

STROKE



Vol 2 | Issue 7 | 2023

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you “Stroke Newsletter” which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

- 1. Evaluating the association between post-stroke left ventricular dysfunction and intense isolated ischemia sores in intravenous thrombolysis patients**
- 2. Evaluating the effect of left atrial or left atrial appendage thrombus on the outcome of strokes**
- 3. A Prospective Cohort study evaluating the impact of vertebral and amygdala metabolic activity on stroke recurrence**
- 4. Moyamoya syndrome associated with Graves's disease in a 17-year-old female ischemic stroke patient: A Case Report**

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd



Evaluating the association between post-stroke left ventricular dysfunction and intense isolated ischemia sores in intravenous thrombolysis patients

Introduction: Ischemic stroke frequently causes cardiovascular effects, such as increase in troponin level, cardiac arrhythmia, left ventricular (LV) dysfunction, sudden cardiac death etc even in the absence of primary cardiac disease. Cardiovascular problems after an ischemic stroke are associated with a significantly poorer outcome. These cardiac abnormalities related to stroke are termed stroke-heart syndrome.¹ Because ischemic strokes typically occur in older patients, cardiac comorbidities are common, and vascular risk factors are prevalent, patients with ischemia stroke are especially vulnerable to cardiac harm. Importantly, cardiac problems after ischemic stroke are linked to a poor functional prognosis and are the second greatest cause of mortality in the first few weeks after the event.²

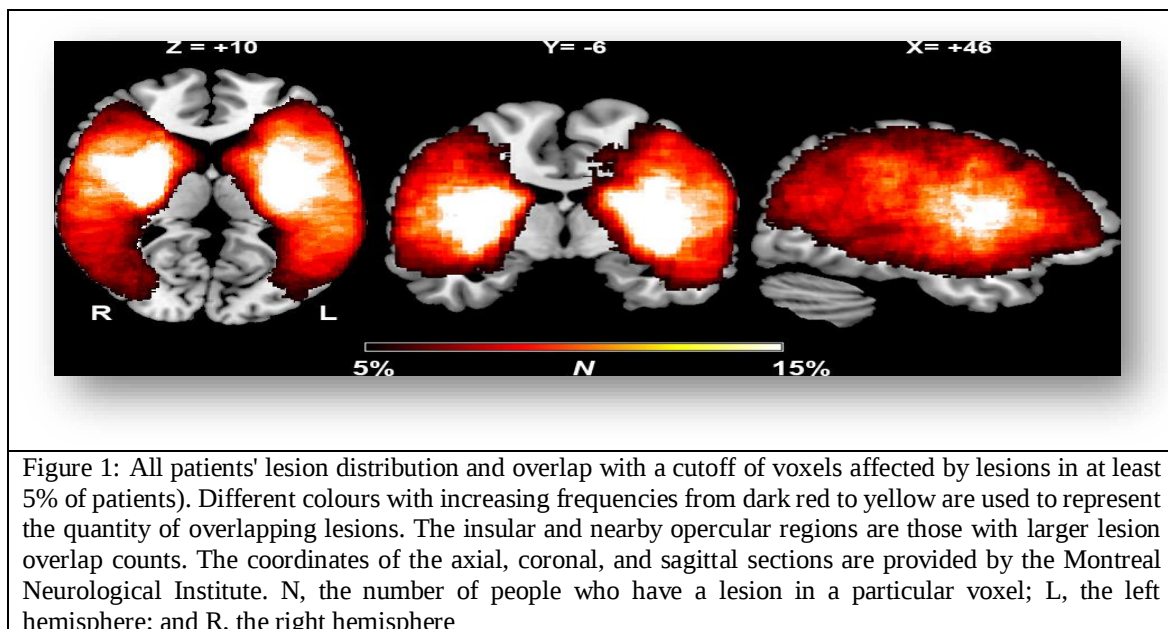
This study aimed to determine relationships between the supratentorial stroke lesion site and changed LV function by using cardiac ultrasonography to assess LV function and voxelwise lesion-symptom mapping (VLSM).

