Epilepsy Research 123 (2016) 1–5

Contents lists available at www.sciencedirect.com

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Acute seizures in cerebral venous sinus thrombosis: What predicts it?

Rohan Mahale*, Anish Mehta, Aju Abraham John, Kiran Buddaraju, Abhinandan K. Shankar, Mahendra Javali, Rangasetty Srinivasa

Department of Neurology, MS Ramaiah Medical College & Hospital, MSRIT Post, New BEL Road, Bangalore 560054, Karnataka, India

ARTICLE INFO

Article history:
Received 11 October 2015
Received in revised form 1 December 2015
Accepted 30 January 2016
Available online 11 March 2016

Keywords:
Seizure
Predictors
Cerebral venous sinus
Thrombosis
Acute

ABSTRACT

Background: Seizures are the presenting feature of cerebral venous sinus thrombosis (CVST) in 12–31.9% of patients. 44.3% of patients have seizures in the early stage of the disease. Acute seizures (AS), refers to seizures which take place before the diagnosis or during the first 2 weeks afterward.
Objective: To report the predictors of acute seizures in cerebral venous sinus thrombosis (CVST).
Methods: 100 patients with CVST were included in the study. The occurrence of acute seizures was noted. The predictors of acute seizure were evaluated by univariate analysis including the demographic (gender, age), clinical (headache, focal neurological deficit, papilloedema, GCS score), type and number of risk factors, MRI findings (Type of lesion: hemorrhagic infarction or hematoma, location of lesion) and MRV findings (superficial or deep sinus, cortical veins).
Results: A total of 46 patients had acute seizures. On univariate analysis, altered mental status ($p < 0.001$), paresis ($p = 0.03$), GCS score <8 ($p = 0.009$), hemorrhagic infarct on imaging ($p = 0.04$), involvement of frontal lobe ($p = 0.02$), superior sagittal sinus ($p = 0.008$), and high D-dimer levels ($p = 0.03$) were significantly associated with acute seizure. On multivariate analysis, the hemorrhagic infarct on MRI and high D-dimer was independently predictive for early seizure.
Conclusion: The predictive factors for the acute seizures are altered mental status (GCS < 8), focal deficits, hemorrhagic infarct, involvement of frontal lobe and superior sagittal sinus with high D-dimer levels.

Introduction

Seizures are more specific to cerebral vein and sinus thrombosis (CVST) than to other types of stroke (Conrad et al., 2013). About 12–31.9% of patients with CVST have seizures as the presenting feature of the disease. Among them, 44.3% of patients have seizures in the early stage of the disease (Ferro et al., 2003; Masuhr et al., 2006). The rate of mortality is three times higher in CVST patients with seizures than those without seizures (Masuhr et al., 2006). Seizures in CVST can occur during different periods of the disease's course and can be categorized as either "early/acute seizures", which take place before the diagnosis or during the first 2 weeks afterward, or as "late/remote seizures", which occur in the years following CVST development (Ferro et al., 2004). The risk of an acute seizure after the diagnosis of CVT is unknown. However, based on the previous case series, following risk factors have been identified for acute seizures that include motor or sensory deficits, cortical vein thrombosis, and hemorrhagic brain lesion on admission (Masuhr et al., 2006; Preter et al., 1996). The incidence of CVST appear more in India as compared to the western countries as many large hospital-based series of puerperal CVST have been reported from India. The exact incidence of CVST in India is still not known; due to the lack of any population-based study or nationwide multicentric hospital-based studies. And, there are no elaborative studies that have evaluated the predictors of acute seizures in CVST. The present study was aimed at determining the predictors of acute seizures in patients with CVST.

Subjects and methods

Subjects

This is a retrospective, cross-sectional, single centre, hospital-based study. The study was approved by the institutional scientific committee and ethics review board. The hospital registry was screened to identify records with a diagnosis of CVST from January 2011 to January 2015. 100 consecutive patients with CVST were

* Corresponding author. Tel.: +091 80 40503125/+091 80 40503189; fax: +091 22183276.
E-mail addresses: rohanmahale83@gmail.com (R. Mahale), anishmehta1302@gmail.com (A. Mehta), aaajohn99@gmail.com (A.A. John), kiranb@gmail.com (K. Buddaraju), abhiks@yahoo.com (A.K. Shankar), jvmahend@gmail.com (M. Javali), Srinivasa-drsrinivas@hotmail.com (R. Srinivasa).

http://dx.doi.org/10.1016/j.eplepsyres.2016.01.011
0920-1211/

included in the study. Patients with epilepsy and on anti-epileptic drug treatment were excluded.

Data

Demographic data and clinical characteristics

Data on the demographic characteristics, presenting symptoms that include headache, vomiting, seizures, fever, altered mental state, duration of symptoms were recorded. The type (focal–simple partial or complex partial, focal with secondary generalization or generalized tonic clonic) and frequency of seizure (single, cluster attacks or convulsive status epilepticus) were recorded. The seizures were categorized into early seizure and late seizure as described earlier. Convulsive status epilepticus was defined if the seizure lasted for more than 5 min. The following risk factors for CVST and number of risk factors were noted: oral contraceptive, pregnancy, systemic and central nervous system infection, dehydration, malignancy, deep vein thrombosis, spontaneous abortion, and family history of venous thrombosis. The level of consciousness was assessed by Glasgow Coma Scale (GCS) at admission and at 1 week. Vital signs, oculomotor abnormalities, presence of papilloedema and cranial nerve palsy were noted. The muscle power as per medical research council (MRC) scale, muscle tone and tendon reflexes were also noted.

