Open Access Article

Ann. Acad. Med. Siles. (online) 2024; 78: 248–252
eISSN 1734-025X
DOI: 10.18794/aams/184312
www.annales.sum.edu.pl

OPIS PRZYPADKU
CASE REPORT

Bruns-Garland syndrome in patient with long-term type 2 diabetes

Zespół Brunsa-Garlanda u pacjentki z wieloletnią cukrzycą typu 2

Edyta Cichocka[1], Sabina Widenka[2], Janusz Gumprecht[1]

[1]Department of Internal Medicine, Diabetology and Nephrology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland

[2]Independent Public Healthcare Centre Provincial Specialist Hospital No. 3 in Rybnik, Poland

ABSTRACT

The Bruns-Garland syndrome (diabetic amyotrophy) is a rare disorder that affects fewer than 1% of patients with diabetes. It is manifested by unilateral or bilateral pain, weakness and muscle wasting in the proximal part of the lower limbs (proximal motor neuropathy).
We present a 72-year-old patient with long-term type 2 diabetes mellitus and with the Bruns-Garland syndrome. All the symptoms, including neurological manifestations, were reversible and resolved after the implementation of intensive treatment. Optimizing diabetes treatment, rehabilitation, pain management and the use of benfotiamine and alpha-lipoic acid preparations were crucial to accelerate the treatment effects of diabetic amyotrophy.

KEYWORDS

diabetes, diabetic neuropathy, amyotrophy

STRESZCZENIE

Zespół Brunsa-Garlanda (amiotrofia cukrzycowa) to rzadkie zaburzenie, które dotyka mniej niż 1% pacjentów chorujących na cukrzycę. Objawia się jednostronnym lub obustronnym bólem, osłabieniem i zanikiem mięśni w bliższej części kończyn dolnych (proksymalna neuropatia ruchowa).
W prezentowanej pracy przedstawiono przypadek 72-letniej pacjentki z długotrwałą cukrzycą typu 2 i zespołem Brunsa-Garlanda. Wszystkie objawy, w tym objawy neurologiczne, były odwracalne i ustąpiły po wdrożeniu intensywnego leczenia. Optymalizacja leczenia cukrzycy, rehabilitacja, leczenie bólu oraz stosowanie preparatów benfotiaminy i kwasu alfa-liponowego miały kluczowe znaczenie dla przyspieszenia efektów leczenia amiotrofii cukrzycowej.

SŁOWA KLUCZOWE

cukrzyca, neuropatia cukrzycowa, amiotrofia

Received: 12.11.2023 **Revised:** 23.01.2024 **Accepted:** 19.02.2024 **Published online:** 09.10.2024

Address for correspondence: dr n. med. Edyta Cichocka, Klinika Chorób Wewnętrznych, Diabetologii i Nefrologii, Wydział Nauk Medycznych w Zabrzu, Śląski Uniwersytet Medyczny w Katowicach, ul. 3 Maja 13, 41-800 Zabrze, tel. +48 32 370 44 25, e-mail: ecichocka@sum.edu.pl

Publisher: Medical University of Silesia, Katowice, Poland

INTRODUCTION

The Bruns-Garland syndrome (diabetic amyotrophy) is a rare disorder that affects fewer than 1% of patients with diabetes [1]. It is manifested by unilateral or bilateral pain, weakness and muscle wasting in the proximal part of the lower limbs (proximal motor neuropathy). It is more prevalent in elderly patients with long-term type 2 diabetes. The course of the disease is prolonged. It usually starts in one leg and spreads to the other leg over weeks or months. It may spread to the upper extremities in 30% of cases [2]. The patient's condition may deteriorate slowly or gradually over a period of up to 18 months. Then the process stabilizes and gradually improves, although recovery may take many months. Patients should be informed that some permanent weakness may persist despite the treatment.

Considering the extent of pathological involvement, diabetic amyotrophy is currently defined as diabetic lumbosacral radiculoplexus neuropathy (DLRPN) [3].

The disease is characterized by the following [4]:

1. onset mainly in the elderly (5–7th decade of life)
2. a gradual or sudden onset that is sometimes unilateral; the other side is involved with disease progression
3. severe and deep pain predominantly in the thighs, hips, or buttocks
4. (mostly asymmetric) weakness of the proximal muscles of the lower limbs, making it impossible to get up from a sitting position (positive Gowers' sign)
5. it often coexists with symmetrical distal polyneuropathy
6. muscle fasciculations (either spontaneous or induced by percussion)
7. weight loss of even 20–30 kg
8. loss of knee and ankle reflexes.