Methods: In this prospective study database, patients who underwent intravenous thrombolysis or mechanical recanalization for acute ischaemic stroke between the years of 2006 and 2016 with acute first-ever ischaemic stroke confirmed by brain imaging but without pre-existing heart disease were included. Left ventricular ejection fraction (LVEF) impairment was classified as mild (35%-50%), moderate (34%-25%), and severe (25%) based on cardiac morphology and transthoracic or transesophageal echocardiography results. In order to compare patients with and without reduced LVEF after stroke, patient age, stroke severity, ischemic lesion volume, the prevalence of troponin I rise (>0.1 ng/mL), atrial fibrillation, and heart wall motion anomalies were evaluated and compared (significance: $p < 0.05$). A multivariate voxelwise lesion analysis linked the locations of ischemic lesions with the LVEF after a stroke.

Results: In this study, a total of 231 patients with the above inclusion criteria were included. After a stroke, there were 40 patients (17.3%) with compromised LVEF. Patients with lower



LVEF experienced aberrant wall motion in 17 cases (42.5%) as compared to 10 cases (5.2%) ($p < 0.001$). In comparison to patients with LVEF of $> 50\%$, patients with lower LVEF exhibited a greater ischemic lesion volume, a higher prevalence of troponin rise of > 0.1 ng/mL, and atrial fibrillation ($p < 0.05$). The reduced EF in four of the 40 patients (10.0%) was so poor that it was less than 25%. 33 patients (82.5%) had slightly reduced EF (35%–50%), while three patients (7.5%) had moderately reduced EF (25%–34%). All patients' lesion distribution and overlap are shown in Figure 1 (with a cutoff of voxels affected by lesions in at least 5% of patients). The multivariate voxelwise lesion analysis found connections between lower LVEF and harmed voxels in the right hemisphere's insula, amygdala, and operculum.



Discussion: A Jimenez-Ruiz A, et al., study showed that cardiovascular consequences occur in up to 31% of individuals after an acute ischemic stroke, and reduced LV function (i.e., EF 50%) afterward affects patient outcome.³ The brain-heart axis is controlled by the insular cortex, which is significant in this investigation. Similar to this investigation, Winder K et al. study showed that the anterior insula and insular cortex integrate visceral arousal states via organotypic viscerosensory representation to guarantee appropriate cardiovascular autonomic control.⁴

Conclusion: The current study concluded that brain-heart axis is significantly influenced by the right hemispheric central autonomic network, particularly the insular cortex. According to preliminary research, heart function may be directly harmed by acute ischemic stroke in



specific central autonomic network brain regions. The study recommended that patients with lesions in these regions be closely monitored for cardiac dysfunction because patients with right-sided ischaemic stroke lesions had a significantly higher probability of cardiac dysfunction, which includes impaired pump function, cardiac arrhythmia, and myocardial damage.

Cardiac dysfunction, such as reduced pump performance, cardiac arrhythmia, and myocardial injury, was much more likely to occur in right-sided ischemic stroke lesions.

References:

1. Winder K, et al. Acute right insular ischaemic lesions and post stroke left ventricular dysfunction. *Stroke and Vascular Neurology*. 2023 Jan 18:svn-2022.
2. Scheitz JF, et al. Stroke-heart syndrome: clinical presentation and underlying mechanisms. *Lancet Neurol*. 2018 Dec;17(12):1109-1120.
3. Jimenez-Ruiz A, et al. Cardiovascular autonomic dysfunction after stroke. *Neurological Sciences*. 2021 May; 42:1751-8.
4. Winder K, et al. Neuroanatomic correlates of post stroke hyperglycemia. *Annals of neurology*. 2015 Feb;77(2):262-8.



