Radiological Spectrum of Cerebral Venous Sinus Thrombosis in Soldiers at High Altitude: A Four-Year Analysis

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ABSTRACT

Objective: To assess the spectrum of radiological findings of cerebral venous sinus thrombosis (CVST) in soldiers serving at high altitudes.

***Study Design*:** Retrospective longitudinal study.

Place and Duration of Study: Combined Military Hospital, Skardu Pakistan, from Jan 2016 to Jan 2020.

Methodology: Thirty-three consecutive soldiers evacuated to Combined Military Hospital, Skardu, with radiologically proven cerebral venous sinus thrombosis on CTV brain were enrolled in the study. Plasma D-dimer levels of all the patients were sent to the laboratory, and clinical data were noted.

Results: Mean age of patients was 28.88 years ± 5.189 (range 20 to 40 years) with a mean duration of stay at high altitude of 59.8 ± 39.3 days and the average height of deployment as 17094 ± 3285 feet. Left transverse sinus was the most commonly involved sinus in 21 (63.6%) patients, followed by left sigmoid sinus 18 (54.5%) and superior sagittal sinus 16 (48.5%). Sixteen cases demonstrated associated findings of venous infarction on CT brain (48.5%). Headache was the most common clinical presentation 13 (93.9%), followed by vomiting 12 (36.4%).

Conclusion: Prolonged stay at high altitude is a key risk factor for cerebral venous sinus thrombosis in young individuals showing a predilection for posteriorly and inferiorly located venous sinuses.

Keywords: Computed tomography venography (CTV), Cerebral venous sinus thrombosis (CVST), High altitude.

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is caused by the occlusion of a dural venous sinus or one of the cerebral veins. It is a multifactorial disease, with a variable clinical presentation ranging from headache through focal neurological deficits to seizures. Imaging modalities are essential for diagnosing CVST, among which computed tomography venogram (CTV) brain is considered the gold standard. The mainstay of treatment is anticoagulation with endovascular intervention for those with severe symptoms. The outcomes are favourable in those who receive early diagnosis and treatment.[1]

The diagnosis of CSVT demands high clinical suspicion and a close liaison between clinical and radiological departments. The diagnosis becomes more challenging at high altitudes due to variable clinical presentation and evacuation of suspected cases to centres having appropriate imaging modalities with implications for human and material resources. There are many well-defined risk factors for CVST, including thrombophilic states, autoimmune diseases and malignancies.[2,3]

Literature shows that high altitudes of more than 8000 feet are associated with thromboembolism, but there is little work in this area. We were interested in filling in this gap because we have our soldiers deployed at Siachen, which is regarded as the highest battlefield in the world. We were interested in studying CVST at high altitudes because the deployed soldiers are young and fit. Neurological disease in this population has a substantial effect on the soldiers' longevity and quality of life and takes a heavy toll on the military. We studied the spectrum of radiological findings in soldiers with CVST.

METHODOLOGY

This retrospective longitudinal study was undertaken from January 2016 to January 2020 at Combined Military Hospital (CMH), Skardu. Study protocol was approved by the Ethical Review Board (IERB approval certificate no: 005). Military personnel deployed at high altitude locations above 8000 feet with clinical suspicion of CVST were enrolled in this study.

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Inclusion Criteria: Patients with age 20-40 years who were confirmed to have CVST on radiological imaging were included in the study. These included patients presented with a history of symptoms including headache, vomiting, nausea, focal neurological deficit, vertigo, diplopia or seizures.

Exclusion Criteria: All the cases not found to have CVST on radiological imaging were excluded from the study.

CMH Skardu receives the significant bulk of causalities evacuated from a high altitude ranging from 8000-22000 feet. All the soldiers undergo basic medical examination and baseline investigations, including serum blood profile, echocardiogram (ECG) and chest radiograph (CXR) before deployment to forward areas. Military troops must follow a strict acclimatisation regime designed as per international guidelines to ensure utmost physical preparation before proceeding to higher locations. All the evacuated patients received at CMH Skardu with high altitude sickness were initially assessed and provided first aid care by doctors at respective altitudes or evaluated at forwarding treatment centres by specialised doctors.

Baseline haematological workups including blood complete picture, liver and renal profile, D Dimers, coagulation profile, CXR and ECG were also carried out for the patients. All CTV Brain studies were done using a four-slice CT scan machine, and intravenous contrast material was administered by CT automated injector. Before CTV, all the patients had undergone plain CT Brain to analyse any cerebral parenchymal changes.

In preparation for CTV evaluation, intravenous access was obtained in each patient using an 18–20 G catheter through one of the major veins in the forearm. Later on, an automated injector gave 35 mL of non-ionic contrast material (Omnipaque) at a 4.5 mL/sec rate. Following a 45-second delay post-injection of contrast, sections were taken.

Scanning was done with the patient in the supine position in suspended respiration, with both arms of the patient by their side. Scanning was done from the skull base to the vertex with slice thickness between 0.50 to 1.00 mm. Variable dose parameters automated by the CT scan machine itself were used according to the patient's weight (CT maximum range: kV*p*=150, mA=600). The imaging was done in a caudocranial direction.