The pathophysiology of diabetic amyotrophy is not fully understood. Most studies suggest ischemic pathology in the form of non-systemic microvasculitis. Inflammatory infiltration of vascular vessels was found in patients who underwent nerve biopsies. Although diabetic amyotrophy is motor-predominant, there is some evidence that autonomic and sensory nerves are also involved [3].

CASE REPORTS

Patient data was collected from medical records. Patient consent was obtained for data publication.

A 72-year-old patient with type 2 diabetes mellitus for over 15 years was admitted to the Department of Neurology due to increasing gait disturbances and paresis of the lower limbs with predominance of the left lower limb. Moreover, the patient reported memory disorders, pain, numbness and paresthesia of the lower left lower limb. The patient stopped leaving home and fell down the stairs several times. She also reported symptoms of polydipsia and polyuria as well as weight loss (about 10 kg over six months), which were most likely related to hyperglycemia. The patient did not control her blood glucose level or blood pressure. Additionally, she did she follow a diet. She had not been monitored for diabetes for many years. Diabetes was treated only with metformin 1000 mg/day. In addition, due to arterial hypertension, treatment with ramipril 5 mg, amlodipine 5 mg and bisoprolol 2.5 mg was used.

The patient had no history of alcohol or stimulant use. She had not smoked cigarettes for 10 years. Before the hospitalization she used only metformin and antihypertensive drugs (ramipril, amlodipine, bisoprolol).

During the neurological examination the patient was conscious, verbally responsive, with memory problems. A limping gait affected the left lower limb. Weakness and atrophy of the proximal muscles in the left lower limb with reduced muscle tone and areflexia of the lower limbs was observed. The femoral nerve stretch test (also known as Mackiewicz sign) was positive in the left lower limb.

On admission, laboratory tests showed hyperglycemia (474 mg/dl; normal range: 70–99 mg/dl, HbA1c – 16.5%; normal range for a diabetic patient: 6.5% or below), the serum sodium concentration was 132 mmol/l, and sodium correction in hyperglycemia was 139 mmol/l (normal range: 135–145 mmol/l), glucosuria and ketonuria were present. The blood gas analysis was without diabetic ketoacidosis. The blood counts were normal and the inflammatory parameters were negative. The serum creatinine concentration was 0.72 mg/dl (normal range: 0.5–0.9 mg/dl) with estimated glomerular filtration rate (eGFR) 79 ml/min/1,73 m^2. Thyroid function was also normal (thyroid-stimulating hormone (TSH) 2.9 mIU/l, normal range: 0.4–4 mIU/l). The vitamin B12 concentration was within the normal range (620 pmol/l; normal range: 148–740 pmol/l). The head computed tomography (CT) showed generalized cortical atrophy.

Electromyographic (Table I) and electroneurographic examinations (Table II) revealed clear signs of neurogenic damage to the left rectus muscle of the thigh and axonal damage (peroneal and left tibial nerves). The diagnostic procedure was extended to magnetic resonance imaging lumbosacral (MRI L-S) spine (T1 TSE, T2 TSE, T2 TRIM in the sagittal projection and T2 ME2D in the axial projection), which revealed degenerative changes. No compression of the nerve structures was reported. The patient underwent cardiac consultation. Ultrasound examination showed a preserved ejection fraction, no segmental contractility disorders, and no valvular defects.

