Received: 19 May 2023 | Revised: 17 November 2023 | Accepted: 29 November 2023

DOI: 10.1002/ccr3.8322

CASE REPORT

Clinical Case Reports Open Access WILEY

Transient perivascular inflammation of the carotid artery—A transient but potentially recurrent disease

Marieta Peycheva[1,2] | **Tina Zdravkova**[3] | **Dora Zlatareva**[3,4] | **Ekaterina Viteva**[1] | **Zdravka Harizanova**[5] | **Thomas R. Meinel**[6] | **Mirjam R. Heldner**[6]

[1]Department of Neurology, Medical University Plovdiv, Plovdiv, Bulgaria

[2]Research Institute, Medical University Plovdiv, Plovdiv, Bulgaria

[3]Translational Neuroscience Complex, Medical University of Plovdiv, Plovdiv, Bulgaria

[4]Department of Imaging Diagnostics, Medical University of Sofia, Sofia, Bulgaria

[5]Department of Human Anatomy, Histology and Embryology, Medical University of Plovdiv, Plovdiv, Bulgaria

[6]Inselspital, University Hospital and University of Bern, Bern, Switzerland

Correspondence
Mirjam R. Heldner, Inselspital, University Hospital and University of Bern, Freiburgstrasse 10, Bern, Switzerland.
Email: mirjam.heldner@insel.ch

Funding information
Medical University Plovdiv, Grant/Award Number: project code 17/2020

Key Clinical Message

Transient perivascular inflammation of the carotid artery (TIPIC syndrome) is a rare, unclassified vascular syndrome that usually affects the distal part of the common carotid artery and has a favorable prognosis. The disease is often misdiagnosed even by neurologists due to the moderate intensity of clinical symptoms and their transient character. We present a case of a 52-year-old man who experienced two episodes of transient neck pain and moderate local tenderness one and a half years apart. Different imaging modalities, such as ultrasound, CT angiography, and high-resolution 3T MR, were applied to better visualize the perivascular inflammation of the common carotid arteries. Based on the clinical-radiological characteristics of our case and applying the diagnostic criteria, we established the diagnosis of TIPIC syndrome. The patient was treated with nonsteroidal anti-inflammatory drugs for few weeks, and reduction in perivascular changes was observed in both episodes. The case raises questions about the phases of the disease, its duration and the intervals between follow-ups. Our article also increases the awareness of this rare clinical-radiological entity and presents recent data from the literature.

KEYWORDS

carotidynia, neck pain, perivascular infiltration, TIPIC syndrome

1 | INTRODUCTION

Transient perivascular inflammation of the carotid artery (TIPIC syndrome) is a rare, unclassified vascular syndrome with a prevalence of 2.8% in patients with acute neck pain.[1,2] The disease usually affects the distal part of the common carotid artery and was thought to have a monophasic course with a favorable prognosis after treatment with anti-inflammatory drugs.[2,3]

2 | CASE DESCRIPTION

A 52-year-old man visited the neurology clinic at the University Hospital "Saint George" Plovdiv, Bulgaria, in June 2021. He had moderate but persistent neck pain (4 points on the VAS pain score) on the right side and tinnitus. His complaints started 1 month ago, and he recalled a fall while descending stairs without a head injury 6 months ago. The patient was a smoker and suffered from

arterial hypertension and dyslipidemia. Pathological findings were not observed on his physical and neurological examination. There was no local swelling or bruising, but there was mild tenderness at the site. An ultrasound examination revealed an irregular longitudinal thickening of the anterior wall of the right common carotid artery near the bifurcation (Figure 1A,B). The patient was sent for CT angiography, which did not show local stenosis (Figure 1C), but mild wall hyperdensity at the site (Figure 1D). On high-resolution 3T magnetic resonance imaging (Figure 2A), an eccentric spindle-shaped thickening of the right common carotid artery wall was found. The lesion affected the middle and distal segments of the artery on the ventral side and was 28 mm long with the largest width being 5 mm. Postcontrast T1-weighted magnetic resonance imaging revealed an eccentric enhancement around the carotid artery in a perivascular but not clearly delimited manner (Figure 2B). Laboratory investigations of the patient showed normal values for high-sensitivity C-reactive protein and erythrocyte sedimentation rate. Hence, differential diagnoses such as vasculitis, carotid dissection, thrombus, and local infections were considered unlikely. Based on the clinical-radiological characteristics of our case and applying the diagnostic criteria, we established the diagnosis of TIPIC syndrome. The patient was treated with a nonsteroidal anti-inflammatory drug (ibuprofen) for 4 weeks, after which the wall thickening decreased and his symptoms disappeared completely. High-resolution 3T control MR 1 year later showed resolution of the wall thickening without contrast enhancement on T1-weighted images (Figure 2C). At the end of 2022, one and a half years after his first event, the patient again complained of neck pain, this time on the contralateral (left) side. He denied any new trauma or other trigger factors. Ultrasound examination showed a hypoechogenic eccentric lesion about 2 mm wide and 15 mm long in the anterior part of the left common carotid artery near the bifurcation (Figure 2D,E). Laboratory investigations of