Evaluating the effect of left atrial or left atrial appendage thrombus on the outcome of strokes

Introduction: Stroke is known to be caused by nonvalvular atrial fibrillation (NVAf), which is usually correlated with cardiovascular mortality and morbidity. A five-fold rise in the rate of ischemic stroke was linked to NVAf. However, few studies have shown a 62% relative risk decrease in stroke was related to the usage of a dose-adjusted vitamin K antagonist. Direct oral anticoagulants are recognized as the most effective way to prevent thromboembolic events in NVAf due to the decreased risk of bleeding. A cardiac embolism is a major cause of the majority of ischemic strokes in NVAf patients.¹ The prevalence of cardioembolism occurs in 14.6%-36.0% of patients with increased age. There are several underlying causes of thromboembolism, however the majority of patients with atrial fibrillation tend to develop thrombi that originate from the left atrial appendage (LAA).² The aim of this study was to investigate the outcomes of stroke in patients with LA/LAA thrombus.

Methods: A retrospective study was conducted on patients who were admitted to a hospital in Korea. Data was collected from January 2012 to December 2020. This study included patients with NVAf who underwent transesophageal echocardiography or multi-detector coronary computed tomography. A modified Rankin Scale score of >3 at 90 days was considered a poor outcome. The incidence of treatment weighing analysis was performed inversely.

Results: In this study, a total of 631 patients with NVAf were included, among 68 (10.7%) patients with LA/LAA thrombus. Congestive cardiac failure (22.1% vs. 5.7%) and persistent/permanent atrial fibrillation (95.6% vs. 73.5%) were more common in patients with LA/LAA thrombus than in patients without LA/LAA thrombus (Table 1). Patients with LA/LAA thrombus were significantly more likely to be prescribed a vitamin K antagonist than patients without a thrombus at the time of discharge. Inverse probability of treatment weighting analysis revealed that patients with LA/LAA thrombus had a significantly higher risk of poor outcomes than patients without LA/LAA thrombus ($P < 0.001$). Patients with LA/LAA thrombus showed longer hospital stays (8 vs. 7 days, $P < 0.001$) and were more likely to have significant artery blockage on angiography (36.3% vs. 22.4%, $P = 0.047$).



Variables	LA/LAA thrombus (+) (n=68)	LA/LAA thrombus (-) (n=563)
Age (>75 years)	48 (70.6)	345 (61.3)
Male sex	39 (57.4)	325 (57.7)
Hypertension	51 (75.0)	450 (79.9)
Diabetes	22 (33.8)	173 (30.7)
Dyslipidaemia	10 (14.7)	122 (21.7)
coronary artery occlusive disease	27 (39.7)	201 (35.7)
congestive heart failure	15 (22.1)	32 (5.7)
Persistent/permanent atrial fibrillation	65 (95.6)	414 (73.5)
Left ventricular thrombus	1 (1.5)	2 (0.4)
Low GFR (<30 mL/min/1.73 m ²)	19 (27.9)	127 (22.6)
High initial NIHSS score (≥10)	16 (26.2)	95 (27.5)
Reperfusion therapy	8 (13.1)	79 (22.9)

Table 1. Baseline characteristics of patients. - Values are expressed as median [interquartile range] for continuous variables and number (%) for categorical variables.

Discussion: This study showed congestive heart failure and persistent or permanent atrial fibrillation were associated with a LA/LAA thrombus. A Bertaglia E, et al. study showed that female sex, hypertension, diabetes, low ejection fraction, or congestive heart failure may all be risk factors for LA/LAA thrombi.³ A Di Minno MN, et al. study showed that LA/LAA thrombus was found in 9.8% of stroke patients,⁴ which is similar to Heo J, et al. investigation of 10.7% of stroke patients with atrial fibrillation.

Conclusion: The current study concluded that patients with ischemic stroke and LA/LAA thrombus increased their risk of having poor functional outcomes after 3 months. Patients with LA/LAA thrombus had longer hospital stays, and relevant arterial occlusions occurred more frequently than in patients without LA/LAA thrombus. Prognostic implications may be helpful for estimating clinical outcomes and managing acute stroke.

Estimation of the clinical outcome and management of acute stroke can be done with the help of prognostic implications.

