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Case Report

Polycystic Ovary Syndrome (PCOS) an Emerging Risk Factor of Cerebral Venous Sinus Thrombosis (CVST): A Case Report and Literature Review

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Abstract

Cerebral venous sinus thrombosis (CVST) is responsible for about 0.5% to 3% of all strokes, with a markedly higher frequency noted in young women. This condition is determined by several factors; in addition to established risk factors, new contributors that have become better recognized but less well-documented in the tropics include obesity, polycystic ovary syndrome (PCOS), COVID-19 infection, and vaccine-associated thrombocytopenia and thrombosis. We describe the third known case, and the first described in Africa, of CVST in a woman with PCOS and no recognizable pro-thrombotic disorder. A 42-year-old female patient, right-handed, nulligest, and obese presented with a history of infertility and menstrual cycle disorders. She was admitted to our department due to the onset of atypical headaches that progressed subacutely and were associated to generalized tonic-clonic seizures. Neurological assessment upon admission revealed intracranial hypertension syndrome. Brain MRI showed extensive CVST on the left side, involving the lateral sinus and the internal jugular vein. The diagnosis of PCOS was made according to the Rotterdam criteria. A multidisciplinary management strategy was implemented. Comprehensive studies are essential to elucidate the factors associated with CVST in women diagnosed with PCOS, which will facilitate risk assessment and the formulation of preventive measures.

Keywords

Polycystic Ovary Syndrome (PCOS), Cerebral Venous Sinus Thrombosis (CVST), Risk Factor, Case Report, Abidjan

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1. Introduction

Cerebral venous sinus thrombosis (CVST) is an important cause of strokes in young adults, particularly affecting women, who make up approximately two-thirds of the cases. It is responsible for 0.5% to 3% of all strokes [1, 2]. Historically viewed as a rare condition, with an estimated incidence of 3 to 4 cases per million annually, a recent retrospective study conducted in Adelaide, Australia, has identified an incidence of 15.7 cases per million per year [3]. This increase is attributed to technological advancements in diagnostic neuroradiology, as well as improved access to and utilization of MRI for the evaluation of unusual headaches and first-time seizures, even in developing regions [1, 4]. In West Africa, the hospital prevalence of CVST ranges from 0.47% to 3% [5-7], with an acute mortality rate of approximately 10% in these regions [8]. Headache is the most frequently reported symptom [9]. The prognosis is generally favorable when diagnosis is made promptly and effective anticoagulant therapy is initiated.

This condition is multifactorial, involving conventional risk factors as well as both endogenous and exogenous estrogen, particularly from combined oral contraceptives, pregnancy, and the puerperium, along with thrombophilic disorders and rare hematological conditions [1, 4, 10, 8]. Emerging factors such as obesity, polycystic ovary syndrome (PCOS), COVID-19 infection, and vaccine-induced thrombocytopenia and thrombosis are gaining recognition, though less documented in tropical regions [11]. PCOS represents the most prevalent endocrine disorder affecting women of reproductive age [12]. Diabetes, hypertension, dyslipidemia, and obesity are commonly linked to PCOS, all of which contribute to a heightened risk of cardiovascular diseases, such as myocardial infarction, stroke, and venous thromboembolism (VTE) [13]. Research conducted by Antonio et Al. revealed that the prevalence of VT among women diagnosed with PCOS was threefold greater than that of the control group [14]. Additionally, recent investigations have shown that the risk of VTE is independent of other variables, such as obesity and the use of hormonal contraceptives [15]. Although large-scale studies specifically addressing the risk of CVST in women with PCOS are currently lacking, two cases of CVST have been documented in reproductive-age women with PCOS, without any other associated prothrombotic conditions [16, 17]. Our patient also presented with a hemorrhagic polymyomatous uterus, which was accompanied by moderate iron-deficiency anemia. In this study, we will discuss the impact of these various factors on the occurrence of CVST.

