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Case Report

# Acute Ischemic Stroke in a 19-Year-Old Male Due to a Rare Genetic Disorder of Collagen (Ehlers-Danlos Syndrome): A Rare Case Report

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## Abstract

A rare case report illustrating an unusual and instructive case of acute ischemic stroke (AIS) in a 19-year-old male, attributed to vascular Ehlers-Danlos Syndrome (vEDS), a rare autosomal dominant genetic disorder affecting Type III collagen synthesis. The patient presented with acute right-sided hemiplegia and aphasia. Neuroimaging revealed an ischemic infarct in the left middle cerebral artery (MCA) territory, precipitated by a dissection of the left internal carotid artery (ICA). Genetic testing confirmed a pathogenic mutation in the COL3A1 gene, confirming vEDS. Early intervention, including thrombolysis and a tailored rehabilitation program, led to partial neurological recovery. This case underscores the critical importance of recognizing genetic disorders as underlying causes of ischemic strokes in young adults. We emphasize the necessity for a multidisciplinary approach to diagnosis, acute treatment, and prevention of recurrence in such patients.

**Keywords:** Acute Ischemic Stroke; Vascular Ehlers-Danlos Syndrome; Collagen Disorders; Genetic Stroke Syndromes; Arterial Dissection

## Introduction

Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide, but its occurrence in young adults (under 45 years) constitutes only 5–10% of cases. Unlike strokes in older populations, which are typically linked to atherosclerosis and traditional cardiovascular risk factors, ischemic events in younger individuals often stem from uncommon causes such as genetic or structural abnormalities, hypercoagulable states, or inflammatory conditions.

Ehlers-Danlos Syndrome (EDS) is a heterogeneous group of inherited connective tissue disorders, with vascular EDS (vEDS) being among the most severe subtypes. vEDS, resulting from mutations in the COL3A1 gene, is characterized by fragility of arteries, veins, and hollow organs, predisposing affected individuals to spontaneous arterial dissections, aneurysms, and rupture. Despite its rarity, with an estimated prevalence of 1 in 100,000, vEDS is a significant cause of young-onset ischemic stroke.

This case report highlights the presentation, diagnostic challenges, and management of AIS caused by ICA dissection in a

young male with undiagnosed vEDS, underscoring the value of a comprehensive approach to young-onset strokes [1-7].

## Case Presentation

### Clinical Presentation

A 19-year-old male presented to the emergency department with a sudden onset of right-sided weakness, facial droop, and inability to articulate speech. Symptoms began abruptly two hours prior to arrival. The patient denied preceding trauma, headaches, chest pain, or palpitations.

### Medical history

- The patient reported hypermobile joints, frequent bruising, and atrophic scars on minor injuries.
- No history of chronic medical conditions, substance use, or smoking.
- Family history included sudden unexplained deaths of maternal relatives in their 30s and 40s.

### Physical examination

### Neurological findings

- Glasgow Coma Scale: 13/15.
- Right hemiplegia (Grade 0/5 strength in the upper and lower limbs).
- Expressive aphasia with preserved comprehension.
- Hyperreflexia and positive Babinski sign on the right side.

### Systemic features

- Hyperextensible skin with visible subcutaneous veins.
- Thin, translucent skin over the chest.
- Atrophic scars over knees and elbows.

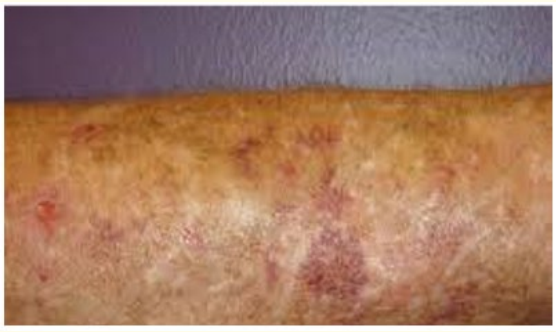

**Figure 1:** Clinical Features.

Atrophic scars on the knees and translucent skin with visible veins.

| System | Findings |
|---|---|
| Skin | Thin, translucent, scars |
| Neurological | Hemiplegia, aphasia |
| Family History | Sudden deaths (maternal) |
| Vascular Imaging | ICA dissection |

**Table 1:** Key Clinical Features of vEDS in This Patient.

### Diagnostic evaluation

### Neuroimaging

- **MRI Brain (DWI):** Acute infarction in the left MCA territory.
- **MRA:** Dissection of the left ICA with luminal narrowing and intramural thrombus.