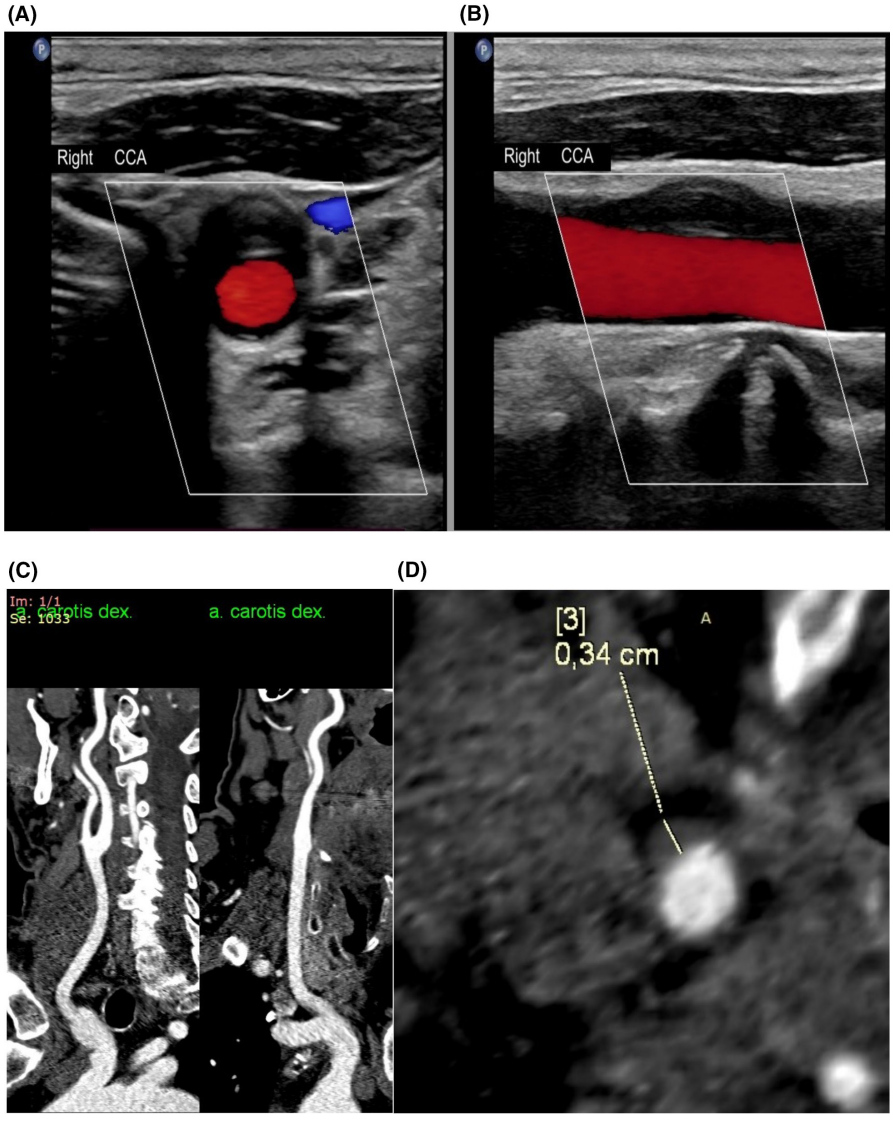


FIGURE 1 Images of the right common carotid artery in longitudinal and transverse views on ultrasound (A, B), on CT angiography (C), and wall thickening and mild hyperdensity of perivascular infiltration in transverse view on CT (D).