2. Case Presentation

A 42-year-old right-handed female patient, nulligest, obese, with a body mass index of 31 kg/m^2 with a history of infertility and menstrual cycle disorders characterized by Spaniomenorrhea without gynecological follow-up. The patient was admitted to our neurology department due to recent, unusual headaches that appeared suddenly and progressed subacutely. The symptoms began approximately ten days prior to her admission, manifesting as diffuse headaches that occurred abruptly, radiating to the neck, described as pulsatile, persistent, and increasing in intensity, reaching a level of 9 out of 10 on the visual analog scale (VAS). The patient's pain was minimally alleviated by standard analgesics and was accompanied by photophobia and visual disturbances, without any signs of phonophobia or projectile vomiting.

Three days later, the patient experienced a generalized tonic-clonic seizure lasting three minutes, followed by a postictal confusion lasting approximately 30 minutes, after which she returned to a normal state of consciousness without any associated motor deficits. This situation prompted a consultation at a peripheral hospital, where initial examinations yielded negative results, leading to her transfer to our department for specialized care.

Upon admission, the neurological examination suggested the presence of intracranial hypertension syndrome, with no signs of meningeal irritation, sensory-motor deficits, or cranial nerve involvement. The physical examination of the abdomen revealed a hypogastric bulge, and upon palpation, several small, rounded, non-tender masses were noted, which were firm in consistency and mobile relative to the superficial plane, appearing to be associated with the uterus.

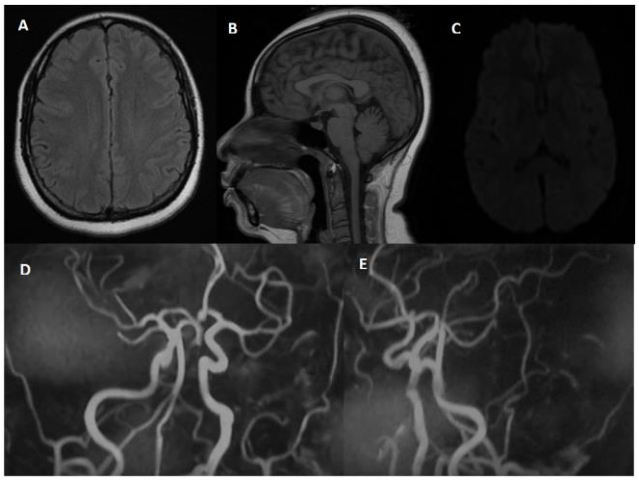

Figure 1. *Brain MRI with arterial sequences.*

Legend: The axial brain MRI T2-FLAIR spin-echo sequence (SES) (A), sagittal section (T1 SES) without gadolinium, (B), diffusion sequence (C), and Maximum intensity Projestion (MIP) reconstruction (front view, D; profile view, E) indicate no parenchymal or arterial vascular lesion

The Brain MRI revealed extensive thrombosis on the left side, extending from the transverse sinus to the left internal

jugular vein (Figure 2), with no associated parenchymal or arterial vascular anomalies (Figure 1). The pelvic ultrasound indicated a hemorrhagic polymyomatous uterus and microfollicular ovaries. The complete blood count indicated moderate hypochromic microcytic anemia, measuring 8.8 g/dl. Additional blood tests, including those assessing thrombophilia (Table 1), along with cerebrospinal fluid analysis (Table 2), yielded negative finding.

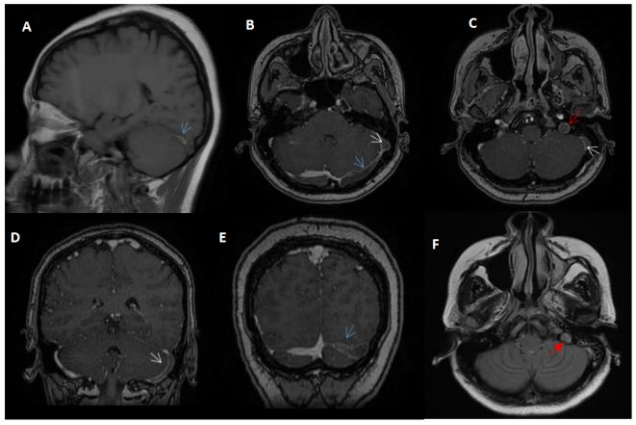

Figure 2. *Brain MRI with gadolinium.*

Legend: Significant CVST is identified in the transverse sinus (blue arrow), left sigmoid sinus (white arrow), and left jugular vein (red arrow). It appears as hyperintensity on the sagittal T1 SES imaging without gadolinium (A). Following gadolinium administration, the sinus wall shows enhancement and appears hyperintense around the thrombus, which is hypointense on the axial section T1 SES 3D images with gadolinium (B and C) and on the coronal section images (D and E). Additionally, the thrombus causes a slowdown in blood flow, shown as hyperintense on the axial T2 FLAIR SES image (F).