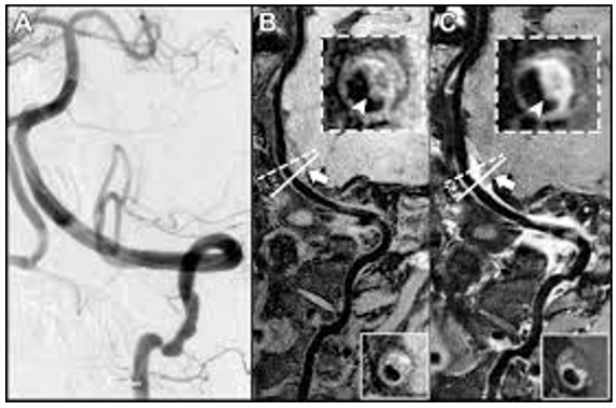


**Figure 2:** MRA of the Neck.

Revealing left ICA dissection with thrombus.

| Parameter | Observation |
|---|---|
| MRI Brain | Acute infarction in MCA territory |
| MRA | Left ICA dissection |
| Genetic Mutation | COL3A1 mutation (pathogenic) |
| Homocysteine Level | Elevated (22 µmol/L) |

**Table 2:** Summary of Diagnostic Findings.

### Laboratory investigations

- Blood counts, renal profile, and coagulation studies: Normal.
- Homocysteine level: Elevated (22 µmol/L, reference <15 µmol/L).
- Inflammatory markers: Negative.

### Genetic testing

- Sequencing of the COL3A1 gene identified a heterozygous pathogenic variant confirming vEDS.

### Literature Review

### Stroke in young adults

Studies estimate that approximately 15% of strokes occur in individuals aged 15–45 years. In this group, ischemic strokes predominate, and traditional risk factors like hypertension and diabetes are less prevalent. Instead, underlying causes often include arterial dissections, prothrombotic states, autoimmune diseases, and rare genetic conditions. A meta-analysis by Pezzini., *et al*. identified arterial dissections as the leading cause in this demographic, contributing to 20–25% of cases.

### Vascular EHLERS-DANLOS SYNDROME

vEDS accounts for 5–10% of all EDS cases but is associated with severe vascular complications. Clinical features such as thin, translucent skin, easy bruising, and atrophic scars can aid early recognition. In a cohort study by Oderich., *et al*., 67% of patients with vEDS experienced arterial dissections, with the carotid and vertebral arteries being the most commonly affected. However, these features are often subtle or absent, delaying diagnosis.

### Genetic testing in AIS

The advent of next-generation sequencing has enabled rapid identification of monogenic causes of stroke. Genetic testing for COL3A1 mutations is pivotal for diagnosing vEDS. Studies emphasize the importance of genetic counseling and family screening in managing hereditary connective tissue disorders.

| Study | Year | Objective | Key Findings | Conclusion |
|---|---|---|---|---|
| Pezzini, A., *et al*. | 2018 | To review the causes of stroke in young adults and their clinical features | Arterial dissections are the leading cause of ischemic stroke in young adults, accounting for 20–25% of cases. | Arterial dissection is a significant cause of stroke in the young, and vEDS should be considered in cases with arterial dissections. |
| Oderich, G. S., *et al*. | 2005 | To evaluate the management of vascular aneurysms in patients with vEDS | vEDS is associated with a high incidence of arterial dissections and aneurysms, commonly affecting the carotid and vertebral arteries. | Early diagnosis and careful vascular surveillance are crucial to managing vascular complications in vEDS. |
| Malfait, F., *et al*. | 2017 | To define the diagnostic criteria for Ehlers-Danlos Syndrome | The genetic mutation in COL3A1 is responsible for vascular EDS, leading to fragile arteries prone to dissection. | Genetic testing for COL3A1 mutations is critical for diagnosing vEDS and preventing vascular complications. |
| Bergqvist, D., *et al*. | 2009 | To examine arterial complications in vEDS and their management strategies | Vascular complications, such as dissections and rupture, are the primary causes of morbidity and mortality in vEDS. | Vascular surveillance and genetic counseling are essential for preventing major vascular events in vEDS patients. |