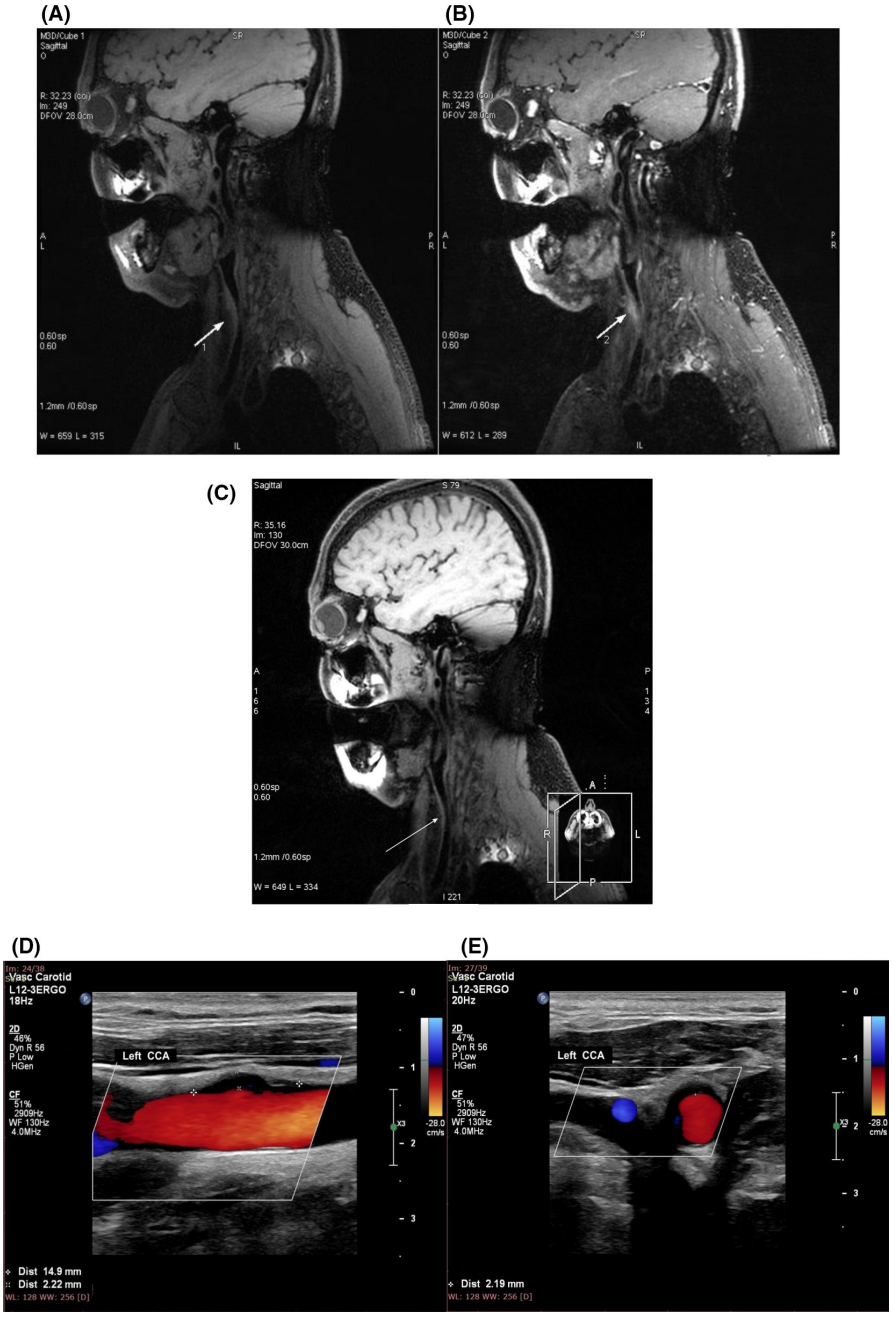


FIGURE 2 3T magnetic resonance T1-weighted images of the right common carotid artery before and after contrast (A, B) and at follow-up 1 year later (C), and ultrasound images of the left common carotid artery in longitudinal and transverse views one and a half years later (D, E).

the patient revealed normal values for high-sensitivity C-reactive protein, erythrocyte sedimentation rate, complete blood count, thyroid hormones, liver and renal function tests, coagulation tests, serology for herpes simplex virus and herpes zoster virus, Ebstein–Barr virus, hepatitis B virus, and hepatitis C virus. The patient was evaluated by a rheumatologist for vasculitis and antinuclear antibodies, and the test for rheumatoid factor and lupus erythematosus antibodies was negative. The patient was treated again with a short course of nonsteroidal anti-inflammatory drugs, and a follow-up examination after 1 month showed a decrease in the wall thickening of the left common carotid artery.

