Case Report

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# Severe neurovascular hypertension in a 17-year-old girl cured by microvascular decompression

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We report a rare case of centrally caused hypertension in a 17-year-old adolescent due to neurovascular compression of the root entry/exit zone of the ninth/tenth cranial nerves of the rostral ventrolateral medulla oblongata on the left side.

The patient underwent a comprehensive diagnostic workup to exclude other causes of secondary hypertension. A cranial magnetic resonance imaging (cMRI) indicated a neurovascular compression. The patient underwent microvascular decompression (MVD) twice. After the first MVD, blood pressure values significantly decreased to normotensive levels without any antihypertensive medication. After one year without clinical symptoms, the patient experienced recurrent hypertension and underwent a second MVD. Again, the blood pressure normalized without any medication or clinical symptoms within six-month follow-up.

This case report highlights neurovascular compression at brainstem level as an important differential diagnosis of centrally caused hypertension, even in the absence of specific cranial nerve deficits. MVD is an effective treatment option.

**Keywords:** microvascular decompression, neurogenic hypertension, neurovascular compression, pediatrics, refractory arterial hypertension, rostral ventrolateral medulla oblongata

**Abbreviations:** BP, blood pressure; CISS, constructive interference in steady state; cMRI, cranial magnetic resonance imaging; CN IX–X, ninth and tenth cranial nerves; EEG, electroencephalography; mmHg, millimeter mercury column; MRA, magnetic resonance angiography; MVD, microvascular decompression; NHT, neurogenic hypertension; NTS, solitary tract nucleus; NVC, neurovascular compression; PICA, inferior posterior cerebellar artery; postop, postoperative; preop, preoperative; PSN, presympathetic neurons; REZ, root entry/exit zone; RVLM, rostral ventrolateral medulla; SNA, sympathetic nerve activity; VA, vertebral artery

## INTRODUCTION

Neurovascular compression (NVC) at the root entry and exit zone (REZ) of the ninth (glossopharyngeal) and tenth (vagal) cranial nerves (CN IX-X) at the rostral ventrolateral medulla oblongata (RVLM) on the left side can cause secondary arterial hypertension. This condition, described by Janetta as neurogenic hypertension, can be treated by neurosurgical microvascular decompression (MVD) normalizing blood pressure (BP) levels [1,2].

Hypertension due to compression of the RVLM involves dysfunction in the neural circuits regulating sympathetic nerve activity (SNA). The RVLM houses presympathetic neurons (PSNs), including C1 cells, that project excitatory signals to sympathetic preganglionic neurons controlling vascular tone. Their inhibition and impairment due to compression can disrupt the balance of SNA, leading to excessive sympathetic output to target organs, increased vascular resistance, and ultimately elevated BP [3].

While the global prevalence of hypertension in adults is around 32–34%, the proportion of hypertension for young adults from 18 to 39 years is approximately 22% and for children from 1–17 years approximately 2–4%. In children, 70–85% of hypertension are caused by secondary causes [4–6]. The prevalence of resistant hypertension (uncontrolled BP on ≥3 agents) is approximately 10–20%, of which circa 3% are refractory hypertensions (uncontrolled BP on ≥5 agents). MRI studies indicate that NVC of CN IX-X at the RVLM, predominantly on the left side, was observed in 74–90% of people with hypertension and in 7–22% of healthy people without hypertension [7–9]. Furthermore, other symptoms of these patients vary widely. While many patients are asymptomatic, others present with headache, nausea, vomiting, chest discomfort, epigastric pain, or sweating. Neurological deficits such as hemiparesis, dysesthesia, dizziness or cranial nerve deficits are also described [10,11].

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This case report presents an instance of centrally caused refractory hypertension in a 17-year-old adolescent due to NVC of CN IX-X at the RVLM on the left side. After excluding all potential causes for secondary hypertension, the patient was successfully treated by MVD twice.