| | | | | |
|---|---|---|---|---|
| Pepin, M., *et al*. | 2000 | To study the clinical and genetic features of Ehlers-Danlos Syndrome Type IV | vEDS patients are at high risk for early-onset strokes, with dissections and ruptures affecting major arteries. | Stroke prevention strategies in vEDS patients should focus on early detection of arterial dissections and prompt treatment. |

**Table 3:** Literature Summary of Vascular Ehlers-Danlos Syndrome (vEDS) and Stroke.

This table summarizes key studies on vascular Ehlers-Danlos Syndrome (vEDS) and its association with stroke. The studies reviewed here underline the importance of early recognition, genetic testing, and vigilant vascular management to mitigate stroke risk in young adults with vEDS.

## Discussion

Pathophysiology of Stroke in Vascular Ehlers-Danlos Syndrome (vEDS). Vascular Ehlers-Danlos Syndrome (vEDS), caused by mutations in the COL3A1 gene, results in the production of defective Type III collagen, which is crucial for maintaining the structural integrity of blood vessels, skin, and internal organs.

The structural weakness of the vascular walls predisposes individuals with vEDS to spontaneous arterial dissections, aneurysms, and rupture. In this case, the left internal carotid artery (ICA) dissection was the primary cause of ischemic stroke. The dissection likely caused a thrombus formation, which led to an embolic occlusion of the left middle cerebral artery (MCA), resulting in the acute infarction.

Arterial dissections, particularly in the carotid and vertebral arteries, are the most common vascular complications in patients with vEDS. The fragility of the vessel walls due to defective collagen synthesis leads to the tearing of the arterial layers. As the tear extends, blood may accumulate between the layers, forming a hematoma that narrows the vessel lumen and can create a thrombus that is prone to embolization. This thrombus can travel to distal cerebral arteries, causing ischemia and subsequent stroke. In our patient, the MCA infarction was a direct consequence of this embolic event.

In addition to dissections, vascular malformations such as aneurysms are also common in vEDS patients. These malformations

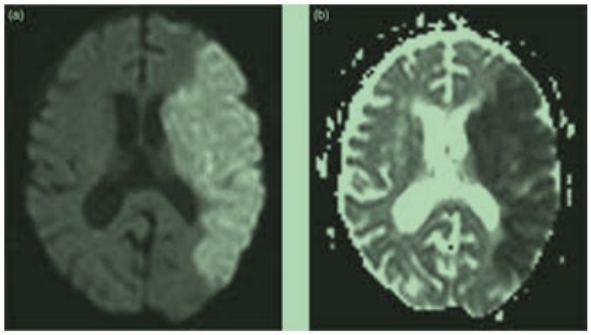

**Figure 3:** MRI DWI: Hyperintense regions in the left MCA territory confirming acute ischemia.

can further contribute to stroke risk by forming areas of turbulent blood flow, making the vessels more susceptible to rupture and thromboembolic events. The presence of vascular anomalies should always be suspected in vEDS patients presenting with neurological deficits.

| Cause | Clinical Features | Diagnostic Tools |
|---|---|---|
| Arterial Dissection | Neck pain, Horner's syndrome | MRI/MRA, Doppler Ultrasound |
| Hypercoagulable States | Recurrent thrombosis | D-dimer, protein C/S, genetic tests |
| Genetic Disorders | Family history, connective tissue signs | Genetic testing, imaging |

**Table 4:** Differentiating Features of Stroke Etiologies in Young Adults.

### Diagnosis of vEDS in young stroke patients

Diagnosing vEDS in the context of an ischemic stroke in a young patient can be challenging. As with many genetic disorders, the clinical signs may be subtle and may not manifest until later in life. In this case, the patient exhibited typical features of vEDS such as

joint hypermobility, atrophic scars, and thin, translucent skin, all of which were key clues that led to the suspicion of a connective tissue disorder. However, these features are often mild or overlooked in the absence of a family history of connective tissue abnormalities or early vascular events. Therefore, a high index of suspicion is critical in young stroke patients who do not present with typical risk factors for cardiovascular disease.