Table 1. *Biological blood test results.*

Parameters	Reports	Reference values
RBC count	4,03.10^6/mm^3	4,8 à5,5.10^6/mm^3
Hb	8,8 gr/dl	12 à16 gr/dl
MCV	59,4 fl	81 à97 fl
MCH	16,3 pg	28 à32 pg
MCHC	27,5 g/dl	32 à36 g/dl
Platelets	142. 10^3/mm^3	150 à400. 10^3/mm^3
TLC	4,71. 10^3/mm^3	4, 5 à10, 5. 10^3/mm^3
P. Neutrophils	2310/mm^3	1800 à7400/ mm^3
CRP	5 mg/l	< 6 mg/l
AST	13,3 UI/l	7-37 UI/L
ALT	11 UI/l	6-40 UI/L
Urea	0,13 g/l	0,13-0,45 gr/L
creatinine	9,5 mg/l	5-14 mg/l
PT	96%	>65%
C Protein	103%	70-130%
S Protein	95%	70-103%
Antithrombin	117%	80-120%
PTT ratio	0,9	0,8-1,2

Legend: RBC: Red blood cell; Hb: Hemoglobin; MCV: Mean Corpuscular Volume; MCH: Mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; TLC: Total leukocytes count; P. neutrophils: Polynuclear neutrophils Cells; CRP: C - reactive protein; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; PT: Prothrombine time; PTT: Partial Thromboplastine Time.

Table 2. *CSF biological analysis results.*

Parameters	Reports	Reference values
Macroscopic analysis		
Appearance	Clear	Clear
Opening pressure	15 cm of water	from 10 to 15 cm of water
Microscopic analysis		
Cytology analysis		
White blood cell counts	9/mm^3	0-268/ mm^3
Red blood cell count	0/ mm^3	0/ mm^3
Atypical cells	0/ mm^3	0/ mm^3
Cytology formula		
Lymphocytes (%)	100	100
Neutrophils (%)	0	0
Lymphoblasts (%)	0	0
Biochemical analysis		
Proteinorrhachia	0.54 g/l	0.40 à0.60 g/l
Glycorrhachia	0.59 g/l	0.45 à0.80 g/l
Chlore	120 mmol/l	110 à130 mmol/l
Bacteriological analysis		
Cultures	No germ	No germ
Molecular biological analysis (PCR)		
MTB	Negative	Negative
Herpes viruses	Negative	Negative

Parameters	Reports	Reference values
Immunological test		
TPHA	Negative	Negative
VDRL	Negative	Negative

Legend: CSF: cerebrospinal fluid, PCR: polymerase chain reaction, TPHA: Treponema Pallidum Hemagglutinations Assay, VDRL: Venereal Disease Research Laboratory.

3. Discussion

This report describes a 42-year-old woman with extensive left-sided CVST, who was incidentally diagnosed with PCOS, uterine fibroids, and moderate microcytic hypochromic anemia. CVST is a significant cause of stroke in young women. The international study on Cerebral venous sinus thrombosis and dural sinus thrombosis (ISCVT) has indicated that approximately 85% of adult patients exhibit at least one risk factor [18]. Within sub-Saharan Africa, there is a notable association between infectious diseases and strokes [19], which remain the leading risk factors for cerebral venous sinus thrombosis (CVST), accounting for 63.1% of instances. The subsequent risk factors include combined oral contraceptives (COCs) at 7.3%, pregnancy and the postpartum phase at 6.2%, and coagulopathies at 2.2% [6]. The factors linked to CVST in tropical regions are still poorly understood, primarily due to diagnostic challenges, a significant shortage of specialized medical personnel, limited access to neuroimaging [1, 20], and a lack of epidemiological studies on this topic [8]. Additionally, emerging risk factors such as obesity, PCOS, COVID-19 infection, thrombocytopenia, and vaccine-induced thrombosis are increasingly underreported in these areas [11].