Table I. Electromyographic examination

EMG IDIVIDUAL MUP TABLE

LEFT RECTUS FEMORIS

Simple	*potentials*	*(96.8%)*			
MUP#	*AMP uV*	*Dur ms*	*Turns*	*Phases*	*SI*
1	*337*	*9.9*	*2.0*	*3.0*	*1.03*
2	*181*	*9.7*	*2.0*	*3.0*	*-0.17*
3	*221*	*6.4*	*2.0*	*2.0*	*-0.13*
4	*283*	*7.2*	*3.0*	*4.0*	*0.12*
5	*1034*	*15.2*	*3.0*	*3.0*	*0.99*
6	*226*	*11.1*	*4.0*	*4.0*	*0.35*
7	*445*	*13.0*	*5.0*	*3.0*	*0.52*
8	*660*	*14.7*	*3.0*	*4.0*	*0.83*
9	*1038*	*16.0*	*7.0*	*3.0*	*1.02*
10	*781*	*10.9*	*4.0*	*4.0*	*1.92*
11	*1124*	*11.5*	*4.0*	*4.0*	*1.51*
12	*1568*	*11.6*	*3.0*	*3.0*	*1.34*
13	*264*	*9.8*	*2.0*	*2.0*	*0.52*
14	*411*	*9.4*	*7.0*	*4.0*	*0.5*
15	*1530*	*7.2*	*2.0*	*3.0*	*1.24*
16	*599*	*7.3*	*2.0*	*3.0*	*-0.005*
17	*922*	*11.5*	*3.0*	*3.0*	*2.0*
18	*379*	*11.4*	*2.0*	*3.0*	*1.84*
19	*497*	*12.0*	*3.0*	*3.0*	*1.72*
20	*2470*	*14.7*	*5.0*	*3.0*	*2.5*
21	*1806*	*17.2*	*5.0*	*3.0*	*1.96*
22	*2818*	*13.8*	*3.0*	*3.0*	*2.2*
23	*1407*	*10.5*	*3.0*	*3.0*	*1.69*
24	*2211*	*12.0*	*3.0*	*3.0*	*2.1*
25	*619*	*12.5*	*2.0*	*3.0*	*2.0*
26	*310*	*12.5*	*2.0*	*3.0*	*1.94*
27	*745*	*10.0*	*2.0*	*3.0*	*1.44*
28	*504*	*11.9*	*2.0*	*3.0*	*1.53*
29	*929*	*13.3*	*5.0*	*3.0*	*1.29*
30	*1069*	*12.5*	*5.0*	*3.0*	*1.69*
means	***913***	***11.6***	***3.3***	***3.1***	***1.25***
Polyphasic	*potentials*	*(3.2%)*			
31	*1676*	*15.5*	*6.0*	*6.0*	*2.0*
means	***1676***	***15.5***	***6.0***	***6.0***	***2.0***
ALL	***POTENTIALS***				
means	***938***	***11.7***	***3.4***	***3.2***	***1.27***
max	***2818***	***17.2***	***7.0***	***6.0***	***2.0***
min	***181***	***6.4***	***2.0***	***2.0***	***-0.17***

LEFT TIBIALIS ANTERIOR

Simple	*potentials*	*(67.9%)*			
MUP#	*AMP uV*	*Dur ms*	*Turns*	*Phases*	*SI*
1	*245*	*15.3*	*3.0*	*2.0*	*2.3*
2	*857*	*11.1*	*3.0*	*4.0*	*1.27*
3	*290*	*10.3*	*2.0*	*3.0*	*0.29*
4	*603*	*11.7*	*3.0*	*4.0*	*2.1*
5	*729*	*10.9*	*5.0*	*4.0*	*1.44*
6	*576*	*12.1*	*3.0*	*3.0*	*1.79*
7	*430*	*10.2*	*2.0*	*2.0*	*1.39*
8	*410*	*13.4*	*3.0*	*4.0*	*1.51*
9	*364*	*8.8*	*3.0*	*3.0*	*0.59*
10	*597*	*9.3*	*2.0*	*3.0*	*0.94*
11	*906*	*8.8*	*4.0*	*3.0*	*1.6*
12	*612*	*9.8*	*2.0*	*3.0*	*1.82*
13	*1306*	*15.3*	*5.0*	*3.0*	*2.5*
14	*1397*	*9.5*	*3.0*	*4.0*	*1.65*
15	*1484*	*10.9*	*5.0*	*3.0*	*1.43*
16	*1545*	*13.0*	*5.0*	*3.0*	*1.61*
17	*1065*	*8.1*	*4.0*	*3.0*	*0.83*
18	*267*	*16.3*	*4.0*	*4.0*	*1.24*
19	*1580*	*16.3*	*7.0*	*3.0*	*1.84*
means	***803***	***11.6***	***3.6***	***3.2***	***1.48***
Polyphasic	*potentials*	*(32.1%)*			
4	*1035*	*12.8*	*6.0*	*5.0*	*2.1*
11	*1401*	*15.0*	*5.0*	*5.0*	*1.82*
18	*1705*	*19.5*	*9.0*	*6.0*	*1.63*
19	*1057*	*13.1*	*5.0*	*5.0*	*1.23*
24	*535*	*14.3*	*4.0*	*5.0*	*1.80*
25	*551*	*14.7*	*4.0*	*5.0*	*1.86*
26	*588*	*12.3*	*7.0*	*7.0*	*0.49*
27	*498*	*11.1*	*5.0*	*6.0*	*0.10*
28	*412*	*10.9*	*6.0*	*7.0*	*-0.030*
means	***865***	***13.7***	***5.7***	***5.7***	***1.22***
ALL	***POTENTIALS***				
means	***823***	***12.3***	***4.3***	***4.0***	***1.39***
max	***1705***	***19.5***	***9.0***	***7.0***	***2.5***
min	***245***	***8.0***	***2.0***	***2.0***	***-0.030***

