

Anorexia Nervosa and Peripheral Vasospasm: A Case Report

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Abstract

Anorexia nervosa is an eating disorder associated with several medical conditions that are directly related to weight loss and starvation, including cardiovascular events and peripheral vascular disorders. We present a case report of a 15-year-old girl with anorexia nervosa and a severe peripheral vasospasm event which correlates directly with a decrease in body mass index without any other risk factor identified. Severe ischemia, as a complication of anorexia nervosa, is not common but has been reported in previous case reports, however, with other risk factors besides anorexia nervosa. Even though the exact pathophysiological mechanisms that predispose patients to vasculopathy in anorexia nervosa are still unknown, the likelihood of these complications increases as the patient further loses weight. Therefore, nutritional rehabilitation is fundamental to avoid these complications.

Keywords: Adolescent; Anorexia Nervosa/complications; Body Mass Index; Lower Extremity/blood supply; Peripheral Vascular Diseases/etiology

Keypoints

What is known:

- Anorexia nervosa is associated with several medical complications directly related to weight loss and starvation.
- Management of anorexia nervosa is still a challenge and patients should be followed by a multidisciplinary team.

What is added:

- The mechanism of vascular abnormalities in anorexia nervosa is still unclear, but complications increase as the patient further loses weight.
- Benign peripheral vascular disorders are more common, but severe ischemia can also occur.
- A thorough laboratory assessment is required to exclude other disorders, including autoimmune diseases.

Introduction

Eating disorders represent a group of mental health problems characterized by a persistent disturbance of eating or eating-related behavior that results in altered consumption or absorption of food, significantly impairing physical health or psychosocial behavior.

Anorexia nervosa is characterized by a restriction of energy intake, leading to significantly low body weight, associated with an intense fear of gaining weight and distorted perception of body weight and shape.¹ The prevalence of anorexia nervosa in adolescents is unknown. It has been reported to be 0.3% in the United States population.²

It has also been reported that the incidence of anorexia nervosa is increasing in younger girls aged < 15 years.³ Anorexia nervosa has the highest fatality rate of all

mental health disorders.⁴ Roughly half of death events are attributable to physical complications associated with weight loss and starvation.⁵

Malnutrition can virtually affect any organ. Aside from cardiovascular complications, such as bradycardia, hypotension, or arrhythmias, anorexia nervosa is also associated with such peripheral vascular disorders as acrocyanosis, erythema pernio, or Raynaud phenomenon. The conditions inducing vasospasm can lead to nonocclusive arterial ischemia. Although not common, severe peripheral ischemia has been reported in association with anorexia nervosa. However, it has always been associated with other risk factors besides anorexia nervosa.^{6,7} This study presents a case of a patient with anorexia nervosa and severe peripheral vasospasm, without any other risk or causal factor identified besides the decrease in body mass index (BMI).

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Case Report

A 15-year-old girl was admitted to the emergency room for bilateral foot edema and right foot paresthesia during the last 24 hours. No history of trauma, smoking habits, or new drug intake was reported. The patient was medicated with atomoxetine, 50 mg/day, for the last six months. There was no history of previous similar events.

The patient presented with the following vital signs and anthropometric parameters: blood pressure 104/44 mmHg, heart rate 77 bpm, axillary temperature 36°C, weight 58.5kg; height 168.5cm (+0,88 SD); BMI 20.6kg/m² (-0.03SD). On physical examination, she had bilateral edema with erythema of both feet. We also observed bilateral erythematous lesions suggestive of erythema pernio and a dystrophic toenail on the right foot (Fig. 1). Additionally, her hands and feet were cold. There were not any other skin color abnormalities. However, the patient mentioned previous episodes of blackening toes. Right posterior tibial and pedal pulses were absent without motor deficits. Arterial Doppler ultrasound revealed a triphasic flow at the right anterior tibial artery and a monophasic flow at the right posterior tibial artery and *dorsalis pedis* artery, suggestive of vasospasm. The patient was treated with a 14-day course of low molecular weight heparin (single administration of enoxaparin 1.4 mg/kg/dose, followed by tinzaparin 10 000 IU, once a day) and seven days of pentoxifylline (400 mg, three times a day). A marked improvement was observed since the fifth day of therapy.

The patient had been diagnosed with anorexia nervosa eight months prior to the event (Fig. 2, point B). At the first medical visit (multidisciplinary team with a pediatrician and pediatric psychiatrist), it was found that the patient was already being visited by a nutritionist,

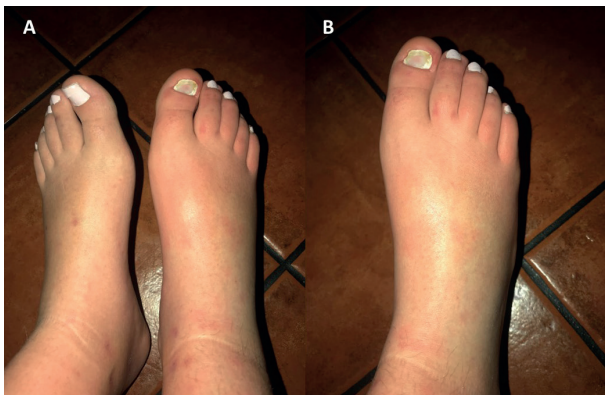


Figure 1. Self-photos taken before emergency room observation showing both feet with bilateral edema, erythema, and erythematous lesions suggestive of erythema pernio in addition to a dystrophic toenail on the right foot (A) and details of right foot (B).

resulting in partial correction of the restrictive diet she had been following in addition to excessive physical activity.