PCOS is recognized as one of the most prevalent endocrine and reproductive disorders, impacting approximately 5 to 20% of premenopausal women globally [21]. The diagnosis is based on the Rotterdam criteria, which require the presence of at least two of the following three features: clinical or biochemical hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [15, 21]. Additionally, various metabolic disturbances, including obesity, insulin resistance, and type 2 diabetes, are often associated with this condition [15, 21]. In the reported case, the diagnosis of PCOS was made due to ovulatory dysfunction linked to infertility, alongside bilateral multifollicular ovarian dystrophy seen on ultrasound.

Numerous observational studies have indicated an elevated cardiovascular risk associated with PCOS. The most recent research highlights a significant overall increase in the risk of cardiovascular diseases (OR, 1.68 [95% CI, 1.26–2.23]), myocardial infarction (OR, 2.50 [95% CI, 1.43–4.38]), and strokes (OR, 1.71 [95% CI, 1.20–2.44]) [21]. PCOS is linked to hemostatic disorders, and epidemiological studies suggest that affected women may face a heightened risk of venous thromboembolism (VTE) [13-15]. Furthermore, many women with PCOS utilize combined COCs, which may also influence this risk [21]. The presence of obesity and insulin resistance, commonly associated with PCOS, further exacerbates cardiovascular risk [13]. Findings from the meta-analysis conducted by Gariana et al. reveal that women with PCOS have a 1.5 to 2 times greater risk of deep vein thrombosis (DVT) compared to unaffected women, regardless of obesity and COC use [15]. This observation is further corroborated by a recent biological study that establishes a connection between free androgen index and the risk of TVE in younger women [22]. The risk of thrombosis appears to escalate with decreasing age; adjusted odds ratios (aOR) reveal that for the age group of 18 to 24 years, the aOR is 3.26 (95% confidence interval, 2.61-4.08). For women aged 25 to 34 years, the aOR is 2.39 (95% confidence interval, 2.12-2.70), while for those aged 35 to 45 years, it stands at 2.05 (95% confidence interval, 1.84-2.38) [13].

Several biological hypotheses have been proposed to elucidate the prothrombotic state observed in women with PCOS. This condition is characterized by a hypofibrinolytic state, indicated by elevated levels of plasminogen activator inhibitor-1 (PAI-1) and thrombin-activatable fibrinolysis inhibitor (TAFI). The secretion of PAI-1 is believed to be stimulated by hyperinsulinemia and reduced levels of sex hormone-binding globulin, which are commonly observed in patients with PCOS [15]. Additionally, a Danish study has reported another mechanism involving a disturbance in thrombin generation [23]. The interplay among hormones, obesity, and insulin resistance in the increased risk of venous thrombosis associated with PCOS remains to be fully clarified; however, obesity may serve as the primary mediator linking insulin resistance and venous thrombosis [15].

Currently, there are two documented instances of CVST in women diagnosed with PCOS who do not present any additional risk factors [16, 17]. The patient in question was a 42-year-old obese female with previously unrecognized PCOS, which was also associated with uterine fibroids. There have been rare reports of CVST and arterial strokes in women with uterine fibroids, often correlated with conditions such as severe anemia (< 6 g/dL) [17], polycythemia [18], or paradoxical emboli [19, 20] in patients with a persistent patent foramen ovale and a right-to-left shunt. A transesophageal echocardiogram was not conducted to exclude this unlikely scenario, given that the patient did not show signs of peripheral venous thrombosis. Anemia poses a considerable risk for CVST, with a greater prevalence in males than in females [24]. The majority of documented cases involve severe anemia [24-26], which was not the case for our patient. In instances of anemia, CVST is linked to reactive thrombocytosis and iron deficiency [23, 24]. Nevertheless, in our patient's case, although she exhibited microcytic anemia, her platelet levels were normal.