References:

1. Heo J, et al. Impact of Left Atrial or Left Atrial Appendage Thrombus on Stroke Outcome: A Matched Control Analysis. *Journal of Stroke*. 2023 Jan 3.
2. Nguyen HT, et al. Prevalence of left atrial appendage thrombus in patients with acute ischaemic stroke and sinus rhythm: a cross-sectional study. *BMJ open*. 2021 Dec 1;11(12): e051563.
3. Bertaglia E, et al. NOACs and atrial fibrillation: Incidence and predictors of left atrial thrombus in the real world. *International journal of cardiology*. 2017 Dec 15; 249:179-83.



4. Di Minno MN, et al. Prevalence of left atrial thrombus in patients with non-valvular atrial fibrillation. *Thrombosis and haemostasis*. 2016;115(03):663-77.

A Prospective Cohort study evaluating the impact of vertebral and amygdala metabolic activity on stroke recurrence

Introduction: Atherosclerosis is a systemic condition that affects the medium- to large-sized artery walls. It is caused by lipid build-up and subsequent inflammation, which causes plaque rupture and thrombus production.¹ Up to 20% of stroke or transient ischemic attack (TIA) patients have atherosclerotic carotid stenosis, which raises the risk of stroke in asymptomatic patients. Positron emission tomography (PET) is an efficient method for non-invasive image analysis to find a plaque metabolism associated with inflammation with the help of ¹⁸F-fluorodeoxyglucose (FDG).² However, the treatment plan focuses on the typical vascular risk factors such as dyslipidemia, hypertension, and diabetes. many patients persist to have vascular events even when they have achieved optimal vascular risk factor control.

The aim of the study is to investigate the metabolic processes of the amygdala and vertebrae affect stroke recurrence and future vascular events in stroke patients.

Methods: A total of 110 acute stroke patients who underwent whole-body F-fluorodeoxyglucose (FDG) positron emission tomography between August 1, 2015 and February 28, 2020 were included. Assessed the FDG uptake between patients with and without recurrent vascular events in the amygdala, vertebrae, liver, spleen, and internal carotid artery. To determine the factors that contribute to recurrent stroke and vascular events, the Cox proportional hazards model was used. According to the severity of the carotid atherosclerosis, the patients were divided into four groups. Group 1, patients with stroke with symptomatic carotid atherosclerosis greater than or equal to 50%; group 2, patients with stroke with non-culprit carotid atherosclerosis greater than or equal to 50%; group 3, patients with stroke with mild carotid stenosis less than 50%; and group 4, patients with stroke without carotid stenosis.

Results: In this study, 29 patients had moderate to severe non-culprit carotid stenosis along with various stroke etiology, including 19 patients with cerebral atherosclerosis and 28 patients had symptomatic carotid atherosclerosis and in addition to these 10 patients with cardio embolism. 15 patients had recurrent strokes over the median follow-up of 18 months. The mechanism of the recurrent stroke included atherosclerosis (n=7; 6 intracranial atherosclerosis



and 1 extra cranial carotid stenosis), cardio embolism brought on by new atrial fibrillation (n=4), miscellaneous aetiologies (n=2, one essential thrombocythemia and the other new cancer-related coagulation disorder), cerebellar haemorrhage (n=1), and unknown etiology (n=1). The amygdala and vertebrae of patients with recurrent vascular episodes absorbed more FDG than those without. According to the Cox proportional hazard model that considered diabetes, renal function, and carotid stenosis into account, a higher FDG uptake in the amygdala was independently linked to total vascular events, while a higher FDG uptake in the vertebrae was linked to stroke recurrence. (Figure 2)