Table II. Electroneurographic examination

MOTOR NERVE CONDUCTION STUDIES

MNCS nerve	Lat		Amp		CV	F-M Lat.
	ms	Ref.Dev.	mV	Rev.Dev.	m/s	Ref.Dev.	m/s
Peroneus Motor Left							
ANKLE- EDB/EDB	4.67	-1.93	3.8	1.8			**57.9**
Fib.head-ankle/EDB	15.5		3.3	1.1	**34.2**	-6.8	
Peroneus Motor Right							
ANKLE- EDB/EDB	3.91		**0.7**	-1.3			31.2
Fib.head-ankle/EDB	14.8	-2.7	**0.56**	-1.64	**35.8**	-5.2	
Tibialis Motor Left							
ANKLE- Abd hal	5.85		4.6	0.6			**62.3**
/Abd hal Knee-Ankle/	18.0	-0.25	3.6	0.8	**33.7**	-6.3	
Adb hal							
Tibialis Motor Right							
ANKLE- Abd hal	3.37		5.5	1.5			**61.3**
/Abd hal Knee-Ankle/	17.2	-2.4	4.4	1.6	**31.2**	-8.8	
Adb hal							

SENSORY NERVE CONDUCTION STUDIES

SNCS nerve	Peak Lat		Amp		CV
	m/s	Ref.Dev.	uV	Rev.Dev.	m/s	Ref.Dev.
Suralis sensory nerve Post Calf 14 cm-Lat.Malleolus	4.23	--0.27	1.34		38.9	
Suralis sensory nerve Post Calf 14 cm-Lat.Malleolus	3.72	-0.78	**2.9**		35.8	

The neuropsychological assessment revealed decreased cognitive function, which could correspond to mild cognitive impairment and dementia that required further monitoring. During a 5-day stay in the Department of Neurology, intensive insulin therapy was initially used, followed by the administration of metformin (in a gradually increasing dose) and an sodium-glucose transport protein 2 (SGLT-2) inhibitor, which significantly improved glycemic control.

The patient was discharged home (a full dose of metformin [3000 mg/d], empagliflozin 10 mg and 10––12 U of neutral protamine Hagedorn (NPH) insulin. Hypertension treatment was maintained. In addition, the patient received benfotiamine 300 mg, pregabalin 150 mg, alpha-lipoic acid 600 mg orally and B vitamins (B1, B2, B6, B12, folic acid). Diabetic amyotrophy was diagnosed based on the entire clinical picture and after excluding other causes of asymmetric weakness of the lower limbs that coexisted with poor metabolic control of diabetes (the patient's feet pulses were preserved and the ankle/brachial systolic blood pressure index was 0.9 bilaterally).

One month after discharge from the Department of Neurology, the patient was admitted to the Department of Neurological Rehabilitation. The patient complained of limb weakness, gait disturbances in addition to memory and concentration problems. On admission, the neurological examination showed paresis of the left lower limb (Lovette scale 2/3), muscular atrophy predominant in the proximal muscles of the left upper and lower limbs, less pronounced in the right upper and lower limbs. Stretch reflexes were impaired in the quadriceps. During hospitalization, pharmacological and dietary treatment of diabetes was continued. On admission, the laboratory tests were as follows: HbA1c 10.7% and fasting glycemia 110 mg/dl (normal range: 70–99 mg/dl). No hypoglycemia was observed by the patient during the outpatient period. During hospitalization, the highest blood glucose levels were observed in the evening, which was associated with dietary errors (glycemia up to 225 mg/dl). The patient was also re-educated in terms of diet.

Ophthalmological consultation revealed features of non-proliferative diabetic retinopathy (NPDR). The patient was evaluated for albuminuria (the urine albumin-creatinine ratio (UACR) was within the normal range 7.41 mg/g). During hospitalization in the Neurological Rehabilitation Department, gradual improvement in gait was noted. Pain was reduced and the patient reported some improvement in cognitive

functions. These findings confirmed the reversible nature of the neurological disorders.

To further optimize the treatment of diabetes and to assess other chronic complications of diabetes, the patient was referred to the Department of Diabetology. The patient did not report to the department on the scheduled date of admission, explaining by phone that her blood glucose levels remained within the range of 100––160 mg/dl, and the neurological symptoms, particularly gait disturbances, were almost completely resolved.

