Spontaneous Arterial Dissection Secondary to Graves' Disease: A Possible Association

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ABSTRACT

Arterial dissection is one of the common etiologies of young ischemic strokes. We report a case of Graves' disease presenting as isolated spontaneous cervical internal carotid artery dissection followed by subarachnoid haemorrhage. A young female in her early 40s presented with 3-day history of headache and left hemiparesis. MRI of the Brain showed acute right hemispheric watershed infarcts. CT Angiogram showed a short segment right cervical internal carotid artery dissection. Her serum TSH was markedly reduced with an elevated free T3/free T4 ratio (1.78) and strongly positive Anti TSH-R antibodies. She was treated with anticoagulants and antithyroid medications. Still, later she developed an episode of focal seizure following right frontal subarachnoid hemorrhage, when anticoagulation was stopped and started on a single antiplatelet, with which she recovered well. Spontaneous cervical internal carotid artery dissection and focal subarachnoid haemorrhage presenting secondary to Graves' disease without any other symptomatic systemic manifestations of hyperthyroidism is probably rare.

Keywords: Carotid Dissection, Subarachnoid Haemorrhage, Hyper Dynamic Flow, Hyperthyroidism

*See End Note for complete author details

INTRODUCTION

Carotid artery dissection accounts for about 10-25% of ischemic strokes in the young population.[1] Headache, ipsilateral facial or eye pain, neck pain and neurological deficits are the usual presenting features. Arterial dissection occurs due to multifactorial aetiology and implies a tear in the intimal layer usually occurring spontaneously or secondary to trauma, leading to mural thrombus formation and distal ischemic symptoms or as a tear in the tunica adventitia, causing aneurysmal dilatation or subarachnoid haemorrhage.[2] About 61% of carotid dissections occur spontaneously secondary to multiple aetiologies, but that secondary to Graves' disease is uncommon.[3] We report a patient with newly detected Graves' hyperthyroidism presenting as acute ischemic stroke due to unilateral cervical carotid artery dissection and later had a focal seizure due to focal subarachnoid haemorrhage.

CASE PRESENTATION

A young female in her early 40s, without any known prior co-morbidities presented with sudden onset left upper and lower limb weakness along with deviation of her mouth towards the right for 3 days duration. She had difficulty in doing her routine household chores due to left upper limb weakness and was able to walk without support. She had a mild headache 3 days back at the onset of symptoms, which subsided gradually over 1-2 days. She did not have vomiting, neck pain, trauma, loss of consciousness or bleeding from nose, ear or mouth. She was neither a smoker nor an alcoholic. She had no history of migraine or significant family history. Her clinical presentation was suggestive of an acute vascular event in the right MCA territory. On examination, she had no markers of hypercholesterolemia or connective tissue disorder. Her blood pressure was within normal range and her pulse

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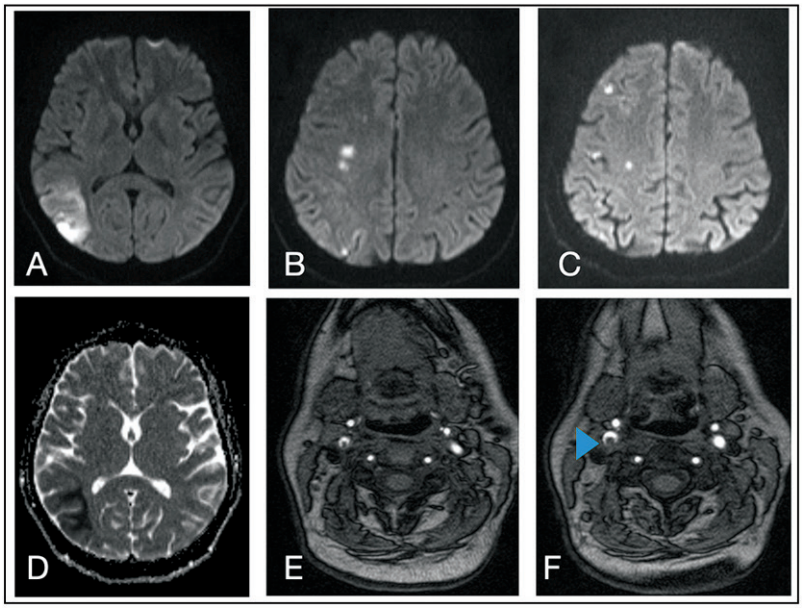

Figure 1. **MRI Brain Axial DWI showing acute infarcts (A-D) MR Angiography showing carotid dissection (E-F)**

was regular and equally felt on both sides. She had no carotid bruit or cardiac murmur. There were no signs of Horner's syndrome. She was alert and oriented, had mild dysarthria, left UMN facial palsy, left upper limb power 3/5 and left lower limb drift, without sensory dulling, ataxia or visual disturbances. Her NIHSS score was 5 and her mRS was 3.