## CASE REPORT

A 17-year-old, healthy girl in normal general and nutritional condition with no previous disease or medication described two episodes of a syncope, headache, dizziness, nausea, nosebleeds and palpation at her initial presentation in September 2022. All symptoms have been described as temporary. An initial ambulatory blood pressure measurement conducted by a primary care physician revealed significantly elevated blood pressure values. Consequently, a 24-h ambulatory blood pressure monitoring was performed, which showed average values of 150/101 mmHg during the day and 119/71 mmHg at night. Therefore, the patient was admitted to hospital for further diagnostics of secondary hypertension causes in October 2022. During this three-week hospital stay, elevated mean BP values of 143/94 mmHg with a maximum of 180/125 mmHg were detected while night dipping was present. The heart rate was regular. A detailed nephrological, cardiovascular, gastroenterological, endocrinological, neurological, neuropsychological examination as well as further diagnostics showed, except for a hypertonic fundus grade I/II on both eyes, no remarkable pathological results (Table 1). A sixfold antihypertensive medication with amlodipine 5 mg 2–0–0, clonidine 0.15 mg 1–0–1, hydrochlorothiazide 25 mg 0–1–0, metoprolol tartrate 50 mg 1–0–1, ramipril 10 mg 0–0–1 and nifedipine 20 mg 1–1–1 did not lead to normotension (BP $\leq$ 120/80 mmHg) [4]. The patient was hospitalized again in December 2022 due to a hypertensive emergency with seizures. Intravenous therapy with clonidine and dihydralazine was initiated, which led to a temporary reduction of BP to normotension. At this time, the 9-fold antihypertensive drug therapy consisted of amlodipine 5 mg 2–0–0, clonidine 0.15 mg 2–0–2, hydrochlorothiazide 25 mg 0–1–0, metoprolol succinate 47.5 mg 1–0–0, ramipril 10 mg 0–0–1, dihydralazine 12.5 mg 1–1–1, minoxidil 5 mg 1–0–1, spironolactone 25 mg 1–0–1 and nifedipine 20 mg 1–1–1 (Fig. 1a).

After four months of investigations without any potential secondary causes for refractory hypertension that have been discovered so far, and despite a ninefold regimen of partly intravenous antihypertensive medication, in January 2023, a cMRI was performed, which indicated NVC on the left side of CN IX-X of the RVLM and branches of the vertebral artery (VA). As well, an elongated inferior posterior cerebellar artery (PICA) on the right side. After weighing up chances and risks, surgical exploration and MVD was indicated. The surgery was performed in prone position under continuous neuromonitoring. The approach involved a laterally extended suboccipital craniotomy that exposed the cerebellar tonsils and brainstem. Vascular nerve contacts of CN IX-X on the left side with branches of the left VA were identified. Identification by stimulation of CN X led to slowing of the heart rate. Then, dissection of the NVC was performed using a Teflon sponge (Fig. 2a). After MVD, BP values decreased and were normotensive (preoperative (preop) mean systolic 156 mmHg, mean diastolic 97 mmHg vs. postoperative (postop) mean systolic 127 mmHg, mean diastolic 71 mmHg) without additionally antihypertensive medication (Fig. 1a). Clinical symptoms remained in complete remission within the one-year follow-up.

In February 2024, the patient reported temporary dizziness, recurrent nosebleeds and headache. Again, hypertensive BP values could be measured (preop mean systolic 165 mmHg, mean diastolic 109 mmHg) (Fig. 1b). Five-fold antihypertensive medication with intravenous clonidine and urapidil as well as oral metoprolol succinate 47.5 mg 1–0–0, enalapril 10 mg 1–0–1 and minoxidil 5 mg 1–0–1 was initiated. A renewed cMRI did not reveal a clear NVC. Due to the patients' medical history and sever intractable symptoms, a reoperation for MVD was suggested. Initially, the inserted Teflon sponge was found in the original position. Scar tissue was present that could have re-established contact with the nerve roots. Re-isolation of CN IX-X on the left side from branches of the VA was performed with implantation of a Teflon sponge (Fig. 2b). Postoperatively, all drug therapy could be discontinued due to normotension. Within the six months follow-up, the patient showed normalized BP values without the need for any drug therapy and no clinical symptoms were present (postop mean systolic 113 mmHg, mean diastolic 63 mmHg) (Fig. 1b).

