MEDICINE



Cerebral Venous Thrombosis in a Young Athlete—an Unusual but Preventable Cause

Siddharth Warrier¹ · Anka Arora¹ · Sanjeev Jha¹ · Vimal Paliwal¹

Accepted: 20 November 2020 / Published online: 6 January 2021 © Springer Nature Switzerland AG 2021

Abstract

Evaluation of cerebral venous sinus thrombosis (CVST) can be challenging, with the etiology often being unrecognized. We report a case of CVST occurring secondary to anti-cancer medication abuse in a young bodybuilder. A 20-year-old male athlete with history of regular gym exercise presented with acute onset behavioral abnormalities and cognitive deficits. Brain magnetic resonance imaging (MRI) showed signal abnormalities in bilateral thalami, with venography showing venous thrombosis. A detailed history highlighted an unusual cause for CVST. Our report suggests that unsupervised drug abuse amongst young athletes is an overlooked and preventable cause of CVST. To the best of our knowledge, this is the first such report.

Keywords Cerebral venous sinus thrombosis · Young stroke · Tamoxifen · Athlete · Bodybuilder · Drug abuse

Background

Cerebral venous sinus thrombosis (CVST) is being increasingly recognized as an important etiology of stroke in young. It is more common in women than men (ratio of 3:1) [1]. While a significant number of cases (34%) have an underlying prothrombotic predisposition, in about 15 to 20% of cases, etiology remains unknown [1]. In such cases, a detailed history often reveals the etiology. Drug-induced CVST is commonly described as occurring in young women taking oral contraceptive pills [2, 3]. We report a 20-year-old male presenting with behavioral abnormality and stroke who was later diagnosed as CVST. Our aim is to highlight the unusual nature of the underlying etiology in this patient and to discuss possible measures in preventing such catastrophes.

Case Report

A 20-year-old male, law graduate, was brought to the emergency unit of neurology by his parents, with complaints of

This article is part of the Topical Collection on Medicine

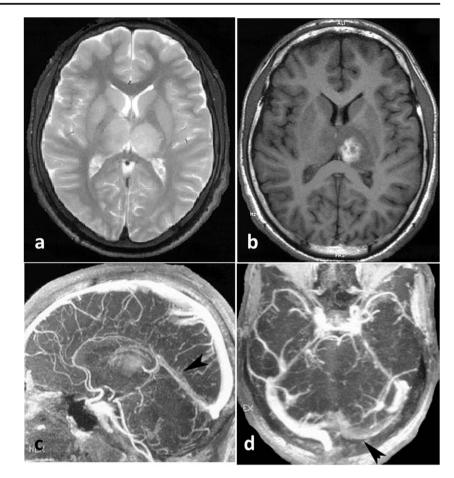
Siddharth Warrier siddharthwarrier@gmail.com headache with vomiting since the past 15 days and progressive deterioration in alertness since 3 days prior to hospitalization. As per the relatives, he appeared disconnected from surroundings. There was no history of associated fever, weakness, diplopia, or seizures. There was no past history of trauma or major medical illness. He was a non-smoker, a teetotaler, and denied any drug addiction or substance abuse. He was an active athlete, passionate muscle-builder, and a consistent visitor to the gymnasium, with a vigorous exercise schedule. He consumed substantial amounts of vitamins and proteins, to supplement his intense workout sessions.

Examination revealed a young muscular man with stable vitals. He was conscious but appeared confused and disoriented. Speech was slurred and he was responding to questions and commands in a lethargic manner. He was unable to recognize simple items of everyday use and had difficulty in identifying his family members including parents. His mini-mental status (of Folstein) examination score was 20/30 on the second day of hospitalization, with points lost in recall, calculation, and writing. There was cognitive deficit in a form of reduced attention span and impaired short-term memory. Pupils were normal, symmetrical, and equally reactive. Fundus examination revealed papilledema. The rest of his neurological examination was normal and he had no motor and sensory deficit.