3 | DISCUSSION

The first clinical description of the disease was done in 1927 by Dr. Fay, who introduced the term carotidynia in the context of atypical neuralgia.[4] The symptom of local tenderness when light pressure is applied on the neck was called Fay's sign. In 1988, the International Classification of Headache Disorders included it as an atypical headache syndrome.[5] It was later excluded from this classification due to controversy whether carotidynia was a distinct clinical entity or a diagnostic symptom of another disease like vasculitis, carotid dissection, sialadenitis, trigeminal neuralgia, and oropharyngeal infections.[6,7]

The hypothesis that the disease is caused by a transient inflammatory process is based mainly on radiological findings and limited histological findings, where lymphocytic infiltration and fibroblast proliferation were observed in the vessel wall.[8] However, the pathogenesis and trigger factors are still unknown, as the symptom may occur in isolation or in association with a neighboring infection or autoimmune disease.[1,2,9]

Imaging features of this entity include signs of perivascular tissue inflammation and vascular involvement such as thickening of the carotid adventitia or the presence of smooth plaques in the intima with slight luminal narrowing but without hemodynamically significant change in blood flow.[1,2]

Based on clinico-radiological features, Lecler et al.[1] introduced the term transient perivascular inflammation of the carotid artery (TIPIC syndrome) and proposed the following diagnostic criteria: (1) presence of acute pain overlying the carotid artery, which may or may not radiate to the head; (2) eccentric perivascular inflammation on imaging; (3) exclusion of another vascular or nonvascular diagnosis with imaging; and (4) improvement within 14 days either spontaneously or with anti-inflammatory treatment.

Two retrospective observational studies with a small cohort of patients are described in the literature.[1,2] The median age of the patients was 48 years with a slight female predominance in both studies. The clinical symptoms were of moderate intensity and self-limiting. In approximately 90% of cases, the main symptom was unilateral transient neck pain. Other signs were local edema (29%), lymphoadenopathy (17%), headache (11%), and fever (6%).[2] Differential diagnoses such as vasculitis, carotid dissection, thrombus, or local infections could be considered[1,2,7] (Table 1). Clinical symptoms that could give rise to a suspicion of the disease were painful palpation or local tenderness (92.9%) and unilateral localization of the pain (92.3%) with moderate intensity (67.7%).[2] The most typical radiological predictor is an eccentric lesion (83.3%) affecting the wall of the common carotid artery or carotid bulb (58.3%), easily visualized by ultrasound.[2]

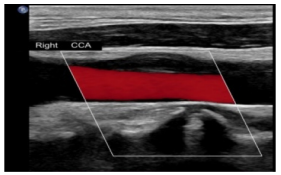
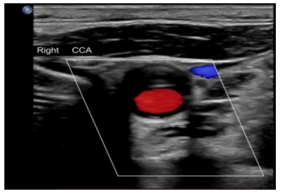
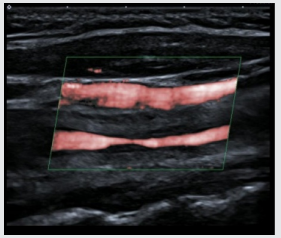
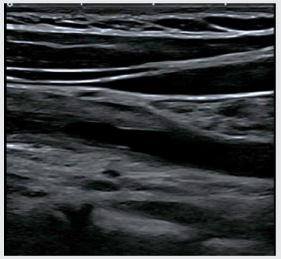
The TIPIC syndrome was thought to have a monophasic course with a favorable prognosis after treatment. Lecker et al.[1] followed 48 cases for a mean period of 3 months. A complete decrease in perivasular changes was observed in 8 of 47 patients and a marked decrease in all. Full clinical recovery was described in all patients, with a median delay of 13 days. The recurrence rate was reported to be 19%, with the same clinical and imaging abnormalities seen at the first presentation. Most of the patients with documented relapse (7 of 9 patients) had a concomitant autoimmune disease. Micieli et al.[2] described the results of 72 patients included in a collaborative multinational study. The authors reported an average of 17 days of symptoms resolution. A linear correlation was observed between baseline and follow-up values regarding the thickness and the length of the carotid lesions, but a possible correlation with the onset and the duration of symptoms was not explored. The recurrence rate after a mean follow-up of 6 months was 18.6%, with a peak in the first 2 weeks. The authors suggested follow-up visits at 14 and 90 days and 1 year later, but noted that data on the long-term course of the disease were lacking. The suggestion that the disease may have a chronic course is also supported by evidence of early fibrosis and vascular proliferation in the only histological report described in the literature.[8] These findings raise questions about the phases of the disease and the duration and intervals of follow-ups. We suggest that patients with proven TIPIC syndrome should be followed up long-term every 6–12 months for the first 5 years and annually thereafter if there are no new or recurrent symptoms requiring urgent evaluation. In case of no clinical improvement, atypical presentation, or frequent recurrent episodes, a concomitant autoimmune disease should be considered.