## DISCUSSION

Guyenet postulated that NVC of the RVLM can lead to hypertension by disrupting the neural circuits regulating SNA. The RVLM harbors presympathetic neurons, including epinephrine-C1 neurons, and receives inputs from different nuclei e.g. the paraventricular hypothalamic nucleus, midline medulla, dorsomedial hypothalamic nucleus or arcuate nucleus. C1 neurons physiologically regulate the vascular tonus by sending excitatory glutamatergic signals via sympathetic preganglionic. NVC can inhibit these neurons and disrupt the SNA balance which results in excessive sympathetic output. If the baroreflex, modulated by the solitary tract nucleus (NTS) and caudal ventrolateral medulla, is simultaneously down-regulated, higher vascular resistance can occur leading to increased BP [3].

DeLalio investigated the role of chronic baroreceptor-activation. Physiologically, arterial baroreceptors, located in the aortic arch and carotid sinus, monitor the BP. Specialized pressure-sensitive sensory endings transmit BP information via A and C type nerve fibers, reaching the brainstem via CN IX-X and synapse with neurons in NTS. Elevated BP triggers increased baroreceptors activity. This signal, relayed to the brainstem, initiates a reflex response to lower BP by additional reducing sympathetic nerve activity due to decreased peripheral resistance and cardiac output. Simultaneously, parasympathetic nerve activity is increased lowering the cardiac output. NVC of REZ of CN IX-X of the RVLM can disrupt this coordinated regulation [12].

Hering examined pulsatile vascular compression between vessels and nerves at the REZ of CN IX-X of the RVLM. The compression mostly arises from PICA or VA