DISCUSSION

The Bruns-Garland syndrome is a rare form of diabetic neuropathy that should be considered, especially in patients with poor glycemic control. The differential diagnosis of diabetic neuropathy is difficult due to the multitude of etiological factors that often cause similar clinical symptoms. The differential diagnosis should take into account other sensory and sensorimotor polyneuropathy in the course of diabetes and other diseases. They include: vitamin B deficiencies, amyloidosis, uremia, alcoholism, celiac disease, sarcoidosis, viral infections, e.g. the human immunodeficiency virus 1 (HIV-1), poisoning, and autoimmune diseases (Sjögren's syndrome). The neuropathy may also be secondary to prior chemotherapy or could be a paraneoplastic syndrome [5,6].

The onset is usually acute with severe pain in the area of the front surface of the thigh or the hip girdle and asymmetric weakness of the lower limbs (mainly flexion in the hip joint). After several weeks, muscle atrophy occurs. The prognosis is good and paresis usually resolves after a few months. Management includes pain control, physiotherapy and glycemic control.

To control pain, opiates may be needed at onset and amitriptyline (10–75 mg) can be administered for pain relief and insomnia. Regular paracetamol or a non--steroidal anti-inflammatory drug and gabapentinoids are also recommended [3,7]. Some studies suggest that pulsed oral or intravenous methylprednisolone may be beneficial for pain reduction if given within 2–3 months of onset of the symptoms. In patients with severe unremitting pain, corticosteroids are recommended. Pulsed methylprednisolone (500 mg/day for two days repeated every two weeks for 8–12 weeks) is also recommended but it is based on reports from uncontrolled studies. However, there is no evidence to support the use of intravenous immunoglobulin, plasma exchange, or cyclo-phosphamide [3,8].

In summary it should be emphasized that a comprehensive approach aimed at optimizing diabetes treatment, rehabilitation, pain management and the use of benfotiamine and alpha-lipoic acid preparations (as in other forms of diabetic neuropathy) may be crucial to accelerate the treatment effects of diabetic amyotrophy. Of note, chronic poor control of diabetes resulted in diabetes complications, including diabetic retinopathy and also led to an acute complication i.e. diabetic amyotrophy.

It is worth noting that unlike diabetic peripheral polyneuropathy, diabetic amyotrophy is mainly related to damage of the proximal parts of the lower limbs and the symptoms develop in a short period (days or weeks). It is reversible and all the symptoms, including the neurological manifestations, resolve after treatment, which is not characteristic of diabetic peripheral polyneuropathy.

Author's contribution

Study design – E. Cichocka, S. Widenka
Manuscript preparation – E. Cichocka, S. Widenka
Literature research – E. Cichocka, S. Widenka
Final approval of the version to be published – E. Cichocka, S. Widenka, J. Gumprecht

REFERENCES

1. Dyck P.J., Kratz K.M., Karnes J.L., Litchy W.J., Klein R., Pach J.M. et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. Neurology 1993; 43(4): 817–824, doi: 10.1212/wnl.43.4.817.

2. Nagsayi S., Somashekhar C., James C.M. Diagnosis and management of diabetic amyotrophy. Endocrinology 2010: 327–329.

3. Dyck P.J., Windebank A.J. Diabetic and nondiabetic lumbosacral radiculoplexus neuropathies: new insights into pathophysiology and treatment. Muscle Nerve 2002; 25(4): 477–491, doi: 10.1002/mus.10080.

4. Llewelyn D., Llewelyn J.G. Diabetic amyotrophy: a painful radiculoplexus neuropathy. Pract. Neurol. 2019; 19(2): 164–167, doi: 10.1136/practneurol-2018-002105.

5. Sobańska A. Diagnostyka różnicowa zaburzeń czucia. Neurol. Dypl. 2013; 8(1): 34–44.

6. Agarwal A., Srivastava M.V.P., Vishnu V.Y. Diabetic amyotrophy (Bruns-Garland syndrome): A narrative review. Ann. Indian Acad. Neurol. 2022; 25(5): 841–844, doi: 10.4103/aian.aian_239_22.

7. Glenn M.D., Jabari D. Diabetic lumbosacral radiculoplexus neuropathy (diabetic amyotrophy). Neurol. Clin. 2020; 38(3): 553–564, doi: 10.1016/j.ncl.2020.03.010.

8. Cohen K., Shinkazh N., Frank J., Israel I., Fellner C. Pharmacological treatment of diabetic peripheral neuropathy. P T 2015; 40(6): 372–388.