Investigations

Following laboratory data were collected: hemoglobin level, total leukocyte count, platelet count, packed cell volume, blood urea nitrogen, serum creatinine, serum electrolytes, random blood sugar, glycated hemoglobin, D-dimer. Serological testing for human immunodeficiency virus, hepatitis-B virus and syphilis, serum homocysteine, protein C, S, anti-thrombin-III, factor V Leiden mutation, anti-nuclear antibodies and anti-phospholipid antibodies. Electroencephalography (EEG) was done in patients with altered mental status and with seizures. Brain magnetic resonance imaging (MRI) (1.5 T) along with gadolinium contrast (if no contraindication for contrast) and MR venography were carried out in all the patients at the time of admission. The following imaging characteristics were noted: type of parenchymal lesions (hematoma, hemorrhagic infarct or none), location of lesion (frontal, temporal, parietal, occipital, multiple sites or basal ganglia and thalamus), whether uni or bilateral, type and number of sinuses affected (superior sagittal, transverse/sigmoid, deep vein, cortical vein or multiple).

Treatment

All patients were treated with low molecular weight heparin for 7 days followed by warfarin. International normalized ratio (INR) was maintained between 2.0 and 2.5. Anti-epileptic drugs were started in patients with seizures. Anti-oedema measures like mannitol during acute stage with oral glycerol were started in all the patients. Patients with malignant cerebral oedema were treated with surgical decompression.

Outcome

The functional outcome was assessed using modified Rankin scale (mRS) and Barthel Index (BI) at 1 week and 3 months. BI was used to evaluate 10 domains of activities of daily living which include feeding, grooming, bowel, and bladder, bed to chair transfer, dressing, mobility, bathing, toilet, and climbing stairs (Mahoney and Barthel, 1965). The number of patients requiring surgical decompression and hospital mortality were also noted.

Statistical analysis

The baseline characteristics of the patients with and without acute seizure were compared by student unpaired t test for continuous variables and Chi square test for categorical variables. The predictors of acute seizure were determined by univariate analysis including the demographic (gender, age), clinical (headache, vomiting, paresis, papilloedema, GCS score), type and number of risk factors, magnetic resonance imaging (MRI) findings (hemorrhagic infarct or hematoma, location of lesion), venography findings (superficial sinus or deep veins, cortical veins and number of sinuses involved). The power of the study was fixed at 80%. Variables with a significant p value (≤ 0.05) in univariate analysis were considered for multivariate analysis (logistic-regression analysis). Statistical analyses were performed using SPSS software (version 17).

Results

100 consecutive patients with CVST were included in the study. The mean age of the patients were 35.9 ± 14 (range: 21–68) years. A total of 60 (60%) patients were males. 9 patients had recurrent CVST. Out of 100 patients, 46 (46%) patients had acute seizure and 54 (54%) patients did not have seizures. The mean duration of symptoms before the diagnosis of CVST ($n = 100$) was 7.6 ± 11.1 (range: 1–60) days. In patients with CVST, the mean duration of symptoms before the diagnosis of CVST ($n = 46$) was 6.9 ± 10.6 (range: 1–60) days. The median duration of symptoms before the diagnosis of CVST ($n = 46$) was 3.0 days. Hemorrhagic infarction on brain MRI was seen in 64 (64%), hematoma in 10 (10%) and no lesion in 26 (26%) patients. Hemorrhagic infarction was seen in 38 (82.1%) and hematoma in 3 (6.5%) patients with seizures. MR venogram showed involvement of superficial sinuses ($n = 91$); deep veins ($n = 5$), and cortical veins ($n = 4$) (Fig. 1).

Early seizures characteristics

The seizures ($n = 46$) were categorized as focal ($n = 4$), focal with secondary generalized ($n = 9$), and generalized tonic clonic ($n = 33$). Focal seizures were simple partial seizures. There were no complex partial seizures with or without generalization. In terms of frequency of seizures, 7 (15.2%) patients had generalized convulsive status epilepticus, 22 (47.8%) patients had seizures in clusters and 17 (37%) patients had single episode of seizure. All patients with seizure ($n = 46$) were on AED, whereas 10 patients without seizure were on AED and remaining 44 patients without seizures were not on AED. 44 patients with seizures had good control with single AED. 2 patients required 2 AED for seizure control. AED used were phenytoin, sodium valproate, levetiracetam and clobazam. All patients on AED at discharge were on AED at 3 months follow-up.

Predictors of seizure

Acute seizures were more common in the CVST patients with altered mental status ($p < 0.001$), paresis ($p = 0.03$), GCS score <8 ($p = 0.009$), hemorrhagic infarct on imaging ($p = 0.04$), involvement of frontal lobe ($p = 0.02$), superior sagittal sinus ($p = 0.008$), high D-dimer levels ($p = 0.03$) as per univariate analysis. CVST patients with seizures had significant lesser involvement of transverse sinus ($p = 0.04$) and multiple superficial sinuses ($p = 0.009$).

Age ($p = 0.95$), gender ($p = 0.97$), duration of illness ($p = 0.24$), headache ($P = 0.62$), vomiting ($p = 0.75$), aphasia ($p = 0.97$), sensory symptoms ($p = 0.76$), papilloedema ($p = 0.34$), risk factors >2 ($p = 1.00$), and death ($p = 0.96$) were not related to early seizure. The details are summarized in Table 1. On multivariate analysis, the