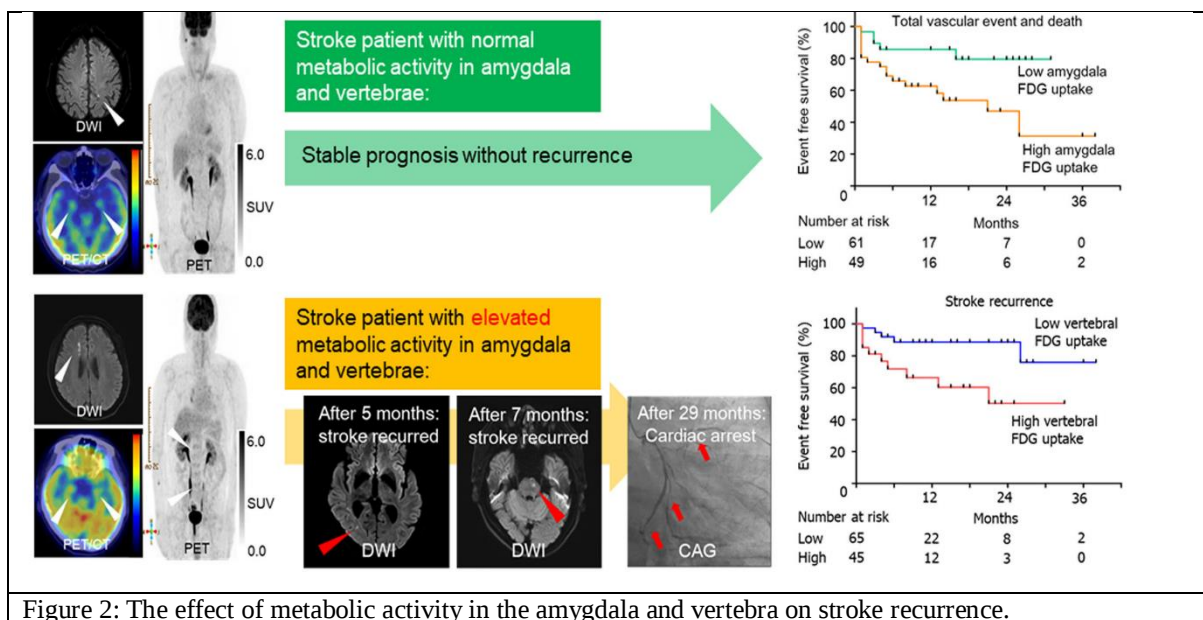


Figure 2: The effect of metabolic activity in the amygdala and vertebra on stroke recurrence.

Discussion: This study showed that serum triglycerides and amygdala glucose uptake positively correlated, which may indicate that the limbic system plays a role in the systemic lipid metabolism in stroke patients. Similarly to this investigation, Woo MH, et al. study showed that atrial fibrillation and cerebral atherosclerosis are both strongly correlated with increased triglycerides. ³

According to Tawakol A, et al., stress-induced inflammation plays a part in the development of future atherosclerotic cardiovascular events because the activated amygdala is directly associated with FDG uptake in the artery wall and haematological organs. ⁴

Conclusion: Stroke recurrence and vascular events in stroke patients can be predicted with the help of glucose uptake status in the amygdala and bone. The raised metabolic activities of the vertebrae and amygdala are associated with future vascular events in stroke patients.



The amygdala and bone glucose uptake status could be used to predict stroke recurrence and vascular events in stroke patients.

References:

1. Kim JM, et al. Impact of Metabolic Activity of Vertebra and Amygdala on Stroke Recurrence: A Prospective Cohort Study. *Circulation: Cardiovascular Imaging*. 2023 Jan;16(1):e014544.
2. Kelly PJ, et al. Carotid plaque inflammation imaged by 18F-fluorodeoxyglucose positron emission tomography and risk of early recurrent stroke. *Stroke*. 2019 Jul;50(7):1766-73.
3. Woo MH, et al. Triglyceride/HDL-cholesterol ratio as an index of intracranial atherosclerosis in nonstroke individuals. *Frontiers in Neurology*. 2021 Jan 18;11:504219.
4. Tawakol A, et al. Relation between resting amygdalar activity and cardiovascular events: a longitudinal and cohort study. *The Lancet*. 2017 Feb 25;389(10071):834-45.