Similar to the two preceding cases, the recent atypical

headache with a subacute evolution was the primary manifestation of the symptomatology [16, 17]. The clinical features associated with CVST are diverse, with this variability being influenced by factors such as the site and extent of the thrombosis, the level of venous obstruction, the age of the patient, and the presence of underlying diseases or specific risk factors pertinent to each case [10]. However, headache is recognized as the most reliable symptom [9]. During the progression of her illness, our patient also experienced seizures, which occur in about 17% of CVST cases in the sub-Saharan African demographic [8]. Additional signs that may be observed include visual impairments, disturbances in consciousness, focal motor or sensory signs, cavernous syndrome, and involvement of other cranial nerves [7, 8]. The recommendations from the European Stroke Organization (ESO) and the American Heart Association (AHA) advocate for the use of magnetic resonance venography or computed tomography venography as reliable diagnostic techniques [1].

The management of CVST is primarily centered on the judicious application of anticoagulants, in conjunction with addressing the identified underlying cause. In this instance, we commenced anticoagulant therapy through a parenteral route, utilizing low molecular weight heparin for a period of three days, followed by a switch to Rivaroxaban, prescribed at 15 mg twice daily for 21 days, and subsequently at 20 mg once daily for five months, adhering to established American guidelines [1]. Results from the SECRET (Study of Rivaroxaban for Cerebral Venous Thrombosis) study indicate that the early initiation of oral anticoagulant therapy, such as Rivaroxaban, can lead to similar clinical outcomes [27]. In rare cases, endovascular treatment may be an option for severe CVST cases that do not show improvement or deteriorate despite appropriate anticoagulation [1]. However, such treatment is not accessible in our clinical setting. Furthermore, the patient was placed on hormonal therapy and is under gynecological supervision, having refused any surgical options for fibroids. Additionally, iron supplementation was provided for three months to rectify her anemia. The clinical course was characterized by a reduction in headache severity within two weeks of treatment, a complete cessation of seizures, and no further neurological incidents reported over a one-year follow-up.

4. Conclusion

Conducting extensive studies is crucial for a comprehensive understanding of the multiple factors that lead to CVST in women diagnosed with PCOS. This knowledge will facilitate risk assessment and the formulation of effective primary prevention and monitoring strategies.

In cases of acute or subacute neurological events in women with confirmed or suspected PCOS, neurologists should consider the possibility of CVST and request appropriate neuroimaging to rule it out. This situation should also raise awareness among gynecologists, who frequently serve as the initial healthcare providers, as well as among all medical professionals involved in the care of this syndrome, to prevent the minimization of neurological events in this demographic. Given the diverse clinical manifestations of venous thrombosis, prompt diagnosis and treatment are vital to avoid compromising both functional and life outcomes.

Abbreviations

CVST	Cerebral Venous Sinus Thrombosis
MRI	Magnetic Resonance Imaging
PCOS	polycystic Ovary Syndrome
COVID-19	Coronavirus Disease
VTE	Venous Thromboembolism
VAS	Visual Analog Scale
ISCVT	International Study on Cerebral Venous Sinus Thrombosis and Dural Sinus Thrombosis
COCs	Combined Oral Contraceptives
aOR	Adjusted Odds Ratios
TAFI	Thrombin-Activatable Fibrinolysis Inhibitor
ESO	European Stroke Organization
AHA	American Heart Association
SECRET	Study of Rivaroxaban for Cerebral Venous Thrombosis

Author Contributions

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Muriel Amon-Tanoh: Funding acquisition, Investigation, Resources, Validation

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Ethical Approval

The study was approved by our local ethics committee.

Consent

Oral informed consent was obtained from the patients for the publication of this case report.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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Research Fields

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Muriel Amon-Tanoh: General Neurology, Cerebrovascular pathologies

Cédric Valéry Kadjo: Neurological Emergency, Neuro immunology, General Neurology

Marceline Sifa Balungwe: Gynecology, obstetric, contraception and reproductive health

Constance Yapo-Ehounoud: Child neurology, Neuro immunology, General Neurology

Abel Christian Tanoh: Neuroepidemiology, Neuroinfectiology, General Neurology

Mariam Doumbia-Ouattara: Child Neurology, Epileptology, General Neurology

Paulette Yapo-Yapi: Neuroradiology, Diagnostic and Interventional Pelvic radiology

Évelyne Aka-Anghui Diarra: Epileptology, Peripheral neurological disorders, Neurophysiology, Abnormal movements disorders, Epileptology

Berthe Assi: Epileptology, Peripheral neurological disorders and muscle pathologies, Neurophysiology