In addition to a detailed clinical history and physical examination, genetic testing for COL3A1 mutations is essential to confirm the diagnosis. The diagnosis of vEDS should be considered in young patients who present with unexplained arterial dissections, especially when there is a family history of sudden vascular events or unexplained deaths. Early diagnosis can help guide management and prevent further complications.

In this case, genetic testing revealed a pathogenic COL3A1 mutation, confirming the diagnosis of vEDS and explaining the patient's susceptibility to arterial dissection and ischemic stroke. Genetic counseling and family screening were offered, as other family members may be at risk for similar vascular complications. Genetic testing plays a crucial role in identifying affected individuals and guiding long-term management strategies.

## Management of acute stroke in vEDS

The management of acute ischemic stroke in vEDS patients requires a careful and tailored approach, given the high risk of arterial rupture. Although intravenous thrombolysis with recombinant tissue plasminogen activator (tPA) remains the standard of care for AIS, it carries inherent risks for patients with vascular fragility. In this patient, thrombolysis was performed within the 2-hour window after symptom onset, with close monitoring for any signs of vascular rupture. It is crucial that clinicians are aware of the heightened risk of complications, particularly in cases of arterial dissection, and take appropriate precautions when administering thrombolytics or anticoagulation.

While tPA was used to dissolve the thrombus, anticoagulation therapy was avoided in this case due to the risk of further hemorrhage from the dissection site. Given the fragility of the patient's vascular system, anticoagulation and fibrinolysis must be approached with caution in vEDS patients. Dual antiplatelet therapy, consisting of aspirin and clopidogrel, was initiated for secondary stroke prevention. The use of statins, such as atorvastatin, was also considered to reduce the risk of future vascular events by stabilizing the endothelial function and lowering cholesterol levels, although statin therapy in vEDS patients should be carefully monitored for any adverse effects.

Long-term management in vEDS patients requires a multidisciplinary approach. Vascular surveillance, including regular imaging of the carotid and vertebral arteries, is necessary to detect any developing aneurysms or dissections that could lead to further strokes or other complications. Blood pressure control is also critical in these patients to reduce the strain on already fragile vessels. Maintaining a low-normal blood pressure (typically <130/80 mmHg) is recommended to prevent further vascular injury and mitigate stroke risk. Additionally, patients with vEDS must be closely monitored for other potential vascular complications, including rupture of arterial aneurysms, which can occur suddenly and without warning.

| Aspect | Recommendation |
|---|---|
| Acute Stroke Treatment | tPA within therapeutic window; avoid heparin |
| Secondary Prevention | Aspirin + Clopidogrel; statins if indicated |
| Long-term Monitoring | Regular vascular imaging and blood pressure control |

**Table 5:** Management Considerations in vEDS-Related Stroke.

## Rehabilitation and Secondary Prevention

Rehabilitation plays a crucial role in the recovery of patients who have suffered a stroke. In this patient, intensive physical therapy was initiated to address motor deficits, including right-sided hemiplegia, and speech therapy was started to help with expressive aphasia. The goal of rehabilitation is to help patients regain as much function as possible and improve their quality of life.

Secondary prevention strategies, including lifestyle modifications (e.g., smoking cessation, physical activity, and dietary changes), should be strongly encouraged. Additionally, genetic counseling for the patient and their family members is critical to understand the inherited nature of vEDS and to prevent future vascular events. Family screening and preventive monitoring,

including regular imaging of major arteries, can significantly improve outcomes by identifying high-risk individuals before the onset of major complications.