INVESTIGATIONS

MRI Brain showed multiple patchy acute infarcts in the right MCA-PCA cortical watershed region and right MCA-ACA internal watershed region. MR Angiography showed dissection in the right internal carotid artery at its origin extending for about 2 cm and causing significant luminal narrowing **(Figure 1).** CT Angiography also showed similar findings and there was no evidence of large artery atherosclerotic disease in other vessels **(Figure 2).**

Routine haematological and biochemical investigations including a lipid profile, HbA1C and serum homocysteine levels were normal. Serum TSH was 0.005 miIU/mL (normal 0.5-5 mIU/L), free T3 was 11.25 pg/mL (normal 2.3-4.1 pg/mL) and free T4 was 6.32 ng/dL (normal 0.8-1.8 ng/dL). Free T3/Free T4 ratio was 1.78. TSH Receptor Antibody was strongly positive, suggestive of Graves' disease. ANA-IF was 2+ and ANA profile was negative. ECG showed normal sinus rhythm and 2D ECHO showed normal ejection fraction with grade 1 diastolic dysfunction.

TREATMENT

She was managed conservatively with anticoagulation. She was started on methimazole 5mg/day and slowly up titrated to 20mg/day. She was also started on propranolol as she had persistent resting tachycardia, though asymptomatic.

OUTCOME AND FOLLOW-UP

On day 7 of hospitalization, our patient developed a brief episode of left-sided focal motor seizure with impaired awareness. Imaging showed subarachnoid hemorrhage in the right frontal region **(Figure 3).** Anticoagulation was stopped and she was initiated on levetiracetam and a single antiplatelet. She had no further seizures and her neurological deficits improved. She was advised to avoid activities predisposing to cervical injury for at least 6 months. On follow-up after 1 month, she had improvement in neurological deficits with only residual dysarthria. Her NIHSS was 0 and mRS was 0. She is kept on regular follow-ups with an endocrinologist for the management of hyperthyroidism.

DISCUSSION

Arterial dissection accounts for about 1-2% of all ischemic strokes and is more common in younger individuals. About 7% of young ischemic strokes were secondary to arterial dissection in an Indian study.[4]

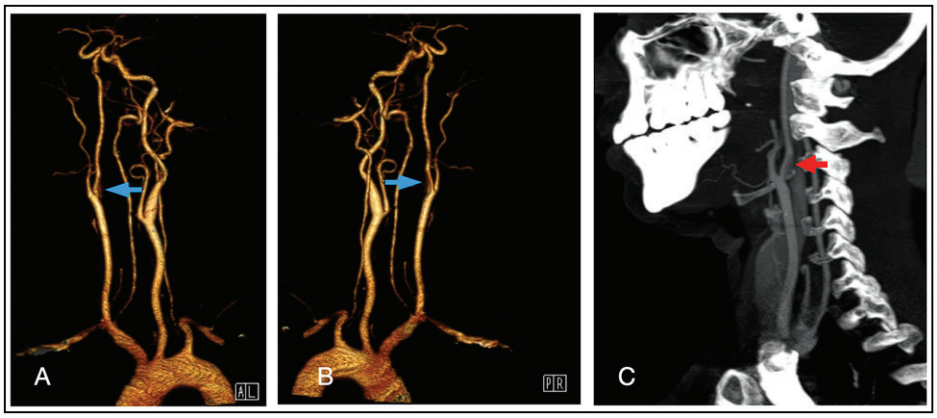

Figure 2. **CT Angiography showing right internal carotid dissection at its origin (A-C)**