Imaging is the gold standard investigation for the diagnosis of TIPIC syndrome.[9] Various studies addressed the issue of which techniques can best be used to diagnose and follow up the syndrome.[1,10,11] B-mode ultrasound and magnetic resonance imaging can easily visualize perivascular and intravascular changes,[9,12,13] whereas CT angiography and DSA may miss pathology as vascular stenosis or occlusion are not typical.[14] 18F-FDG positron emission tomography can also be used to evaluate patients with TIPIC syndrome showing abnormal radiotracer uptake in the carotid artery wall and in cases when oncologic or systemic disease is suspected.[15] As ultrasound is noninvasive, radiation-free, and easily reproducible, it has been shown to be the tool of choice for the evaluation of TIPIC syndrome, especially when contrast enhancement is applied to demonstrate perivascular inflammation.[1,2,11]

4 | CONCLUSION

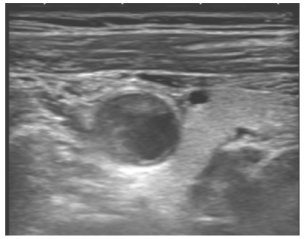
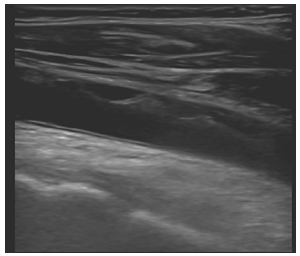
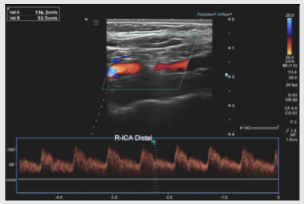
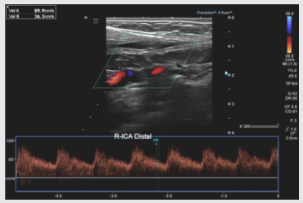
Transient perivascular inflammation of the carotid artery is a rare, clinico-radiological entity that can easily be misdiagnosed even by neurologists due to the moderate intensity of clinical symptoms and their transient character. Long-term follow-ups are needed as recurrent episodes are possible.

TABLE 1 Differential diagnosis of vascular diseases with symptoms and imaging findings similar to TIPIC syndrome.

Disease	Clinic	Laboratory findings	Imaging/description of findings	Stroke risk and prognosis	Treatment
TIPIC syndrome	• Local pain at the level of the carotid artery with irradiation towards the neck and face • local swelling • lymphadenopathy • fever • headache	Slightly elevated inflammatory biomarkers possible	  Perivascular hypoechoic lesion affecting common carotid artery without artery stenosis (longitudinal and transverse views)	No risk for stroke, favorable prognosis but possible recurrent episodes	Nonsteroidal anti-inflammatory drugs or corticosteroids
Vasculitis	• Headache • focal neurological deficits • cognitive impairment • seizures • fever • systemic manifestation	Elevated inflammatory biomarkers, immune complexes, or antibodies	  Long and homogeneous concentric arterial wall thickening of the common carotid artery with artery stenosis in Takayasu's arteritis	Increased risk of ischemic or hemorrhagic stroke, stepwise or progressive course of the disease	Corticosteroids or immunosuppressive drugs

(Continues)

TABLE 1 (Continued)

Disease	Clinic	Laboratory findings	Imaging/description of findings	Stroke risk and prognosis	Treatment
Cervical artery dissection	• Local pain • headache • Horner's syndrome • tinnitus • cranial nerve palsy • focal neurological deficits	No abnormal findings	  Double lumen and intraluminal flap in common carotid artery dissection with artery stenosis (transverse and longitudinal views)	Low risk of ischemic stroke, favorable prognosis of the disease, low risk for recurrent event	Antithrombotics or endovascular treatment
Fibromuscular dysplasia	• Dizziness or vertigo • headache • tinnitus • focal neurological deficits • neck pain • vision problems	No abnormal findings	  String-of-beads sign in internal carotid artery with slight artery stenosis due to fibromuscular dysplasia	Risk of ischemic or hemorrhagic stroke, progressive course of the disease	Antihypertensive drugs and endovascular treatment

Abbreviation: TIPIC, transient perivascular inflammation of the carotid artery.

