Demyelinating polyneuropathy and lymphoplasmacytic lymphoma coexisting in 36-year-old man: A case report

Lesia Rozłucka, Elżbieta Semik-Grabarczyk, Marta Pietrukaniec, Agnieszka Żak-Gołąb, Małgorzata Grabarczyk, Sebastian Grosicki, Michał Holecki

Lesia Rozłucka, Department of Internal Medicine, Allergology and Clinical Immunology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice 40-752, Poland
Elżbieta Semik-Grabarczyk, Marta Pietrukaniec, Agnieszka Żak-Gołąb, Michał Holecki, Department of Internal Medicine, Autoimmune and Metabolic Diseases, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice 40-752, Poland
Małgorzata Grabarczyk, Student Scientific Society at the Department of Internal Medicine, Autoimmune and Metabolic Diseases, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice 40-752, Poland
Sebastian Grosicki, Department of Hematology and Cancer Prevention, Faculty of Health Sciences in Bytom, Medical University of Silesia, Bytom, 41-902, Poland

Corresponding author: Lesia Rozłucka, MD, Doctor, Department of Internal Medicine, Allergology and Clinical Immunology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Medykow 14, Katowice 40-752, Poland. lesia.rozlucka@gmail.com

Abstract

BACKGROUND
Lymphoplasmacytic lymphoma is a rare non-Hodgkin’s lymphoma, occurring mostly in the elderly. It develops slowly and leads to malignant proliferation of lymphoid line cells in the bone marrow, lymph nodes and spleen. It may also affect nerve roots and meninges; some patients develop sensorimotor polyneuropathy which may precede general symptoms of lymphoma.

CASE SUMMARY
We present a case of a 36-year-old man diagnosed in 2012 with chronic inflammatory demyelinating polyneuropathy (CIDP), then he was hospitalized in 2019 due to progressive symptoms of heart failure and significant weight loss over the previous four months. Based on clinical and laboratory findings a diagnosis of lymphoplasmacytic lymphoma was suspected and confirmed by bone marrow flow cytometry. There was no improvement in the results of laboratory tests and the patient’s condition after immediate implementation of chemotherapy. Patient died on the fifth day of treatment.

CONCLUSION
While CIDP and malignant disease co-occurrence is rare, it should be suspected and investigated in patients with atypical neuropathy symptoms.
A 36-year-old man diagnosed with CIDP and hypothyroidism seven years ago, was

**CASE PRESENTATION**

**Chief complaints**

A 36-year-old man diagnosed with CIDP and hypothyroidism seven years ago, was
admitted in April 2019 to the Department of Internal Medicine, Autoimmune and Metabolic Diseases due to progressive weakness, peripheral edema, weight loss (approximately 10 kg within the previous four months, 31 kg in total since CIDP diagnosis), deterioration of appetite and impairment of the muscular system (the patient moved around the house with the help of others). On admission, the patient complained of "stiffness of the torso", sensory disturbances affecting hands and feet in a glove and stocking distribution.

History of present illness
The patient’s condition deteriorated significantly about five months before admittance, with particular aggravation of symptoms during the last month. In December 2018 patient was hospitalized due to concomitant edema, protein deficiency and heart failure. Despite intensive diuretic treatment, the improvement was temporary. In the meantime, due to increasing abdominal pain, patient underwent gastroscopy and was diagnosed with gastritis. Proton pomp inhibitors treatment resulted in only partial improvement. The patient’s neurological condition continued to deteriorate despite intravenous immunoglobulin and glucocorticosteroid treatment leading to his necessity of hospitalization.

History of past illness
Patient was diagnosed with CIDP and hypothyroidism in 2012. Since then he was treated using INN–human normal immunoglobulin (Kiovig 60 mg), with the last administration one month before current hospitalization and methylprednisolone (in intravenous pulses followed by an oral therapy). Hypothyroidism was treated with Levothyroxine (50 μg/d).