She was also amenorrheic (after menarche at 11-years-old) for almost four months. The patient had an initial recovery and satisfactory evolution during the first four months (Fig. 2, point B to C) and had menstrual bleeding twice (Fig. 2, point C to D).

The time-event of vasospasm matched the point E in Fig. 2, showing overlap with a severe decrease in BMI. The difference between maximum BMI of 27.4 kg/m² (point A) and BMI of 20.6 kg/m² (point E) corresponded to a total weight loss of 24%.

Laboratory assessment after the vasospasm event excluded the diagnosis of vasculitis, autoimmune diseases, and thrombophilia. Prior severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was also excluded. No other alterations were found except for factor VII deficit (Table 1). The patient had no history of dyslipidemia. During follow-up, there was no other severe vascular intercurrent, despite persistent weight loss in the following six months (Fig. 2).

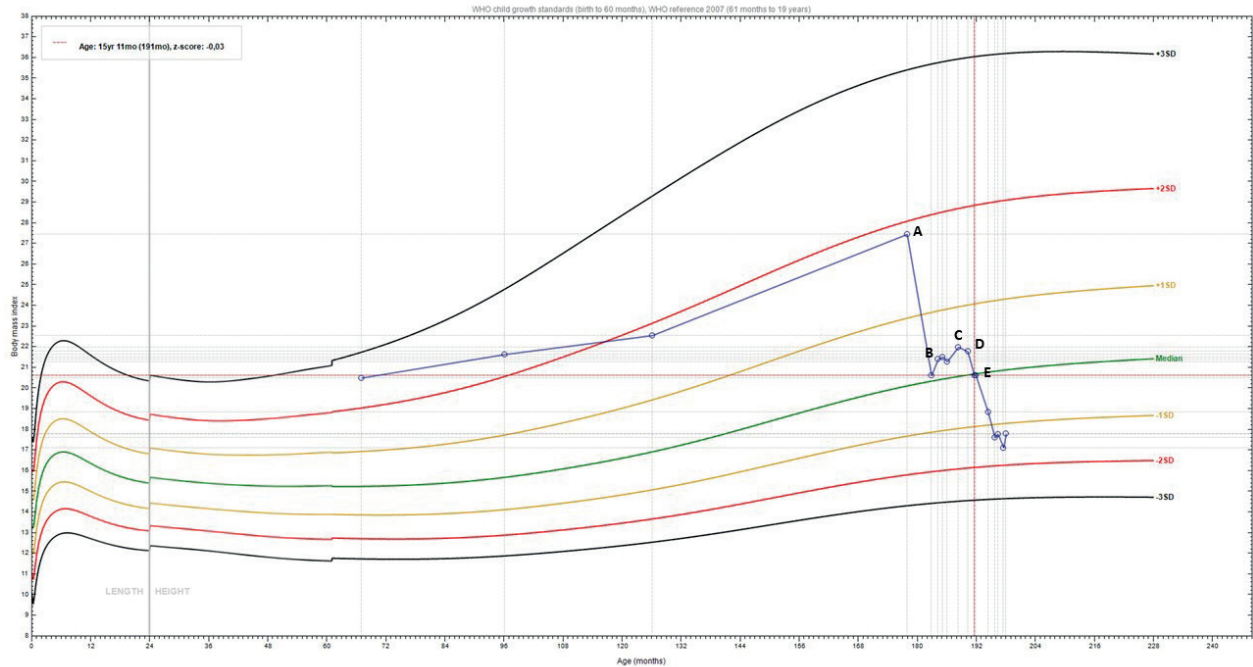
Discussion

Anorexia nervosa has been broadly associated with peripheral vascular disorders such as acrocyanosis and Raynaud phenomenon. The reason for the occurrence of such disorders is still unclear. It has been hypothesized that it can be due to dysregulation between peripheral vasoconstriction and vasodilatation.⁸ Weight loss can also lead to a loss of subcutaneous and perivascular adipose tissue, which in turn leads to an increase in vasospastic events.⁸

Acrocyanosis could represent a more extreme form of heat-conserving mechanisms that are not uncommon in anorectics.⁹ Severe ischemia is not common but has been reported.^{6,7,10}

However, previous case reports indicated other risk factors besides anorexia nervosa. In the presented case, the vasospasm event led to acute lower limb ischemia with the pale and cold right foot with paresthesia (degree IIa of Rutherford acute limb ischemia classification¹¹), and the only apparent risk factor was the severe BMI decrease in a teenager with anorexia nervosa. To our knowledge, our findings have not been reported in any other case reports.