**TABLE 1. Differential diagnosis**

| Disorders | Tests | Results |
|---|---|---|
| Adrenal-related | | |
| primary aldosteronism, mineralocorticoid excess syndromes | Serum aldosterone and renin, potassium | Aldosterone 64.8 ng/l (reference 25.2–392), renin 33.6 mU/l (reference 2.8–46.1), ARR 1.93 (reference <12) |
| Genetic-related | | |
| Liddle Syndrome, Pseudo Hyperaldosteronism type II | Genetic testing | Unremarkable |
| Heart-related | | |
| heart rate | Clinical examination, pulse measurements | Normal, Unremarkable |
| valve stenosis or insufficiency, increased cardiac output | Transthoracic echocardiogram | Unremarkable |
| Kidney-related | | |
| parenchymal or urinary tract disease | Serum creatinine, eGFR, electrolytes (sodium, potassium, calcium, phosphorus), serum UA, urinalysis, CBC, lipid profile | Unremarkable |
| renal artery stenosis | angiography, renal artery duplex ultrasonography | Unremarkable |
| Neurogenic-related | | |
| CNS infection | Lumbar puncture, CSF culture and PCR | Unremarkable |
| CNS lesions (stroke, tumor, hemorrhage, trauma, compression of lateral medulla) | cMRI | Vascular compression of the left rostral ventrolateral medulla, prolonged PICA right side, otherwise unremarkable |
| Fundus hypertonicus | Fundoscopy | hypertonic fundus grade I/II on both eyes |
| Neurological symptoms | Clinical examination | syncope, headache, dizziness, nausea, nosebleeds |
| Seizures, migraine | EEG | once while hypertensive crisis otherwise unremarkable |
| Others | | |
| drugs and toxins | Laboratory tests | Unremarkable |
| ear, nose, throat conditions | Otoscopy, rhinoscopy, laryngoscopy | Unremarkable |
| gastrointestinal conditions | Ultrasonography | Unremarkable |
| gynecological conditions | Ultrasonography | Unremarkable |
| porphyria | Hoesch test | Unremarkable |
| psychogenic | Child psychiatrist consultation | Unremarkable |
| systemic infections | CBC, CRP | Unremarkable |
| (Para)thyroid-related | | |
| Hyperparathyroidism | Serum iPTH, calcium, phosphorus | Unremarkable |
| Hyper/hypothyroidism | TSH, T3 and free T4 hormones | Unremarkable |
| Pheochromocytoma and paraganglioma | hormone vanillic acid (24-h urine), vanillin mandelic acid (24-h urine) | hormone vanillic acid 3.1 nmol/μmol Crea urine, reference upper normal value 7.95, vanillin mandelic acid 4.0 nmol/μmol Crea urine, reference upper normal value 4.72 |
| adrenal congenital hyperplasia | Testosterone, DHEA-S, ACTH | Unremarkable |
| Pituitary-related | | |
| Acromegaly | GH and IGF-1 | Unremarkable |
| Morbus Cushing | Serum cortisol, ACTH, morning cortisol levels in saliva | Unremarkable, Unremarkable, slightly elevated (9.9 μg/l) |
| Rheumatism and Collagenoses related | | |
| Sjörgens syndrome, systemic lupus erythematosus, mixed collagenosis, scleroderma | SjS, SLE, U1 RNP, SM, SSA, SSB, Scl-70, Jo-1 | Unremarkable |
| Risk Factors | | |
| height, weight, family history, unhealthy lifestyle | Clinical history and examination | 169 cm (72nd percentile), 48,5 kg (9th percentile), all Unremarkable |
| Vascular-related | | |
| coarctation of aorta and other cardiac diseases | Ankle-brachial index, cardiovascular auscultation/palpation, 12-lead ECG, transthoracic echocardiogram, MRI | Unremarkable |
| Vasculitis and collagen vascular diseases | ANA, ANCA, C3, C4, CRP, ESR, liver and kidney function tests | Unremarkable |

Here, all the differential diagnosis which were considered and tested. As well, the results are presented.
ACTH, adrenocorticotropic hormone; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; C3, complement component 3; C4, complement component 4; CBC, complete blood count; CNS, central nervous system; Creatinine (crea), serum creatinine; CRP, C-reactive protein; DHEA-S, dehydroepiandrosterone sulfate; EEG, electroencephalogram; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; GH, growth hormone; IGF-1, insulin-like growth factor 1; iPTH, intact parathyroid hormone; Jo-1, histidyl-tRNA synthetase antibody; PCR, polymerase chain reaction; Scl-70, scleroderma antibody; Serum UA, serum uric acid; SjS, Sjögren's syndrome; SLE, systemic lupus erythematosus; SM, Smith antibody; SSA, Sjögren's syndrome antibody A; SSB, Sjögren's syndrome antibody B; T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone; U1 RNP, U1 ribonucleoprotein antibody.

branches. Oxygen deficiency resulting from the compression is likely to cause deafferentation of the NTS leading to loss of inhibitory effect transmitted from the NTS and sympathoexcitation of C1 neurons [13]. As a new neurosurgical treatment option, vagal modulation triggers a reduction of sympathetic activity and increase in parasympathetic tonus leading to reduced BP. However, long-term effectiveness and follow-ups are needed [14].

Here, we present a case of a young adolescent with refractory hypertension treated succesfully by MVD twice.