### Considerations in family screening and genetic counseling

One of the most important aspects of managing vEDS is genetic counseling and family screening. Since vEDS is inherited in an autosomal dominant manner, the patient's relatives are at risk for inheriting the mutation and may be predisposed to similar vascular complications. In this case, the patient's family members were offered genetic testing, which revealed that a sibling also carries the COL3A1 mutation. Preventive strategies, such as regular vascular imaging and lifestyle modifications, were recommended for the affected family member. Early detection through family screening can significantly reduce the risk of stroke and other vascular events, improving long-term outcomes and enabling early intervention when necessary.

As more families are diagnosed with vEDS, there is growing recognition of the importance of genetic counseling and the need for awareness of the potential vascular risks. With better screening, more individuals at risk of vascular complications can be identified earlier, leading to timely intervention and reducing the burden of vascular events in this population.

### Treatment

This table outlines the comprehensive management strategy for young patients with acute ischemic stroke related to vascular Ehlers-Danlos syndrome (vEDS). The treatments listed are tailored to address both the immediate needs for stroke care and long-term prevention, with special emphasis on the unique risks posed by the vascular fragility seen in vEDS.

| Treatment Modality | Indication | Management Approach | Considerations |
|---|---|---|---|
| Acute Stroke Treatment | For patients presenting with acute ischemic stroke due to arterial dissection | Intravenous thrombolysis with tPA (if within the therapeutic window) | Avoid systemic anticoagulation due to high risk of arterial rupture. |
| Antiplatelet Therapy | Secondary prevention of stroke and management of dissection-related thrombus formation | Aspirin (81 mg/day) + Clopidogrel (75 mg/day) | Monitor for signs of bleeding. |
| Statins | To stabilize endothelial function and reduce recurrent vascular events | Atorvastatin (20 mg/day) | Be cautious in cases of renal or hepatic dysfunction. |
| Blood Pressure Control | To minimize stress on fragile vasculature and reduce stroke risk | Calcium channel blockers or ACE inhibitors | Maintain blood pressure within a low-normal range (e.g., <130/80 mmHg). |
| Surgical Intervention | In cases of significant arterial dissection or aneurysm formation | Surgical revascularization or stenting if necessary | Risk of vessel rupture; should be done by specialized vascular surgeons. |
| Rehabilitation | To address motor deficits, aphasia, and restore function post-stroke | Physical therapy, speech therapy, and occupational therapy | Ongoing therapy required for long-term recovery. |
| Genetic Counseling | To evaluate the presence of vEDS in family members and prevent future events | Family screening for COL3A1 mutations | Early detection in family members can lead to preventive monitoring. |

**Table 6:** Treatment Modalities for Acute Ischemic Stroke in Vascular Ehlers-Danlos Syndrome (vEDS).

## Conclusions

This case underscores the importance of considering rare genetic conditions, such as vEDS, in young adults presenting with ischemic stroke. Early recognition, informed by genetic testing and a thorough clinical evaluation, is critical to prevent recurrent events. Lifelong surveillance, multidisciplinary care, and patient education are vital for managing such cases. Increased awareness among clinicians and further research into vEDS-related strokes will enhance outcomes for this vulnerable population.

## Declarations

- **Ethical Approval**: Taken from concerned authorities.
- **Human subjects**: Consent was obtained or waived by all participants in this study.
- **Consent to publish** -also taken
- **Authors' contributions**
  - Mohammed Quader Naseer and MohammedAfshar Alam wrote the main manuscript text
  - Iqra Hoor, Uday Sankar Akash Vinayaka, Subhana Musquan Shaik collected figures and wrote the cover letter
  - All authors reviewed the manuscript
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- **Availability of data and materials**: Can be asses via mail at mdquader69@gmail.com or databases search including pubmed, scopus, web of science.
- **Conflicts of interest**: In compliance with the ICMJE uniform disclosure form, all authors declare the following:
- **Payment/services Info**: All authors have declared that no financial support was received from any organization for the submitted work.
- **Financial relationships**: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.
- **Other relationships**: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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