Personal and family history
Patients’ grandfather died of cancer of unknown localization and mother was treated in the past due to thyroid cancer.

Physical examination upon admission
Physical examination revealed dry, thickened, slightly flaky skin of the whole body and swelling of the lower limbs was also noticeable. Peripheral lymph nodes were not palpable. His body weight was 55 kg, height 178 cm (BMI 17.3 kg/m²). Neurological examination revealed disturbances of deep sensation and vibration sense in the lower limbs, reduction of muscle tone in the limbs except for the hands, symmetrical muscle wasting in the face, upper and lower limbs.

Laboratory examinations
The results of laboratory tests are presented in Table 1. The overall clinical picture, as well as the results of laboratory and imaging studies suggested a secondary nature of polyradiculoneuropathy. Despite the negative opinion of a neurologist, the patient underwent a bone marrow aspiration. Bone marrow cytology showed an increased percentage of plasmocytes, which strongly suggested a hematological background.

Imaging examinations
The abdomen ultrasonography revealed abdominal lymphadenopathy and accumulated pericardial and peritoneal fluid. Computed tomography (CT) scan of the chest, abdomen and pelvis revealed streaky fibrous changes at the base of the left lung, and numerous enlarged mesenteric lymph nodes (up to 14 mm × 29 mm, Figure 1).

MULTIDISCIPLINARY EXPERT CONSULTATION
Sebastian Grosicki, MD, PhD, Professor and Chief of Hematology Department, Medical University of Silesia, Poland
In the course of diagnostics, an increased pool of lymphoid cells in the myelogram was found and the patient was referred for further diagnosis in the Hematology Department. Fifty-five percent infiltration with clonal plasma, lymphoplasmic and B cells was confirmed in immunophenotype and bone marrow morphology (Figure 2). Increased concentration of free kappa light chains in peripheral blood serum and urine, and the presence of M protein in the IgM kappa class in serum was confirmed. In peripheral blood counts, leukocytosis $21.9 \times 10^3/\mu L$ (normal range 4.0 $\times 10^3/\mu L$–10.0 $\times 10^3/\mu L$) with granulocytosis, microcytic, sideropenic anemia and reactive thrombocytosis have been noted.
Table 1 Laboratory blood test results at hospital admission