The images were transferred to computer media for interpretation. Two-dimensional (2D) and three-dimensional (3D) multiplanar acquisition, as well as rendering techniques such as maximum intensity projection (MIP) and volume rendering (VR) in three dimensions (sagittal, coronal, and oblique planes), were performed. Removal of bones from the images was achieved by graded subtraction.

The criterion used to diagnose CVST on CTV brain was as follows: 1) Presence of empty delta sign in cases of superior sagittal sinus involvement 2, 2) Luminal filling defect in visualised dural venous sinuses, with a ring of contrast enhancement around partial filling defects, 3) Associated evidence of unilateral/bilateral, cortical/peripheral venous haemorrhage/infarcts and gyral enhancement was also sought on unenhanced scan.[2]

All the patients, after initial management, were transferred to a tertiary care facility for a further detailed evaluation of any associated risk factors, including thrombophillic screening (Protein C, S, antithrombin III and anticardiolipin antibody levels), connective tissue profile (RA and ANA levels) and plasma homocysteine levels.

Demographic data (age, height of deployment, duration of stay, known risk factors), clinical features, and radiological and laboratory results were noted on a pre-designed proforma. Data were entered and analysed using IBM Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were summarized as mean ± standard deviation or median values for continuous variables and numbers and percentages for nominal variables.

RESULTS

A total of 33 consecutive patients with clinical suspicion of CVST deployed at high altitudes (>8000 feet) were enrolled in the study. The mean age of patients was 28.88 ± 5.18 years (range 20 to 40 years), with the majority (45.5%) in 25-30 years. The mean duration of stay was 59.8 ± 39.3 days (range 9-150 days), while the average deployment height was 17094 ± 3285 feet (range 8000-21300 feet).

Headache was the most common clinical presentation 31 (93.9%), followed by vomiting 12 (36.4%). The majority of the patients (90.9%) were non-smokers, while no patient had any evidence of a known significant risk factor. Mean hemo globin levels were 17.17 ± 2.18 g/dL (range 9.6–20.4 g/dL). However, most patients (54.5%) showed raised haemoglobin levels of

more than 17.5 g/dL. Plasma D-dimer levels were only raised in 9% of patients (Table-I).

Table-I: Baseline characteristics and clinical findings (n=33).

Parameters	Values
Age (years)	28.88 ± 5.189
Duration of Stay (days)	59.8 ± 39.3
Mean Altitude of Stay (feet)	17094 ± 3285
Smoker n (%)	3 (9.1%)
Hemoglobin Level (g/dL)	17.17 ± 2.18
D–Dimer Levels n (%)	
< 250	30 (90.9%)
250-500	3 (9.1%)
Clinical Features	
Headache	31 (93.9%)
Vomiting	12 (36.4%)
Focal neurological deficit	9 (27.3%)
Vertigo	4 (12.1%)
Diplopia	3 (9.1%)
Seizures	2 (6.1%)

All the patients were screened for thrombophilic and vasculitic diseases and found negative. None of the patients showed elevated homocysteine levels or a history of thrombotic disease, trauma, tumour or surgery. In the absence of all other risk factors, prolonged stay at a high altitude was the only thrombogenic risk factor in our study group.

Radiological evaluation on CTV Brain showed left transverse sinus to be the most common dural venous sinus with thrombosis in 21 (63.6%) patients followed by left sigmoid sinus in 18 (54.5%) and superior sagittal sinus 16 (48.5%) patients.

Sixteen cases demonstrated associated finding of venous infarction on unenhanced CT brain (48.5%) while one case had evidence of intracranial bleed (ICB) (Table-II).

Table-II: Spectrum of radiological findings.

Radiological Findings	n (%)
Superior Sagittal Sinus	16 (48.5%)
Inferior Sagittal Sinus	2 (6.1%)
Straight Sinus	3 (9.1%)
Left Transverse Sinus	21 (63.6%)
Right Transverse Sinus	14 (42.4%)
Confluence of Sinuses	4 (12.1%)
Left Sigmoid Sinus	18 (54.5%)
Right Sigmoid Sinus	11 (33.3%)
Left Internal Jugular Vein	6 (18.2%)
Right Internal Jugular Vein	2 (6.1%)
Brain Parenchymal Changes	
Venous Infarcts	16 (48.5%)
Intracranial Bleed	1 (3.0%)

DISCUSSION

In our study, high altitude was found a significant risk factor for CVST in young soldiers. The diagnosis of this potentially fatal entity diagnosis rests on radiological imaging. CVST has a predilection for posterior and inferior dural venous sinuses. The correct diagnosis followed by prompt treatment can save the lives of our soldiers.

