: N, HCY ↑, Hb<br>↓      | T3-T6                  | A&D          | VitB12, high<br>pressure<br>oxygen | Improvement | Zhao et<br>al.2020       |

Age: the unit is years old; Na: age which were not mentioned in literature; M: male; F: female; VitB12: Vitamin B12; HCY: homocysteine; Hb: hemoglobin; MCV: Mean corpuscular volume; MMA: methylmalonic acid; N: normal; ↑ : increase; ↓ : decrease; /: data which were not mentioned in literature; EMG: Electromyography; A: axonal; D: demyelination; IVIG: intravenous immunoglobulin

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