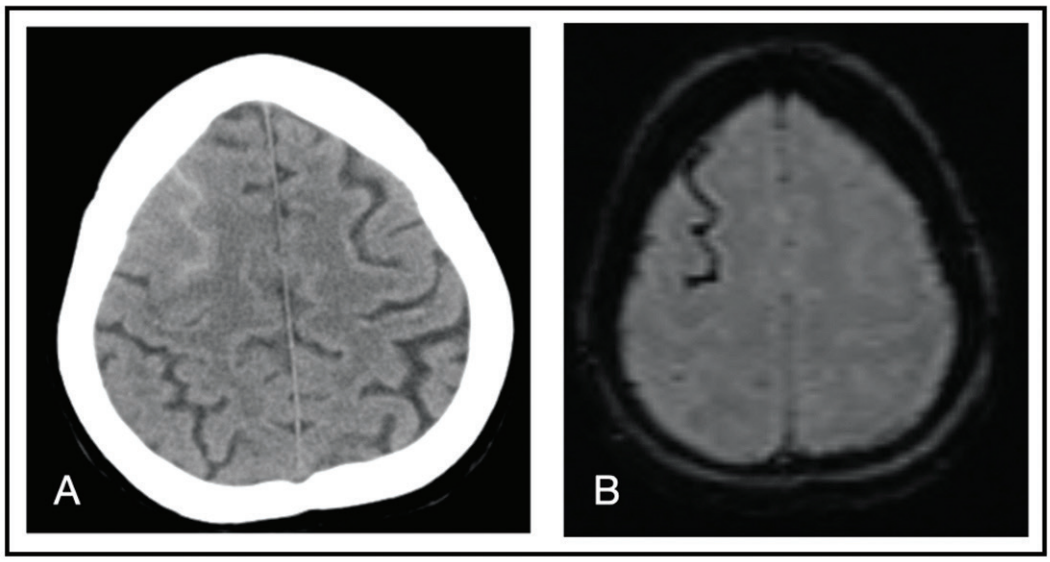

Figure 3. **A) CT Brain showing right frontal subarachnoid hemorrhage. B) Axial SWI sequence showing blooming in the same region**

Carotid artery dissections are multifactorial but are usually either traumatic or spontaneous. The carotid and vertebral arteries are more prone to dissection as compared to other arteries of similar size like coronary or renal arteries, probably due to their greater mobility and the propensity to get injured by contact with surrounding bony structures like cervical vertebrae and styloid process.[6-8] The tears in arterial walls are notoriously difficult to identify but a sub-intimal tear leads to intramural hematoma causing stroke either due to ischemia or embolic phenomenon and a sub-adventitial tear leads to aneurysmal dilatation of the artery or subarachnoid haemorrhage.[8] **(Figure 3).** In addition to classical presenting features of dissection like headache, facial pain and neck pain, the other reported features are Horner's syndrome, cranial nerve palsies especially lower nerves and pulsatile tinnitus.[9]

Spontaneous internal carotid artery dissection causes ischemic strokes in the majority like our patient, while other presentations include transient ischemic attacks, ischemic optic neuropathy, amaurosis fugax and retinal infarct.[9] Traumatic arterial dissection can occur due to significant insults following motor vehicle accidents, falls or direct blunt injuries to the neck. Though spontaneous dissections are attributed to variety of genetic (Ehlers-Danlos syndrome type IV, Marfan's syndrome, autosomal dominant polycystic kidney disease, Osteogenesis imperfecta I) and environmental factors (minor precipitating events like dancing, practicing yoga, coughing, vomiting, sneezing, anesthesia recipient, amusement park rides or chiropractic neck manipulations), the etiology is usually speculative and definite precipitant remains elusive in most cases as in our patient.[5,6]

The association of carotid dissection with thyroid dysfunction is a rarely reported entity. Campos et al first reported two cases with bilateral carotid dissection with Graves' disease who eventually succumbed, and postmortem evaluation of one of those patients showed segmental medial arteriopathy, which was a