The magnetic resonance imaging (MRI) of the cranium, done immediately on hospitalization, revealed bilateral thalamic hyper-intensities (Fig. 1a). Possibilities of acute viral encephalitis like Japanese encephalitis (JE), which is endemic

¹ Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Fig. 1 Brain MRI of 20-year-old athlete. a Cranial MRI (T2weighted) showing bilateral thalamic hyper-intensities. b Cranial MRI (T1-weighted) showing hemorrhagic transformation in left thalamus. c The MR venography (sagittal view) revealing thrombosis in straight sinus and vein of Galen (black arrow). d The MR venography (axial view) revealing thrombosis in left transverse sinuses (black arrow)



in Uttar Pradesh, Herpes simplex encephalitis, Wernicke's encephalopathy, and a cerebral deep venous thrombosis were the possible differential diagnoses. Cerebrospinal fluid (CSF) examination was normal. Serological tests for JE and Herpes simplex antibodies were negative. An MR imaging with venography was repeated on the eighth day of illness, which revealed a hemorrhagic infarct in the left thalamus (Fig. 1b), with occlusion of the left transverse sinus, sigmoid sinus, straight sinus, and vein of Galen suggestive of CVST (Fig. 1c, d). All the laboratory investigations, including a complete hematological and thrombophilic profile, were normal. Tests for a genetic prothrombotic condition were normal. The patient was started on anticoagulation with Enoxaparin 0.6 ml subcutaneously twice a day. His symptoms started resolving after 72 h and there was complete recovery by the end of second week. He was again questioned regarding risk factors. He had never used steroids or any weight-losing medications and denied consuming recreational drugs like cocaine or cannabis. On further targeted interrogation (specifically regarding the use of hormonal supplements), he confessed to taking a daily tablet of Nolvodex since a month prior to the onset of illness.

He was discharged from the hospital on oral anticoagulation therapy (2 mg alternating with 3 mg of

Warfarin) and he returned to his normal schedule in another 2 weeks. When he reported for follow-up after a month of illness, there was no evidence of any residual neurological deficit (with resolution of papilledema).

Discussion

We report a young man presenting with thalamic infarcts caused by a deep CVST. However the etiology behind this thrombotic episode was not initially established. He was an aspiring model and obsessed with strenuous gymnasium workouts. Despite initially denying any drug intake, he eventually admitted using Nolvodex. Nolvodex is a trade name for tamoxifen, which the patient was consuming to counteract the gynecomastia, which sometimes appears after long-term, rigorous muscle building exercises. Excess androgen gets converted to estrogen in the peripheral tissues by aromatase enzyme, which, in turn, is responsible for the gynecomastia. The gynecomastia may be further aggravated by the use of exogenous anabolic steroid intake. This is often a source of embarrassment for youngsters, who resort to pharmacological means of correcting this [4, 5].

tamoxifen is a selective estrogen receptor modulator having mainly anti-estrogenic action, but also acts as partial estrogen agonist. Approved in 1977 as an anti-breast cancer medication, it blocks the estrogen receptors and inhibits tumor growth in the breast. But its estrogen agonist properties can lead to disastrous effects like venous thromboembolism [6]. Multiple studies have established that tamoxifen does lead to an increased risk of venous thrombotic events. However, all these studies have been conducted only in women undergoing treatment for breast cancer [7, 8].

Use of anabolic steroids in body builders and athletes is well documented and has been the subject of intense discussion and debate in competitive sports. Androgen abuse in young males leading to CVST has been reported previously [9, 10]. Use of tamoxifen in body builders for the purpose of reducing gynaecomastia has been reported [11, 12]. In the UK alone, the use of tamoxifen amongst bodybuilders has been escalating, with 22% amongst them admitting to consuming the drug [13]. While the risk of thromboembolism with tamoxifen in men with male breast cancer and idiopathic infertility has been studied previously, our report highlights the adverse effects of its use as a body-building supplement, and therefore as a preventable cause of thrombosis [14, 15]. Larger studies are required to further establish the risk and causation.

