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A Stroke of Undetermined Source in Geriatrics

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Authors' contributions

This work was carried out in collaboration among all authors. Author FG collected the clinical case record. Authors FM and PO drew the scientific conceptual content and revised the paper critically, according to literature. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Presentation of the Case: Criptogenetic strokes represent a challenge, particularly in geriatrics as the patient's clinical complexity, the polipharmacotherapy, the epigenetic modifications of a life course may complicate the case clinical presentation and the prognosis. We report the case of a young old woman admitted to hospital for an ischemic stroke recurrence associated to a leg deep venous thrombosis. The medical history was negative for traditional cardiovascular risk factors, excluding a mild carotid atherosclerotic plaque, for rheumatologic/autoimmune or oncological diseases. Haematological malignancies were also ruled out. The coagulative panel showed the prothrombin G202110A gene heterozygote mutation.
Discussion: The clinical case adds an interesting narrative frame to the issue of criptogenetic strokes in geriatrics; the mutation of the prothrombin G202110A gene might act synergistically to comorbidity disrupting the atherosclerotic plaque. Immunosenescence, clinical frailty, gender difference and the epigenetic modifications might contribute to stratify a higher pro thrombotic risk for this individual patient.

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Conclusion: This case strengthens the need to tackle the elderly clinical complexity, through tailored approaches on the single patient.

Keywords: Criptogenetic strokes; elderly frailty cumulative index; prothrombin G202110A gene mutation.

1. INTRODUCTION

Criptogenetic strokes represent a challenge, accounting for 30/40% of strokes. So far, the pathogenesis is unclear, since many risk factors have been implicated without conclusive features [1]. The issue of strokes of undetermined origin is even more complicated in geriatric patients; the age- related anatomic-functional alterations, the multifactorial origin of diseases, the comorbidity status and the polipharmacotherapy of older adults heavily affect the common onset of diseases, the clinical course and the prognosis.

To date, hypercoagulative states have been included among the putative causes for criptogenetic strokes; they are defined as innate and/or acquired alterations of the coagulation that may constitute the biological background for the development of venous thrombosis and ischaemic infarction in unusual anatomical locations. To date, there is no evidence-based result that thrombophilias are associated to an increased risk of stroke [2]. However, a recent metanalysis has included the mutation of the prothrombin G202110A gene, the most frequent coagulative disorder in the Mediterranean area with different degrees of penetrance, as a potential risk factor for the pathogenesis of stroke and venous embolism [3]. Furthermore, hypercoagulative states and aging are complex processes; haemostasis factors progressively rise within aging, hence high levels of the coagulation markers in elderly does not necessarily mirror an higher risk of arterial or venous thrombosis [4].

2. PRESENTATION OF THE CLINICAL CASE

We reported the clinical case of a woman of 65 years old, who presented an ischemic stroke associated to a left leg deep venous thrombosis, and was admitted to our acute geriatric ward IRCCS AUO San Martino Hospital Genoa, Italy.

The patient's history reported one pregnancy with eutocic delivery, a knee arthroprosthesis without major complications and a previous right hemisphere ischemic stroke (involving extensively temporoparietal and frontolateral regions) with left brachiocrural hemiparesis at the age of 63 with *restitutio ad integrum*. The patient's history was negative for traditional risk factors (hypertension, dyslipidemia, cardiac disease and/or malformation, diabetes, hyperhomocysteinemia) and for rheumatologic/autoimmune or oncological diseases. Her life style habits included active slight smoking (less than 5 cigarettes a day in the last twenty years) and regular physical activity. The patient's drugs regimen included acetyl salicilate 160 mg o.p.d and a protein pump inhibitor o.p.d. The neurological examination showed a mild left brachio-crural hemiparesis (F3/5), with brachial predominance, a postural instability (Tinetti 15/28) and a functional dependence (Barthel 60/100). The patient's cognitive status (Mini mental state examination 29/30) and mood (geriatric depression scale 3/15) resulted unaffected. The CT brain scan showed a non-lacunar ischemic stroke, characterized by a vast hypodense area in the right hemisphere, involving right temporal insular nuclear, parietal inferior regions, frontolateral and frontorolandic region with passive dilation of the homonymous lateral ventricles (Image 1).