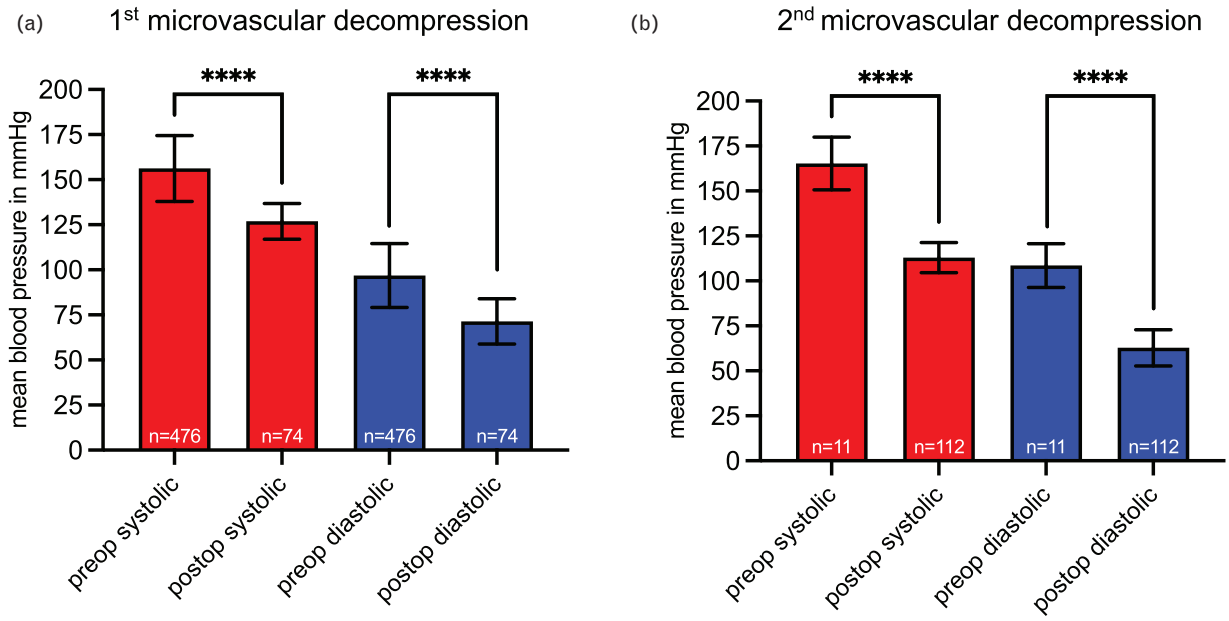


**FIGURE 1** BP values before and after MVDs. From September 2022 to June 2024, noninvasive and invasive BP measurement was regularly taken multiple times per day with a maximum of four measurements per day which went into analysis. In case of invasive BP measurement, mean values of morning, noon, evening and night were used. (a) After 1st MVD, preop mean systolic 156.2 mmHg and mean diastolic 96.9 mmHg BP values (measured from initial presentation in September 2022 until the 1st MVD) significantly decreased to postop mean systolic 126.9 mmHg and mean diastolic 71.4 mmHg ($n = 476$ for preop values and $n = 74$ postop values; mean systolic difference $-29.3 \pm$ SEM 2.2 and 95% confidence interval $-33.6$ to $-25.0$, mean diastolic difference $-25.4 \pm$ SEM 2.1 and 95% confidence interval $-29.6$ to $-21.2$). (b) After 2nd MVD, mean systolic 165.3 mmHg and mean diastolic 108.5 mmHg BP values (measured from February 2024 until the 2nd MVD) significantly decreased to postop mean systolic 112.9 mmHg and mean diastolic 62.8 mmHg ($n = 11$ for preop values and $n = 112$ postop values; mean systolic difference $-52.3 \pm$ SEM 2.9 and 95% confidence interval $-58.0$ to $-46.6$, mean diastolic difference $-45.7 \pm$ SEM 3.2 and 95% confidence interval $-52.1$ to $-39.3$). Unpaired Student's *t*-test ****$P$ value $< 0.0001$. Column bar graph shows mean with standard deviation. *x*-axis shows systolic and diastolic state preop and postop, *y*-axis shows BP values in mmHg. preop = preoperative. postop = postoperative. SEM = standard error of the mean.