Conclusion

We conclude that this off-label use of tamoxifen is possibly an overlooked and preventable cause of CVST. Further studies are indicated to establish this risk. Creating health awareness and deploying proper legislation can prevent such unsupervised drug consumption and their complications. To the best of our knowledge, this is the first case report of CVST in a young male with no other co-morbidities occurring secondary to tamoxifen abuse.

Authors' Contributions SW analyzed and interpreted data regarding clinical treatment and outcome. AA analyzed and interpreted data regarding MRI. SJ and VP supervised the management of patient, and were major contributors to the preparation of manuscript.

Data Availability Data used for the case report is available with the corresponding author.

Compliance with Ethical Standards

Ethics Approval and Consent to Participate Waived in view of observational nature of the case report.

Consent for Publication Patient's consent for use of data and publication of image received.

Competing Interests The authors declare that they have no competing interests.

Abbreviations CVST, cerebral venous sinus thrombosis; MRI, magnetic resonance imaging; JE, Japanese encephalitis; CSF, cerebrospinal fluid

References

- Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F, ISCVT Investigators. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke. 2004;35:664–70.
- Martinelli I, Sacchi E, Landi G, Taioli E, Duca F, Mannucci PM. High risk of cerebral-vein thrombosis in carriers of a prothrombingene mutation and in users of oral contraceptives. N Engl J Med. 1998;338:1793–7.
- de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Casecontrol study of risk of cerebral sinus thrombosis in oral contraceptive users and in carriers of hereditary prothrombotic conditions. The Cerebral Venous Sinus Thrombosis Study Group. BMJ. 1998;316:589.
- Willoughby DS, Taylor L. Effects of sequential bouts of resistance exercise on androgen receptor expression. Med Sci Sports Exerc. 2004;36(9):1499–506.
- Johnson RE, Murad MH. Gynecomastia: pathophysiology, evaluation, and management. Mayo Clin Proc. 2009;84:1010–5.
- Christoph R. Meier and Hershel Jick: tamoxifen and risk of idiopathic venous thromboembolism. Br J Clin Pharmacol. 1998;45: 608–12.
- Saphner T, Tormey DC, Gray R. Venous and arterial thrombosis in patients who received adjuvant therapy for breast cancer. J Clin Oncol. 1991;9:286–94.
- McDonald CC, Alexander FE, Whyte BW, Forrest AP, Stewart HJ, for the Scottish Cancer Trials Breast Group. Br Med J. 1995;311: 977–80.
- Jaillard AS, Hommel M, Mallaret M. Venous sinus thrombosis associated with androgens in a healthy young man [abstract]. Stroke. 1994;25:212–3.
- Sahraian MA, Mottamedi M, Azimi AR, Moghimi B. Androgeninduced cerebral venous sinus thrombosis in a young body builder: case report. BMC Neurol. 2004;4:22.
- Spano F, Ryan WG. Tamoxifen for gynecomastia induced by anabolic steroids? N Engl J Med. 1984;311:861–2.
- Parker LN, Gray DR, Lai MK, Levin ER. Treatment of gynecomastia with tamoxifen: a double-blind crossover study. Metabolism. 1986;35(8):705–8.
- Baker JS, Graham M, Davies B. Gym users and abuse of prescription drugs. J R Soc Med. 2006;99(7):331–2.
- Eggemann H, Bernreiter AL, Reinisch M, Loibl S, Taran FA, Costa SD, et al. Tamoxifen treatment for male breast cancer and risk of thromboembolism: prospective cohort analysis. Br J Cancer. 2019;120(3):301–5.
- Allasia S, Motta G, Mirabelli M, Tagliabue MP, Lanfranco F. A case of deep vein thrombosis in a young male treated with tamoxifen for idiopathic infertility. Asian J Androl. 2017;19(5):615–6.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.