| Result                      | Normal range          |
|-----------------------------|-----------------------|
| **Hematology**              |                       |
| White blood cell count      | $20.31 \times 10^3/\mu L$ (4.0-10.0) |
| Red blood cell count        | $4.93 \times 10^6/\mu L$ (4.2-5.7) |
| Hemoglobin                  | 12.3 g/dL (13.5-6.5)   |
| Hematocrit                  | 38.7% (40-53)          |
| MCV                         | 78.5 fL (84-98)        |
| MCH                         | 24.9 pg (27-31)        |
| MCHC                        | 31.8 g/dL (32-36)      |
| Platelets                   | $704 \times 10^3/\mu L$ (130-400) |
| Lymphocytes                 | 47.6% (20-45)          |
| Monocytes                   | 7.1% (3-9)             |
| Neutrophils                 | 44.2% (45-70)          |
| Eosinophils                 | 0.20% (1.00-5.00)      |
| Basophils                   | 0.4% (0-1)             |
| ESR                         | 9 mm/h (3-8)           |
| **Coagulation**             |                       |
| aPTT                        | 29.0 s (25.4-36.9)     |
| Thrombin time               | 16.6 s (10.3-16.6)     |
| Prothrombin time            | 11.3 s (9.4-12.5)      |
| INR                         | 1.00 ng/mL (0.80-1.20) |
| D-dimer                     | 1744.0 (≤ 500.0)       |
| **Biochemistry**            |                       |
| C-reactive protein          | 7.3 mg/L (≤ 5.0)       |
| Glucose                     | 116.00 mg/dL (74.00-106.00) |
| Creatinine                  | 1.10 mg/dL (0.84-1.25) |
| MDRD GFR                    | > 60 mL/min (> 60)     |
| Uric acid                   | 6.37 mg/dL (3.50-7.20) |
| Lactate dehydrogenase       | 196 U/L (≤ 248)        |
| Lactate (Lac)               | 2.10 mmol/L (1.10-2.40) |
| Alkaline phosphatase        | 95 U/L (38-126)        |
| Alpha amylase               | 75.0 U/L (≤ 90.0)      |
| Lipase                      | 44.00 U/L (21.00-67.00) |
| Serum iron                  | 26.00 µg/dL (60.00-180.00) |
| UIBC                        | 150.00 µg/dL (155.00-300.00) |
| TIBC                        | 176.0 µg/dL (250.0-450.0) |
| Total cholesterol           | 133.0 mg/dL (≤ 200)    |
| Triglycerides               | 160.00 mg/dL (0.00-150.00) |
| **Hormones**                |                       |
| Anti-TPO                    | < 5.00 IU/mL (≤ 34.00) |
| TSH                         | 5.230 µU/mL (0.27-4.2) |
| Cortisol                    | 12.60 µg/dL (4.82-19.50) |
| **Electrolytes**            |                       |
| Sodium                      | 134.2 mmol/L (136.0-146.0) |
| Potassium                   | 4.95 mmol/L (3.50-5.10) |
| Calcium-total               | 7.70 mg/dL (8.80-10.60) |
| Phosphates inorganic        | 3.95 mg/dL (2.50-4.50) |
| **Liver enzymes**           |                       |
| ALT                         | 17.0 U/L (≤ 45.0)      |
| AST                         | 20.0 U/L (≤ 35.0)      |
| GGT                         | 15.00 U/L (≤ 55.00)    |
| Total bilirubin             | 0.19 mg/dL (0.30-1.20) |
| Cardiac biomarkers          |                       |
### Troponin T high sensitivity
47.74 ng/L (0.00-14.00)

### Creatine Kinase
41 U/L (< 170)

### Creatine Kinase -MB
18 U/L (< 25)

### CKMB
43.9% (< 6.0)

### Pro-BNP
288.30 pg/mL (0-125)

### Serum protein electrophoresis

| Protein Type | Value     | Reference Range |
|--------------|-----------|-----------------|
| Albumin      | 49.2%     | (53.8-65.2)     |
| Alpha 1      | 7.2%      | (1.1-3.7)       |
| Alpha 2      | 21.1%     | (8.5-14.5)      |
| Beta         | 17.1%     | (8.6-14.8)      |
| Gamma        | 5.4%      | (9.2-18.2)      |
| A/G ratio    | 0.97      | (1.27-1.96)     |
| Total protein| 4.30 g/dL | (6.60-8.30)     |
| Albumin      | 2.30 g/dL | (3.5-5.2)       |

### Virology tests
- Anti-HCV: Negative
- HbsAg: Negative
- Anti-HIV: Negative

### Immunoglobulins
- Immunoglobulin A: 25 mg/dL (70-400)
- Immunoglobulin G: 193 mg/dL (700-1600)
- Immunoglobulin M: 142 mg/dL (40-230)

### Rheumatology profile
- ANA profile: Negative
- Anti-CCP: 0.47 RU/mL (< 5.00)
- Anti-dsDNA: 13.9 IU/mL (< 100)
- p-ANCA: Negative
- c-ANCA: Negative
- Complement C3: 134 mg/dL (90-180)
- Complement C4: 35 mg/dL (10-40)

### Onconeural antibodies
- Chromogranin A: 363.250 µg/L (< 100)
- Anti-neuronal autoantibodies (Hu. Yo. Ri. CV2. Ma2/Ta. amphiphysin. anti-GAD): Negative

### FINAL DIAGNOSIS
Taking into account all the symptoms, a diagnosis of LPL was stated.

### TREATMENT
Given the rapidly worsening clinical condition of the patient, R-COP (rituximab 600 mg iv 1 d, vincristin 2 mg iv 1 d, cyclophosphamide 1200 mg iv 1-5 d, methylprednisolone 125 mg iv 1-5 d,) immunochemotherapy as an emergency treatment was started. Unfortunately, despite intensive supportive treatment the general clinical and neurological condition of the patient deteriorated.
OUTCOME AND FOLLOW-UP

The patient died on the fifth day of treatment in the Hematology Department.

