Hypercoagulability in patients with indirect carotid cavernous fistulas

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Introduction

Indirect carotid cavernous fistulas (CCFs) are a subgroup of brain dural arteriovenous fistulas (DAVFs). Untreated cases may cause significant morbidity due to complications of orbital venous stasis. Pathogenesis is multifactorial and poorly understood. Recent studies suggest association of DAVFs with underlying hypercoagulable state (HS).

We hypothesized that patients with indirect CCFs may also have an underlying HS.

Objective

To assess the largest cohort of patients with indirect CCFs to date for evidence of HS by combination of comprehensive medical questionnaire and laboratory testing.

Methods

Design:
Descriptive, investigational study based on a retrospective cohort of patients having been diagnosed and treated for CCF at a University-based hospital between 2003 to 2019.

70 patients diagnosed and treated for CCF were identified:
55 were diagnosed with indirect CCFs and considered for enrollment into the study

Patients over 18 years of age with confirmed diagnosis of indirect CCF on neuro-imaging were identified on retrospective chart review. Consenting individuals able to complete questionnaire and undergo laboratory testing were enrolled.

Procedure:
Comprehensive clinical questionnaire screened for hereditary, situational and acquired risk factors of HS.

Laboratory investigations included:

- Complete blood count (CBC)
- Prothrombin time (PT)
- Partial thromboplastin time (PTT)
- Platelets
- Protein C and protein S
- D-dimer
- Factor V Leiden
- Prothrombin time (PT)
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- Prothrombin 20210A
- CalR
- HPT Platelet factor 4

- Participants with abnormal laboratory testing and/or past history of ischemic stroke, atrial fibrillation, cancer or hypercoagulability-associated hereditary disorders were deemed to have HS.

Results

Patient sample:
Twenty-two patients out of a total of fifty-five patients with indirect CCFs treated at the same institution between 2003 to 2019 fulfilled inclusion criteria and underwent hypercoagulability assessment.

- Mean age at CCF diagnosis was 59.4 years
- 17 (77%) patients were female

Clinical evidence of HS: clinical questionnaire and laboratory investigation (Tables 1, 2 and 3):

- 16 (73%) had clinical or laboratory evidence of HS:
  - 5 with history compatible with HS
  - 5 with laboratory evidence of HS
  - 6 with evidence of HS on both clinical history and laboratory investigation

Eleven (50%) had abnormal hypercoagulability markers:

- 1 had a diagnosis of Klippel-Trenaunay syndrome (hereditary disease predisposing to HS)
- No others had evidence of hereditary thrombophilia
- 9 were on anti-coagulation
- No patient reported a history of pulmonary embolism (PE) or deep vein thrombosis (DVT)

Of the nine patients on anti-coagulation therapy, 8 had started medication for an indication discovered on average 5.5 years after CCF diagnosis (Figure 1).

Study Limitations:

- Small sample size: nature of the prevalence of indirect CCFs
- Selection and survival biases: only a subset of patients who were available met inclusion criteria and consented to participate in the study and it was not control-based
- Retrospective nature: given patients having already been diagnosed and treated for CCF, data related to laboratory investigations for HS at time of initial presentation is lacking thus trend analysis is deficient

Conclusion:

We describe the presence of risk factors for HS in the largest cohort of patients with indirect CCFs to date. Our results indicate that patients with indirect CCFs have a very high prevalence of HS which contributes to increasing evidence that DAVFs are associated with HS.

This study supports the need for patients with newly diagnosed indirect CCFs to undergo a comprehensive hypercoagulability screen in order identify HS early and mitigate the risk of future thrombo-embolic events.