

Supplementary materials

Patients

Altogether 25 patients above the age of 18 with were initially surveyed in the study. We included patients that presented with suspected reversible cerebral vasoconstriction syndrome according to clinical course and initial imaging. The clinical inclusion criteria included headache with or without thunderclap component, with or without focal neurological signs at presentation combined with subsequent suggestive imaging (magnetic resonance [MR] angiography or computed tomography [CT] angiography). Patients without definite vasoconstriction on the imaging were excluded from the analysis (two patients), as well as patients without available MR imaging due to artificial implants (one patient). In addition, we excluded from the study patients with initial intracranial stenosis on presentation, which on follow-up was proven to be due to either severe atherosclerosis or vasculitis (two patients). The retrospective evaluation of patient files was approved by the ethical committee of the Chaim Sheba Medical Center (Helsinki committee approval number 6067-19). Clinical data was gathered and documented, including the incidence of brain ischemia and seizure episodes.

Imaging

All our patients underwent brain CT angiography and transcranial ultrasound Doppler imaging. In several patients, conventional digital subtraction angiography (DSA) was also performed at presentation and follow-up.

In most cases MR imaging, including MR angiography, was performed during the first few days of presentation. In some cases, the MR scan preceded the established diagnosis of cerebral vasoconstriction on angiography. Most of the patients underwent a follow-up magnetic resonance imaging (MRI) scan. All the clinical data is summarized in Supplementary Table 1.

CT imaging was performed on either a General Electric Revolution 256 scanner or a Philips ICT256 station. Injected contrast media was based on iohexol solution (Omnipaque 350 mg I/mL) by General Electric Healthcare (Chicago, IL, USA). DSA was performed by experienced interventional neuroradiologists, on a biplane Siemens Artis (Munich, Germany) angiography system, utilizing the same iohexol based solution mentioned above.

MRI imaging was acquired on a Philips™ Ingenia 3.0 Tesla scanner, injected contrast media included gadoteric acid solution (Dotarem, at a concentration of 9.1 g/100 mL).

Image processing

The diagnosis of cerebral vasoconstriction on CT angiography was established via consensus of a neuroradiologist and an in-

terventional neurologist. Two vascular neurologists confirmed cerebral vasospasm on transcranial Doppler imaging. MR imaging was reviewed independently by two neuroradiologists and an interventional neurologist. The degree of cerebral vasoconstriction was determined by quantifying the number of affected vessels (middle cerebral artery, anterior cerebral artery, posterior cerebral artery, superior cerebellar artery, basilar artery, anterior inferior cerebellar artery, posterior inferior cerebellar artery) and also by transcranial Doppler velocities measurements of the affected vessels on presentation and follow-up.

We graded the severity of reversible cerebral vasoconstriction syndrome (RCVS) by a composite neurological score that included posterior reversible encephalopathy syndrome (PRES) like edema appearance on MRI (0, 1), clinical seizures (0, 1), subarachnoid hemorrhage (0, 1), brain ischemia (0, 1) and thunderclap headache on initial presentation (0, 1). Multivariate logistic regression analysis was used to assure that the score components were not affected by demographic or clinical variables. The score was devised according to previously described markers of RCVS severity.⁶ The grading of contrast enhanced fluid attenuation inversion recovery (CE FLAIR) included the composite of intensity of sulci enhancement by contrast (0, no signal; 1, for mild signal; 2, for substantial signal) with its distribution throughout the brain (1 point for each involved lobe—including cerebellar hemispheres; 0–10).

Inter-rater agreement was excellent on every radiological evaluation (MRI, MR angiography, CT angiography, DSA, transcranial Doppler imaging).

Laboratory studies

All the patients underwent basic and advanced laboratory studies based on routinely accepted studies at the Sheba Medical Center Laboratory Division, including ruling out of rheumatologic and hypercoagulable conditions. Most of the patients also underwent a lumbar puncture to exclude subarachnoid bleed as a possible trigger and/or active inflammation to rule out vasculitic pathology.

Statistical analysis

Pearson correlation coefficient was calculated to establish various effects on either composite neurological outcome or CE FLAIR scoring. Multivariate analysis was performed as well in order to rule out mixed effects on the scores. Cutoff for statistical significance was set up at $P < 0.05$. The analyses were performed using Excel Statistical functions (Microsoft Corporation, Redmond, WA, USA) and GraphPad Prism software (San Diego, CA, USA).