Cryptogenic Stroke: Cryptic Definition?

To the Editor:

We have read with great interest the article entitled “May-Turner Syndrome in patients with cryptogenic stroke and patent foramen ovale” which appeared in Stroke.1

The article is innovative, being the first large-scale analysis of the association between May-Turner Syndrome, cryptogenic stroke, and patent foramen ovale (PFO). Nonetheless, it arises some uncertainties concerning the definition of “cryptogenic stroke”. In the present study, cryptogenic stroke was defined as “a sudden focal neurological event in the absence of an identifiable cause such as uncontrolled hypertension, intracranial hemorrhage, ipsilateral carotid lesion, atrial fibrillation, intracardiac thrombus, degenerative neurological disorder or neoplasm.”1

In literature, the term cryptogenic stroke usually refers to strokes with no clearly definable cause even after extensive workup.2 Approximately 30% to 40% of ischemic strokes are cryptogenic.3 This means that in a large part of our patients we are unable to identify stroke etiology because: (1) the cause is reversible, and the workout is not performed at the appropriate time; (2) the causes of stroke are not fully investigated; and (3) some causes of stroke remain unknown.3 In the TOAST classification, the stroke is of undetermined etiology when the presence of multiple, concomitant risk factors force the physician to be unable to determine a final diagnosis.4

Paradoxical embolism via PFO has been documented as a stroke mechanism. Nevertheless, data are still conflicting, and PFO remains associated with cryptogenic stroke.4 In the present study all patients had undergone PFO closure, but a comprehensive workout was also performed to rule out other causes of stroke. Interestingly, they found a statistically significant higher incidence of thrombophilia screen abnormalities in the May-Turner Syndrome group. Some of these factors are known to be independent risk factors for arterial stroke (ie, 1 patient had antiphospholipid syndrome). Others are independent risk factors for venous thrombosis, but also a probable cofactor for arterial stroke (2 patients had Factor V Leiden mutation, 2 patients had prothrombin gene mutation, 4 patients had anticardiolipin antibody titer).5

We believe that these cases reported above exclude the definition of cryptogenic stroke. As a matter of fact, the presence of a thrombophilic abnormality (especially if acting in the venous system) and the PFO are not only concomitant risk factors, but pathophysiologically connected to the etiology of these strokes. Therefore, these are not cryptogenic strokes.

This consideration is not only speculative, because it relates to the debate concerning the indication of percutaneous closure of PFO. In presence of a thrombophilic factor, when lifelong antithrombotic or anticoagulant therapy is recommended, the advantage of closure is minor, while the risk of its complications are still not trivial.

To conclude, in the light of studies investigating new putative risk factors for stroke, it is urgent to revise the definition of cryptogenic stroke, to clarify the diagnostic doubts, and the possible clinical approach.

Disclosures

None.

Marta Altieri, MD, PhD
Pina Troisi, MD
Ilaria Maestrini, MD
Gian Luigi Lenzi, MD
Clinica Neurologica A
Sapienza Università di Roma
Viale dell’Università 30
Rome, Italy


Cryptogenic Stroke: Cryptic Definition?
Marta Altieri, Pina Troisi, Ilaria Maestrini and Gian Luigi Lenzi

Stroke. published online June 18, 2009;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/early/2009/06/18/STROKEAHA.109.553966.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/