The reported symptoms syncope, temporary headache, dizziness, nausea, nosebleeds, and palpitations, were not typical manifestations of CN IX-X dysfunction. Instead, they align with long-term elevated BP values and hypertensive crisis. While intravenous treatment with clonidine and urapidil could normalize the BP, 9-fold oral treatment was ineffective. Nonadherence regarding medication intake could be ruled out by supervised intake. However, concentration measurements and drug levels from blood or urine were not determined. A medication response test was not performed, which could have identified the patient as a potential nonresponder. Moreover, no oral alpha-blocker was prescribed which could be considered [15].

The patient's successful treatment twice suggests MVD's efficacy in refractory hypertension. Nevertheless, several studies show a transient effect of MVD [10], which we can also confirm. To date, there are no prospective efficacy studies that indicate objective selection criteria for MVD in patients with neurogenic hypertension. Based on our case report we suggest in cases of resistant/refractory hypertension, that all potential differential diagnoses should be investigated first. If there are no conclusive findings, centrally caused hypertension by NVC of the REZ of CN IX-X of the RVLM should be considered as a differential diagnosis, even in the absence of specific cranial nerve deficits. Then, a thin-layer cMRI/MRA with CISS-sequences should be

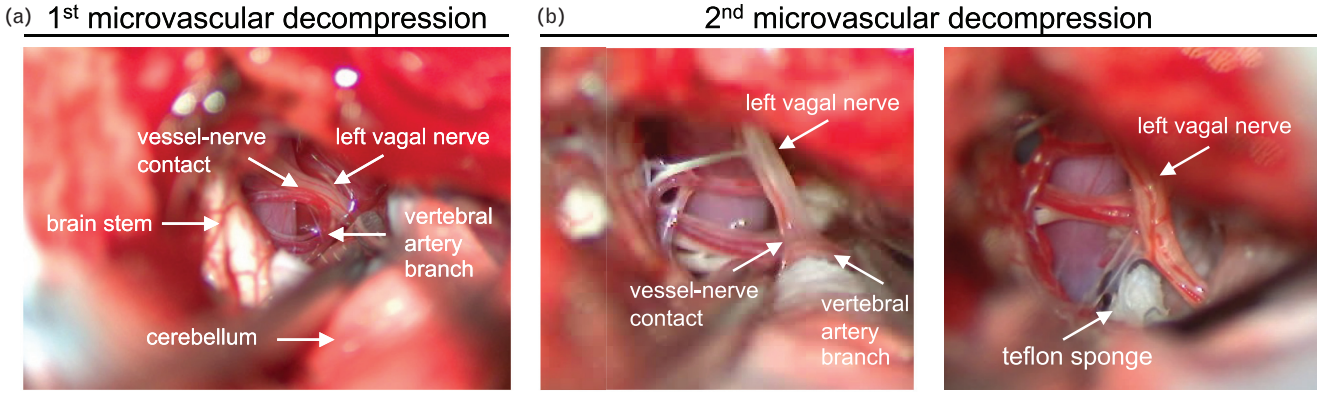


**FIGURE 2** Intraoperative anatomy of 1st and 2nd MVD. Intraoperative anatomy in both operations showing a vessel-nerve contact of the left vagal nerve at the REZ of the RVLM and a vertebral artery (VA) branch and (a) anatomy before first MVD, (b) anatomy before and after second MVD.

performed. The results should be discussed in an interdisciplinary setting with hypertension specialists, neuroradiologists and neurosurgeons considering potential benefits and risks of the operation.

Finally, this case report presents an instance of a 17-year-old adolescent with centrally caused resistant/refractory hypertension due to NVC of the left REZ of CN IX-X of the RVLM. The patient was successfully treated by MVD twice leading to normal BP levels after both operations which indicates MVD as potential causal treatment option in these cases.

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### Conflicts of interest

There is no conflict of interest.

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