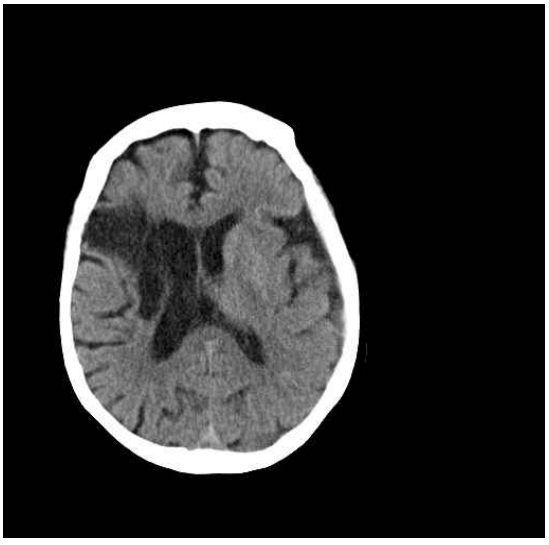

Image 1. CT brain scan showing a vast right hemisphere non-lacunar ischemic stroke, involving right temporal insular nuclear, parietal inferior regions, frontolateral and frontorolandic region with passive dilation of the homonymous lateral ventricles

As the pathogenesis of the stroke was undefined, a further assessment of cardiovascular risk factors was performed; a mild bilateral carotid atherotic plaque (eco- color doppler of sovraortic trunks with a left stenosis of near 40%) was detected, non responsible for stroke onset. The serum lipid profile was within the normal range. A serum autoimmune panel was also performed (including LAC, APLA and anti-cardiolipin) yielding non-significant results. The ECG monitoring (ECG HOLTER) ruled out a paroxysmal atrial fibrillation. The echocardiographic examination ruled out any congenital heart malformation and reported a normal ejection fraction (Ejection fraction: 65%) with preserved left ventricular function and no atrial dilation. A chest X-ray was performed and it resulted negative for infective pulmonary disease, pulmonary embolism or malignancies. The screening for haematological disorders (including protein C and S deficiency, antithrombin III deficiency and mielodisplastic conditions such as Polycythemia vera, sickle cell anemia, sickle-C disease, and essential thrombocythemia) as major disorders of formed blood elements causing stroke were also ruled out. Then, the coagulative panel for thrombophylia was performed and the heterozygote mutation of the prothrombin G202110A gene was detected.

The patient fully recovered after an intensive 2 months rehab therapy, (Barthel 90/100; Tinetti 19/28); an oral anticoagulant (warfarin within 2-3 INR therapeutic range) was introduced, as secondary prevention, and the patient was successfully discharged at home.

3. DISCUSSION

The clinical case adds an interesting narrative frame to the issue of strokes of undetermined source. As the cerebrovascular event is considered of an unknown cause, it is important to rule out haematological diseases as unusual causes (almost 6% of the cerebral infarcts), as well as systemic infections, inflammatory disorders and a series of miscellaneous clinical conditions. In this clinical case, the accurate blood panels and the clinical examinations of the patient allowed excluding these causes as source for the cerebral insult [5,6].

It is conceivable to consider the mutation of the prothrombin G202110A gene a thrombophylic background, which might contribute to the onset of the criptogenetic stroke, trough a multifactorial origin.

So far, a growing body of evidence indicates that genetic diseases which carries different degrees of heterozygous, and polymorphisms may present with specific late life disease [7], addressing a new challenge in the field of genetics and elderly. Indeed, the comorbidity status and, specifically, the atherosclerosis burden may act synergistically to the innate thrombophylia to disrupt the local plaque, fostering the onset of the cerebrovascular accident. Moreover, the immunosenescence, the cumulating of clinical deficits as postulated by Rockwood frailty indicator, [8] associated to the gender difference for stroke and the epigenetic modification of a life course (herein the smoking habit and the orthopaedic surgery) [9] might contribute to stratify an higher pro thrombotic risk for this single patient.

4. CONCLUSION

To date, evidence based results in the field are missing; the diagnostic workup for the stroke does not routinely include the testing for prothrombotic conditions but this narrative case strengthens the need to tackle the elderly clinical complexity, through tailored approaches on the single patient.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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