Even when considering the potential role of anorexia nervosa in the vasospasm event, it is crucial to exclude any other disease or risk factor for vascular complications, including drug intake. A bidirectional



mo - months; yr - years.
 Point A: maximum body mass index 27.4 kg/m² at 14 years and 9 months. Point B: first medical visit and anorexia nervosa diagnosed, body mass index 21.4 kg/m² at 15 years and 4 months. Point C: first menstrual bleeding after seven months of amenorrhea, body mass index 22 kg/m² at 15 years and 8 months. Point D: last menstrual bleeding, BMI 21.8 kg/m² at 15 years and 10 months. Point E: vasospasm event, body mass index 20.6 kg/m² at 15 years and 11 months.

Figure 2. Body mass index evolution and relevant events.

Table 1. Laboratory assessment after the vasospasm event (only relevant results)

Analysis / test	Result	Reference values / interpretation
Autoimmunity		
Antinuclear antibodies (ANA)	negative	-
Antibodies against Ro/SSA and La/SSB, Sm, RNP, Scl70, JO1	negative	-
Cytoplasmic antineutrophil cytoplasmic antibodies (anti-C-ANCA)	negative	-
Perinuclear antineutrophil cytoplasmic antibodies (anti-P-ANCA)	negative	-
Antibodies anti-mieloperoxidase (anti-MPO)	negative	-
Antibodies anti-proteinase 3 (anti-PR3)	negative	-
Infection markers		
Anti-SARS-CoV-2 IgG	0.120	NR < 0.7, R ≥ 1.4
Anti-SARS-CoV-2 IgM	0.030	NR < 1.0, R ≥ 1.0
Hemostasis		
INR	1.26	Normal
PT (seconds)	14.9	10.0-14.1
aPTT (seconds)	38.2	24.6-38.4
Factor VII*	39 %*	55.4-133.1
Molecular studies		
PRT20210 G/A	normal	-
Factor V Leiden	normal	-
Thrombophilia risk: F2, c.20210G>A; F5, c.1691G>A, p.R506Q	negative	-

aPTT - activated partial thromboplastin time; Ig - immunoglobulin; INR - international normalized ratio; NR - not reactive; PT - prothrombin time; R - reactive; SARS-CoV-2 - acute respiratory syndrome coronavirus 2.

* Abnormal values.

relationship was reported between eating disorders and autoimmune diseases in females.¹² In our case report, all the laboratory assessments were negative. However, some analysis could have also been added, such as D-dimer, antiphospholipid antibodies, protein C, and protein S, due to their potential association with thrombotic events. Atomoxetine was the only medication the patient was taking (50 mg daily).

Even though severe cardiovascular and vasospasm events have been associated with drugs used for attention deficit hyperactivity disorder, mostly after overdosing,¹³ there are no reports of vasospasm leading to severe limb ischemia with the use of atomoxetine. Of note, an incidence rate of 1%-3% was reported for cold extremities during atomoxetine use.¹⁴

The patient was treated with a temporary course of anticoagulant therapy to prevent distal artery thrombosis during the vasospastic event. The association with a vasodilator therapy such as pentoxifylline led to the increase of blood flow to the affected microcirculation. The patient had a full recovery. During the follow-up, there were not any other vascular complications besides cold extremities, but always with palpable pulses, even with persistent weight loss.

Further investigation is required to clarify the association between anorexia nervosa and vascular disorders, which can help identify both patients at risk and new therapeutic targets.

This case report shows severe peripheral vasospasm in a patient with anorexia nervosa, without any other risk or causal factor identified besides the decrease in BMI.

Peripheral vascular disorders are known complications of

anorexia nervosa and the clear mechanisms are still not clear. The same as most eating disorder complications, anorexia nervosa is associated with nutritional status, and the likelihood of disease complications increases as the patient further loses weight.⁴

Author Contributions

AIM, RC and JS participated in the study conception or design. AIM, RC and JS participated in acquisition of data. AIM, RC and JS participated in the analysis or interpretation of data. AIM, RC, JS and JN participated in the drafting of the manuscript. PF participated in the critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013).

Provenance and peer review

Not commissioned; externally peer reviewed

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Anorexia Nervosa e Vasoespasmo Periférico: Caso Clínico

A anorexia nervosa é um transtorno alimentar associado a diversas condições médicas relacionadas diretamente com perda de peso e inanição, incluindo eventos cardiovasculares e alterações vasculares periféricas. Relatamos o caso clínico de uma adolescente de 15 anos com anorexia nervosa e um evento de vasoespasmo periférico grave correlacionado diretamente com uma diminuição do índice de massa corporal e sem qualquer outro fator de risco identificado. A isquemia grave, como complicação da anorexia nervosa, não é comum. Foi relatada em casos anteriores, mas com outros fatores de risco presentes além da anorexia

nervosa. Embora os mecanismos fisiopatológicos exatos que predisõem os doentes a vasculopatia na anorexia nervosa não sejam conhecidos, a probabilidade destas complicações aumenta com a perda de peso. Assim, a reabilitação nutricional é fundamental para evitar essas complicações.

Palavras-Chave: Adolescente; Anorexia Nervosa/complicações; Doenças Vasculares Periféricas/etiologia; Extremidade Inferior/irrigação sanguínea; Índice de Massa Corporal