AUTHOR CONTRIBUTIONS

Marieta Peycheva: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Tina Zdravkova:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Dora Zlatareva:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Ekaterina Viteva:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Zdravka Harizanova:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Thomas R. Meinel:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Mirjam R. Heldner:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing.

ACKNOWLEDGMENTS

We thank our colleagues from the University of Bern for sharing their expertise in the field of rare vascular pathologies.

FUNDING INFORMATION

The article is part of the research project "Cerebrovascular disease—new methods of diagnosis and prevention" (project code 17/2020) funded by Medical University Plovdiv, Bulgaria.

CONFLICT OF INTEREST STATEMENT

Dr Marieta Peycheva was supported by short-term scientific missions "Clinical management of rare vascular pathologies" by the IRENE COST Action (CA18118). All other authors have nothing to disclose related to this case report. All authors report no conflict of interests.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

ETHICS STATEMENT

Our manuscript conforms to "Uniform Requirements for Manuscripts Submitted to Biomedical Journals." Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This study protocol was reviewed and approved by the Scientific Ethics Committee of Medical University—Plovdiv, approval number 2/08-09.04.2020.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Marieta Peycheva https://orcid.org/0000-0002-0045-8420
Mirjam R. Heldner https://orcid.org/0000-0002-3594-2159

REFERENCES

1. Lecler A, Obadia M, Savatovsky J, et al. TIPIC syndrome: beyond the myth of carotidynia, a new distinct unclassified entity. *AJNR Am J Neuroradiol*. 2017;38(7):1391-1398.
2. Micieli E, Voci D, Mumoli N, et al. Transient perivascular inflammation of the carotid artery (TIPIC) syndrome. *Vasa*. 2022;51(2):71-77.
3. Hersh SP, Gerard P, Hersh J. Carotidynia versus transient perivascular inflammation of the carotid artery (TIPIC) syndrome: finding common ground. *Cureus*. 2021;13(9):e17684.
4. Fay T. Atypical neuralgia. *Arch Neurol Psychiatry*. 1927;18:309-315.
5. Society HCCotIH. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia*. 1988;8:1-96.
6. Headache Classification Subcommittee of the International Headache Society. The International Classification of headache disorders: 2nd edition. *Cephalalgia*. 2004;24(Suppl 1):9-160.
7. Forwith KD, Tami TA. Carotidynia: symptom or diagnosis? *Curr Opin Otolaryngol Head Neck Surg*. 1999;7:150-154.
8. Upton PD, Smith JG, Charnock DR. Histologic confirmation of carotidynia. *Otolaryngol Head Neck Surg*. 2003;129:443-444.
9. Mathangasinghe Y, Karunarathne RU, Liyanage UA. Transient perivascular inflammation of the carotid artery; a rare cause of intense neck pain. *BJR Case Rep*. 2019;5(4):20190014.
10. Venetis E, Konopnicki D, Jissendi Tchofo P. Multimodal imaging features of transient perivascular inflammation of the carotid artery (TIPIC) syndrome in a patient with Covid-19. *Radiol Case Rep*. 2022;17(3):902-906.

11. Rafailidis V, Chryssogonidis I, Tegos T, Partovi S, Charitanti-Kouridou A, Staub D. Role of multi-parametric ultrasound in transient perivascular inflammation of the carotid artery syndrome. *Ultrasound*. 2019;27(2):77-84.
12. Burton BS, Syms MJ, Petermann GW, Burgess LP. MR imaging of patients with carotidynia. *AJNR Am J Neuroradiol*. 2000;21(4):766-769.
13. Ulus S, Aksoy Ozcan U, Arslan A, et al. Imaging spectrum of TIPIC syndrome: validation of a new entity with vessel wall imaging. *Clin Neuroradiol*. 2020;30(1):145-157.
14. Baradaran H, Gupta A. Extracranial vascular disease: carotid stenosis and plaque imaging. *Neuroimaging Clin N Am*. 2021;31(2):157-166.
15. Amaravadi RR, Behr SC, Kousoubris PD, Raja S. [18F] fluorodeoxyglucose positron-emission tomography-CT imaging of carotidynia. *AJNR Am J Neuroradiol*. 2008;29:1197-1199.

How to cite this article: Peycheva M, Zdravkova T, Zlatareva D, et al. Transient perivascular inflammation of the carotid artery—A transient but potentially recurrent disease. *Clin Case Rep*. 2024;12:e8322. doi:10.1002/ccr3.8322