Moyamoya syndrome associated with Graves's disease in a 17-year-old female ischemic stroke patient: A Case Report

Introduction: A progressive cerebrovascular condition called Moyamoya syndrome is defined as stenosis or blockage of the proximal middle cerebral artery, the anterior cerebral artery, and the terminus of the internal carotid artery. An autoimmune condition called Grave's disease, in which autoantibodies to thyroid-stimulating hormone receptors produce elevated thyroid hormone in the blood, which results in hyperthyroidism. Moyamoya syndrome commonly presents with one or more underlying systemic disorders. These well-known illnesses include neurofibromatosis type 1, sickle cell disease, Down syndrome, cranial therapeutic irradiation, and other uncommon conditions. ¹ Ischemic stroke with thyrotoxicity is a rare complication of moyamoya vasculopathy associated with hyperthyroidism. Increased morbidity and mortality rates can result from a thyroid storm, an endocrine disorder linked to uncontrolled hyperthyroidism, in a patient with underlying Moyamoya syndrome (MMS). ²



Case presentation: A 17-year-old female was admitted to the hospital in the emergency department with thyrotoxicosis, increasing caries and sudden paralysis of the right limb for 1 day with alopecia for 4 years (Fig. 3A). At the age of 15, the patient developed dental caries due to thyrotoxicosis, and methimazole was prescribed for two years. There was no history of hyperthyroidism, hypertension, diabetes, epilepsy, cerebral infarction, cerebral hemorrhage, or other medical conditions in the family. During the admissions, the blood pressure was 158/72 mmHg, the heart rate was 142 bpm, the ECG showed sinus tachycardia, and the respiratory rate was 28. Physical examination revealed that the patient had goiter and exophthalmos. Patient initial National Institutes of Health Stroke Scale (NIHSS) score was 5 after a neurological examination revealed right limb paralysis.

A head computed tomography (CT) scan indicated that cerebral infarction of the left middle cerebral artery area and magnetic resonance angiography shows bilateral proximal portions of the anterior and middle cerebral arteries were blocked. A lumbar puncture was performed and the presence of bloody cerebrospinal fluid further confirmed the ventricular hemorrhage. The panoramic image of the oral cavity showed several residual crowns and roots on both sides of the jaw (Fig. 3B). Echocardiography revealed mild sinus tachycardia and significant mitral regurgitation, but there was no evidence of atrial fibrillation until 24 hours.