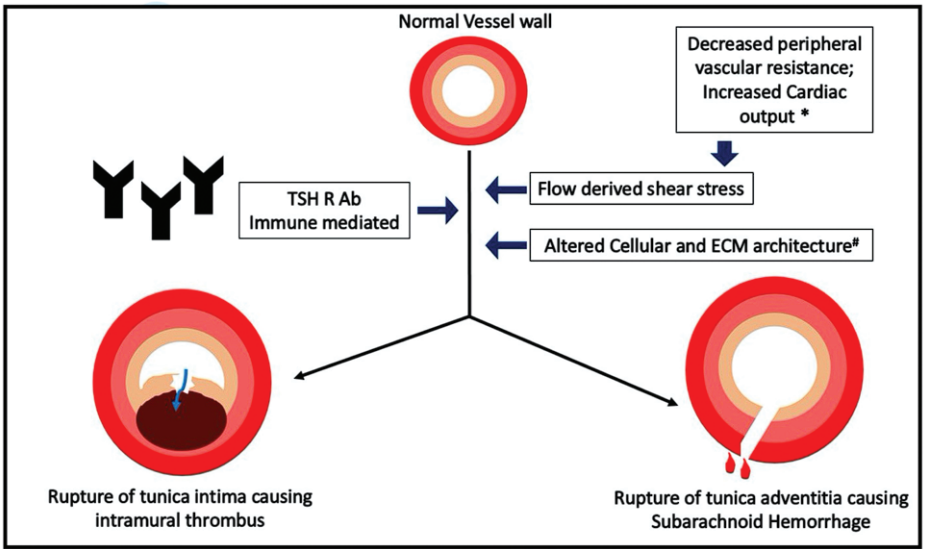

Figure 4. **Proposed mechanisms of arterial dissection due to Graves' disease.**

*Thyroid hormones cause pe-ripheral vasodilatation by direct effect causing decreased peripheral resistance, which activates renin-angiotensin system to increase sodium and water retention, which along with the direct iono-tropic effect of thyroid hormones causes increased cardiac output. # Thyroid hormones have a di-rect effect on vascular smooth muscles, endothelial cells and extracellular connective tissue; TSH R Ab - Thyroid Stimulating Hormone Receptor Antibody. (Illustrated by author L Priya)

lytic process involving tunica media and was attributed to be an immune mediated mechanism similar to the prior reported case with SLE and similar histopathological findings.[10,11] Pezzini et al conducted a retrospective study among 58 spontaneous carotid artery dissection patients and found that antithyroid antibodies were present in 31% of those patients and proposed a hypothesis that arterial disease might be one of the phenotypic expressions of generalized immune activation.[12] Another retrospective study by Shi Z et al showed that antithyroid peroxidase antibodies to be significantly elevated in young ischemic stroke patients with intracranial large artery stenosis (16.5% out of 121 patients), proposing an immune mediated pathogenesis.[13] Thyroid hormone has a direct effect on vascular smooth muscles causing vasodilation, that activates renin-angiotensin system to increase the plasma volume, which in addition to its transcriptional and non-transcriptional effects on cardiac myocytes increases the cardiac output, thereby creating a hyper dynamic circulatory state.[14] Although Graves' disease can be coincidentally detected along with carotid dissection in our patient, we consider it to be less likely in view of the support from existing literature. In our patient, we hypothesize that the hyper dynamic flow state in Graves' disease causes sheer stress on the vessel wall, which is already in a state of altered microstructure (vascular smooth muscle cells, endothelium and connection tissue) due to both direct and probable immune mediated mechanism, making the vessel vulnerable to dissection and perhaps this alteration occurs prior to the manifestation of overt clinical signs and symptoms of hyperthyroidism like ophthalmopathy or dermopathy **(Figure 4).** There had been a report of familial association of Graves' Disease with subarachnoid haemorrhage which had hypothesized hyper dynamic flow state as one of the predisposing mechanisms.[15] However, based on the available literature currently, we neither confirm nor disprove the association between Graves' Disease and spontaneous arterial dissection, but rather speculative.

Our patient had tapering occlusion and vessel wall irregularity on CT angiogram **(figure 2),** which was correlating with clinical picture to conclude carotid dissection. However, an MR Angiogram with fat-suppressed images would have helped to identify intramural hematoma if no clues had been obtained on CT Angiogram.[16] We propose that in our patient hyperthyroidism would have caused a tear in tunica adventitia also leading to subarachnoid hemorrhage, though anticoagulant use may account for rare instances. DSA was deferred to further characterise the aetiology given the risks associated with already existing occlusive thrombus in cervical ICA. Genetic testing is not routinely recommended to patients with carotid dissection, but may be useful in patients with recurrent dissections, positive family history and patients with physical signs suggestive of connective tissue disorders.[17]

As this patient had an occlusive thrombus with no other significant bleeding tendencies initially, she was treated with anticoagulation, but later when she developed subarachnoid hemorrhage, single anti platelet was considered the treatment of choice as per recent AHA guidelines. The risk of recurrent dissections are usually higher in the initial few months after first event.[17] Management of hyperthyroidism is crucial as early and appropriate management prevents further vessel damage.

LEARNING POINTS/TAKE HOME MESSAGES

- There must be a high index of suspicion of carotid dissection in young patients presenting with acute ischemic stroke though the classical symptoms of dissection like headache or neck pain are vague.
- Young females with arterial dissection must be evaluated for Graves' disease even though clinical signs and symptoms of thyroid dysfunction are absent.
- Hyperthyroidism may predispose to arterial dissection at two independent sites causing an occlusive thrombus and subarachnoid hemorrhage.