DISCUSSION

Lymphomas, more commonly B-cell lymphomas including LPL may cause axonal damage or infiltrate peripheral nerves and cause asymmetric mononeuropathy or CIDP[14]. Therefore, there are a number of reports regarding occurrence of CIDP in the course of lymphoma, but only a few describing paraneoplastic CIDP, which preceded the lymphoma diagnosis[15-17]. Vial et al[12] presented nine cases in which CIDP symptoms preceded lymphomas, but none of them where LPL. However, they described a case of 39-year-old man with axonal multiple mononeuropathy which occurs six months before LPL diagnosis and 79-year-old woman with radiculopathy, in whom LPL was diagnosed five months after the first symptoms of radiculopathy. In the first case treatment included doxorubicin-based therapy, intrathecal methotrexate/cyclophosphamide and fludarabine. The second patient was treated with doxorubicin, intrathecal methotrexate and prednisone. In both cases hematological remission and neurological improvement were observed[12].

The patient described by us is an example of paraneoplastic polyradiculoneuropathy and lymphoplasmacytic lymphoma. CIDP was initially diagnosed in 2012, since when remissions and relapses were observed alternately. The patient was treated monthly with intravenous immunoglobulins (Kiovig), and with intermittent intravenous pulses of methylprednisolone sodium succinate (Solu-Medrol). This treatment was initially effective – the patient was able to function normally in everyday life (he worked as a mechanic in the workshop, often travelled abroad, actively spending his spare-time). However, in December 2018 his general health condition (especially neurological) deteriorated. The rapid weight loss was attributed to the intensive diuretic treatment due to concomitant edema, which in turn were caused by protein deficiency and heart failure (not typical for such a young man). Due to increasing abdominal pain, patient underwent gastroscopy and was diagnosed with gastritis. Proton pomp inhibitors treatment resulted in only partial improvement. The patient’s neurological condition continued to deteriorate despite intravenous immunoglobulin and glucocorticosteroid treatment leading to his necessity of hospitalization.

The overall clinical symptoms, the results of laboratory tests and CT scan suggested the secondary background of polyradiculoneuropathy. Despite the different opinion of the neurologists, we stayed with our suspicion of a diagnosis of lymphoma, which was finally confirmed. It seems that the lack of typical symptoms, such as peripheral lymphadenopathy, splenomegaly or low-grade fever, resulted in delaying the diagnosis of lymphoma and worsening its’ prognosis. Disturbing symptoms reported by the patient were not considered to have paraneoplastic origin. It seems reasonable, that such asymptomatic patients should have regular basic laboratory tests such as blood count, blood biochemistry and proteinogram, as well as chest X-ray and an abdominal ultrasound. In case of any abnormalities bone marrow biopsy and...
hematologist consultation should be done. Polyradiculoneuropathy, while mostly primary, may also be secondary to LPL. Such a situation, when symmetrical sensorimotor polyneuropathy (multifocal or mononeuropathy) precedes the diagnosis of lymphoma, is observed even in 30% of patients. This case should be a reminder to consider an oncological diagnosis in patients with CIDP, especially those with an atypical or rapidly progressive course of the disease.

CONCLUSION

CIDP and malignant diseases co-occurrence is rare, nevertheless patients with atypical symptoms of neuropathy should have extended diagnostics and remain under constant supervision of specialists.

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