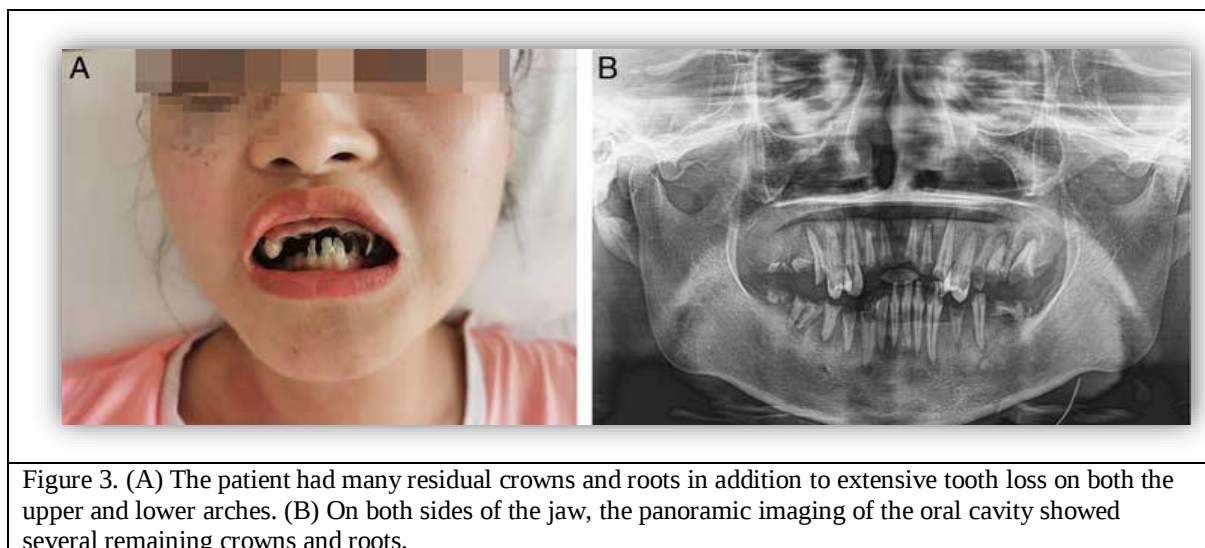


Figure 3. (A) The patient had many residual crowns and roots in addition to extensive tooth loss on both the upper and lower arches. (B) On both sides of the jaw, the panoramic imaging of the oral cavity showed several remaining crowns and roots.

On the first day after admission, treatment plans included nutrition support therapy, propylthiouracil 200 mg PO Q8h (initial dosage doubling), hydrocortisone 100 mg intravenous infusion Q12h, and propranolol 20 mg PO Q8h. The patient's symptoms remained constant and did not worsen after therapy with hydrocortisone and propylthiouracil. Re-examining the head CT scan after 11 days of treatment revealed that the ventricular haemorrhage had been cleared.



The patient's NIHSS was zero after sixteen days of admission and the infarction lesion's MRI signal had minimized.

Discussion: In this study, a head computed tomography (CT) scan revealed that the patient suffered from cerebral infarction of the left middle cerebral artery area, and magnetic resonance angiography showed that bilateral proximal portions of the anterior and middle cerebral arteries were blocked.

Similarly, to this investigation, the Ramirez-Quiones J, et al. study found that bilateral vascular damage similar to Moyamoya disease, while the patient's MRI revealed bilateral acute ischemic lesions in the anterior circulation. Also had clinical and laboratory manifestations of thyrotoxicosis.³

Conclusion: Moyamoya syndrome associated with Graves' illness leads to an acute cerebral infarction and intraventricular haemorrhage. Propylthiouracil and hydrocortisone together had a strong therapeutic effect. After treatment, a CT and MRI re-examination revealed that the infarct lesions were significantly minimized, suggesting that hydrocortisone in combination with propylthiouracil can treat thyroid insufficiency and enhance neurological function.

Propylthiouracil taken with hydrocortisone helps to improve neurological function and correct thyroid dysfunction.

References:

1. Huang M, et al. Ischemic Stroke and Intraventricular Hemorrhage in Moyamoya Syndrome Associated with Graves' Disease: A Case Report. *The Neurologist*. 2023 Jan 1;28(1):42-5.
2. Gill JH, et al. Acute cerebral infarction combined with a thyroid storm in a patient with both Moyamoya syndrome and Graves' disease. *J Cerebrovasc Endovasc Neurosurg*. 2022 Jun 1;24:160-5.
3. Ramírez-Quíñones J, et al. Bilateral Ischemic Strokes Secondary to Moyamoya Syndrome Associated with Graves Thyrotoxicosis in a Patient of Amerindian Descent from Peru: A Case Report. *Cureus*. 2022 Jul 4;14(7).



This scientific input is prepared from the Department of Medical Services, an initiative of M/s Micro Labs Limited under the aegis of Micro Knowledge Academy. The information contained herein is for education purpose only. The content is developed by compiling information from various authentic and published literatures. Although great care has been taken to assure the accuracy of the publication, M/s Micro Labs Limited shall not be responsible or in any way liable for any inaccuracy, errors, or omissions resulting from negligence or otherwise howsoever or any consequences arising there from. In spite of best efforts, the information in this publication may become outdated over time. M/s Micro Labs Limited shall not be responsible in any manner whatsoever, for any action taken, opinions expressed, advice rendered or accepted, any direct, incidental, special or consequential loss and damage caused on the basis of any material or information presented in this publication / update.