END NOTE

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Abbreviations

TSH-R: Thyroid Stimulating Hormone Receptor

ANA: IF Anti nuclear antibody - Immunofluorescence

CT: Computed Tomography

MRI: Magnetic Resonance Imaging

MRA: Magnetic Resonance Angiography

ICA: Internal Carotid Artery

MCA: ACA Middle Cerebral Artery - Anterior Cerebral Artery

MCA: PCA Middle Cerebral Artery - Posterior Cerebral Artery

ECG: Electrocardiogram

ECHO: Echocardiography

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LP, PR, AM, BKK - data collection and drafting of manuscript

PTA, JVM - revision and final drafting the manuscript

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REFERENCES

1. Winter T, Kraut E, Thompson K. Thyrotoxicosis and bilateral internal carotid artery dissections. The American Journal of Emergency Medicine. 2021 Jan 1;39:251-e1.
2. Haneline MT, Rosner AL. The etiology of cervical artery dissection. Journal of chiropractic medicine. 2007 Sep 1;6(3):110-20.
3. Haneline MT, Lewkovich GN. An analysis of the etiology of cervical artery dissections: 1994 to 2003. Journal of manipulative and physiological therapeutics. 2005 Oct 1;28(8):617-22.
4. Lipska K, Sylaja PN, Sarma PS, Thankappan KR, Kutty VR, Vasan RS, Radhakrishnan K. Risk factors for acute ischaemic stroke in young adults in South India. Journal of Neurology, Neurosurgery & Psychiatry. 2007 Sep 1;78(9):959-63.
5. Harriott A. Idiopathic non-atherosclerotic carotid artery disease. Current Treatment Options in Cardiovascular Medicine. 2019 Nov;21:1-2.
6. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. New England Journal of Medicine. 2001 Mar 22;344(12):898-906.
7. Hart RG, Easton JD. Dissections of cervical and cerebral arteries. Neurologic clinics. 1983 Feb 1;1(1):155-82.
8. Sundt TM, Pearson BW, Piepgras DG, Houser OW, Mokri B. Surgical management of aneurysms of the distal extracranial internal carotid artery. Journal of neurosurgery. 1986 Feb 1;64(2):169-82.
9. Baumgartner R, Bogousslavsky J. Clinical manifestations of carotid dissection. Handbook on cerebral artery dissection. 2005;20:70-6.
10. Campos CR, Basso M, Evaristo EF, Yamamoto FI, Scaff M. Bilateral carotid artery dissection with thyrotoxicosis. Neurology. 2004 Dec 28;63(12):2443-4.
11. Juvonen T, Niemelä O, Reinilä A, Nissinen J, Kairaluoma MI. Spontaneous intraabdominal haemorrhage caused by segmental mediolytic arteritis in a patient with systemic lupus erythematosus--an underestimated entity of autoimmune origin?. European Journal of Vascular Surgery. 1994 Jan 1;8(1):96-100.
12. Pezzini A, Del Zotto E, Mazziotti G, Ruggeri G, Franco F, Giossi A, Giustina A, Padovani A. Thyroid autoimmunity and spontaneous cervical artery dissection. Stroke. 2006 Sep 1;37(9):2375-7.
13. Shi Z, Zhang X, Chen Z, Liebeskind DS, Lou M. Elevated thyroid autoantibodies and intracranial stenosis in stroke at an early age. International Journal of Stroke. 2014 Aug;9(6):735-40.
14. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. New England Journal of Medicine. 2001 Feb 15;344(7):501-9.
15. Leblanc R, Lozano AM. Graves' disease and subarachnoid hemorrhage: a possible familial association. Canadian journal of neurological sciences. 1987 Nov;14(4):638-41.
16. Mehdi E, Aralasmak A, Toprak H, Yildiz S, Kurtcan S, Kolukisa M, Asil T, Alkan A. Craniocervical dissections: radiologic findings, pitfalls, mimicking diseases: a pictorial review. Current Medical Imaging. 2018 Apr 1;14(2):207-22.
17. Yaghi S, Engelter S, Del Brutto VJ, Field TS, Jadhav AP, Kicielinski K, Madsen TE, Mistry EA, Salehi Omran S, Pandey A, Raz E. Treatment and outcomes of cervical artery dissection in adults: A scientific statement from the American Heart Association. Stroke. 2024 Mar;55(3):e91-106.