In literature, the prevalence of CVST is 3-4 patients per million population.[3] CSVT is a devastating disease having multifactorial pathophysiology with at least one risk factor involved in about 85% of affected individuals like thrombophilic conditions, infections and vasculitides.[4] It usually occurs in people stationed at high altitudes of about 5000 meters or above (range 2200–5500 meters).[5] However, several cases have also been reported with CVST at high altitudes due to underlying thrombophiliac states.[6] An association between CVST and height is a well-documented phenomenon, but there is limited published data in its support. We conducted this study to explore the occurrence of CVST in fit young individuals at an altitude who had no risk factors for the disease. We studied the involvement of the sinuses in the disease process, which can be used later for advancements like radiological thrombectomy/thrombolysis in future.

In our study, headache was the most typical symptom. The suggested pathology for headache caused by CVST is vascular congestion.[7] The headache associated with CVST is highly variable with no specific site or character.[8] In our study, 27.3% of patients had a neurological deficit. In most cases, neurological deficits manifest as motor weakness in mono-paresis, hemiparesis, or involving both sides in patients with deep venous system thrombosis. Only 6% of patients in our study developed seizures. In a study on 194 patients in Germany with CVST, 44.3% of cases had seizures.[9] Different age populations may explain the lower incidence of seizures in our patients studied, different underlying precipitating factors and sites of thrombosis. In this study, intra-cerebral haemorrhage and cortical vein thrombosis were identified as predictors of seizures and these findings were seen in only one of our patients.

The mean haemoglobin levels of soldiers in our study were 17.17 ± 2.18 g/dL. The average altitude of deployment in our study was 8000-21300 feet. In another local study, most cases (85.7%) were diagnosed at an altitude above 8,000 feet and with mean haemoglobin (Hb) value of 16.7 g/dL. In this study, half of

the individuals had d-dimer levels of more than 1,000 ng/mL, while in our stud, only 9% of patients had elevated D dimers.[10] This difference may be explained by the non-quantitative assay used in our study.

Despite improvements in the identification of CVST in recent times, diagnosis and treatment can be onerous due to the number of underlying patho-physiological mechanisms, clinical signs and the non-availability of standard management protocols.[11] Primary/secondary polycythemia and dehydration have been identified as risk factors for CVST.[12] This may be the underlying pathology of CVST at high altitudes. Other factors like very low temperature, immobilisation during long-distance travel, hypoxia, heat stress and hyperthermia and stress related to occupational hazards at high altitudes have been implicated in thrombosis at high altitudes.

Neuroimaging is the gold standard modality for the diagnosis and localisation of CVST. The intersection of cerebral veins and larger sinuses is believed to be the commonest site of CVST.[13] A plain CT brain scan does not rule out the diagnosis of CSVT as it may be normal or show nonspecific findings in 30% of cases.[14] Plain CT brain findings in CVST include dense clot sign, cord sign, oedema and venous haemorrhages with or without pressure effects.[15] In our study, 48.5% of soldiers had venous infarcts on plain CT brain, and one had associated intracranial bleed. Intracerebral haemorrhage (ICH) associated with CVST is found in about 30–50% of all patients. [16] Venous enhancement following a CT scan aids in the identification of filling defects in the cortical sinuses and veins, increased collateral venous drainage, and enhancement of sinus walls.[17] CTV Brain is extremely useful in patients with the subacute or chronic presentation with an overall sensitivity of about 95%.[18]

In our study, the commonest site of CVST was left transverse sinus occurring in 63.6% of cases, followed by left sigmoid sinus (54.5%) and superior sagittal sinus (48.5%). The involvement of various sites by thrombosis in the brain, as determined by the international study on cerebral vein and dural sinus thrombosis (ISCVT), is as follows: transverse sinus (86%), superior sagittal sinus (62%), straight sinus (18%), cortical veins (17%), jugular veins (12%), the vein of Galen, and internal cerebral vein (11%).[19] The difference in this frequency of involvement may be explained by our smaller sample size that exclusively studied patients at high altitudes. There remains an open avenue for further research about the radiological patterns of involvement in CVST occurring at high altitudes. The latest advancement in imaging of CVST is the Susceptibility Weighted Imaging in MRI brain that can help predict cerebrovascular complications in CVST.[20]

LIMITATIONS OF STUDY

The small sample size was the significant shortfall of our study. It was, however, one of the very few studies about CVST at high altitude in a group of healthy soldiers with no co-morbidities. We suggest larger studies on the subject to follow the ultimate neurological outcome and correlation with the site and severity of the CVST.

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CONCLUSION

Prolonged stay at high altitude is a key risk factor for cerebral venous sinus thrombosis in young individuals showing a predilection for posteriorly and inferiorly located venous sinuses.

Conflict of Interest: None.

Authors' Contribution

ARP: Conception and design of study, data collection, statistical analysis and interpretation of data, article writing, Case reporting, MA: Conception and design of study, data collection, statistical analysis and interpretation of data, article writing, case reporting, SR: Statistical analysis and interpretation of data, article writing, DM: Data collection and interpretation of data, Case reporting, MML: Data collection and interpretation of data (Was on surgical cover at CMH Skardu during conception of study and data collection), UN: Peer review and interpretation of data.

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