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PLAIN CT BRAIN IN PROGNOSTICATION OF PATIENTS WITH GANGLIO CAPSULAR BLEED.

Neurosurgery

Dr.KrishnaKumar.P* Assistant Professor, Department of Neurosurgery, Government T.D Medical College, Alappuzha, Kerala, India *Corresponding Author

Dr.Biju Bhadran Professor .Department of Neurosurgery. Government T.D Medical college, Alappuzha, Kerala

Dr.Sunil Panchal SeniorResident. Department of Neurosurgery, Government T.D Medical College, Alappuzha, Kerala.

Dr.Harrison G Assistant Professor, Department of Neurosurgery, Government T.D Medical College, Alappuzha, Kerala.

Dr.Subrat.K.S SeniorResident. Department of Neurosurgery, Government T.D Medical College, Alappuzha, Kerala

ABSTRACT

Background and Rationale: Capsulo ganglionic bleed is a definite subset of intracerebral haemorrhage with heavy morbidity and high mortality. In this study we examine whether radiological parameters from a plain CT brain can be used for the purpose of prognostication in such cases.

Materials and Methods: We undertook a prospective study of 120 consecutive patients who presented with capsulo ganglionic bleed. Univariate analysis of the radiological predictors was done and those found to attain statistical significance were fit into a multivariate logistic regression model. The model was validated using ROC (Receiver Operating Characteristic) curve.

Results: The mortality rate was 30.8 %.(N=37).The mean age was 63.6 years. On univariate analysis location of haematoma, intraventricular haemorrhage (IVH), volume of haematoma, hydrocephalus, and midline shift were found to be statistically significant. On multivariate logistic regression analysis location (p<.001, OR .020, 95%CI.003-.120) and midline shift (P<.001, OR 19.45, 95%CI 1.47-255.78) were found to be statistically significant.

Conclusion: Capsulo ganglionic bleed forms a definite subset of primary spontaneous intracerebral haemorrhage with its own radiological prognostic variables. Medial location and midline shift were found to be reliable radiological prognostic markers.

KEYWORDS

Capsulo ganglionic bleed , Location, Midline shift.

INTRODUCTION

Hemorrhagic stroke is the most disabling form of stroke with an overall mortality rate approaching 40% and affecting 10-20 in 100000 people every year [1,2,3]. Basal ganglia and internal capsule accounts for 35%-70% of all the locations. Out of this 32%-50% of deaths takes place in the first 30 days and 20% are independent at 6 months[4,5].The best treatment for each individual case has been a conundrum and is often difficult to define[6,7]. It is imperative to make an early and accurate prognostication in all cases to optimize the usage of resources. Literature abounds with several clinical, radiological and biochemical parameters which have been proposed for the matter of prognostication [8,9,10]. Plain computerised axial tomogram (CT) scan of brain is the initial radiological investigation in all cases with capsulo ganglionic bleed. The present study attempts to define certain radiological parameters obtained from a plain CT film of brain which can be used for prognostication.

MATERIALS AND METHODS

The study was approved by Institutional Ethics committee. It is a prospective study which consisted of all patients with primary capsulo ganglionic bleed admitted in emergency section of Government T.D medical college hospital, Alappuzha between April 2017 and November 2017 .For the purpose of study capsulo-ganglionic bleed was defined as spontaneous leakage of blood in to basal ganglia or internal capsule or both, with or without lobar extension as documented by a plain CT study of brain. All cases of pure lobar haematomas, cerebellar haemorrhages, brainstem haemorrhages, traumatic Intracerebral haemorrhage (ICH), and those presenting after 24 hours of ictus were excluded from study. Informed consent was taken either from the patient or their bystanders. A detailed neurological history regarding onset, progression, headache, seizures, and chronology of worsening since ictus was taken. History of hypertension, diabetes mellitus, and family history of strokes, alcoholism, and cigarette smoking were also recorded. The Glasgow Coma Scale (GCS) score of the patient was noted on admission.

All patients underwent a plain CT scan of the brain as part of their treatment protocol. Image analysis was done to note the following parameters-location of haematoma, volume of haematoma, mid line shift, intraventricular haemorrhage (IVH) and hydrocephalus. For defining the location of haematoma the cut passing through the foramen of Monro was taken. A line was drawn along the midline using standard bony landmarks. Two lines parallel to the above line1.5cms (line A) and 2.5cms (line B) from the midline are drawn. The area medial to line A is designated as medial zone and the area between line A and line B as lateral zone. The volume of haematoma was measured using the formula ABC/2,where A is the greatest haemorrhage diameter by CT, B is the diameter at 90 degrees to A, and C is the number of CT slice multiplied by slice thickness[11].The primary end point was either death in hospital or live follow-up at 30 days.

Statistical Analysis

All data were analysed using SPSS software version 16.0(SPSS Inc,Chicago,Illinois,USA). Descriptive statistics were presented as means with standard deviation for continuous variables and as percentages for categorical variables. Univariate analysis for clinical and radiological predictors of the primary end point was done using unadjusted logistic regression analysis. Those radiological predictors having significance were fit in to a multivariate logistic regression model. The Model was validated using AUC (Area under ROC).P value less than .05 was considered significant in all cases.

RESULTS

There were a total of 164 admissions, out of which 120 cases were selected based on the inclusion criteria. The mortality rate was 30.8%(N=37).The mean age was 63.6 years (Median 65 years, Range 31 to79 years).There were a total of 72 (60%) males and 48 (40%) females. Hypertension was present in 60.8% (N=73) patients which constituted the most common risk factor. This was followed by smocking 26.7% (N=32), and diabetes mellitus 20.8% (N=25).Alcohol consumption was present in 20% (N=24) of subjects. The mean GCS was 11 which ranged from 3 to 15.The GCS was significantly low for patients who expired (6 vs14, P <.001). Patients who expired in first 48 hours constituted 51.31% (N=19) of all cases. A surgical procedure was performed in 15 (12.5%) of patients. This constituted decompressive craniotomy in 11 patients (9.1%) and external ventricular drain in 4 (3%) patients.

The mean haematoma volume was 46.02±9.8ml (Range 4ml to 230 ml).The average midline shift was 2.16mm (Range 0-12).Intraventricular haemorrhage (IVH) was present in 35.8% (N=43) and hydrocephalus in 34.2% (N= 41).Out of the 120 patients 34 patients (28.3%) had haematoma occupying the medial zone and out of them 12 had haematoma confined to medial zone only. On univariate analysis zone, midline shift, hydrocephalus, volume and IVH were the radiological variables found to be statistically significant (Table 1). The mean GCS of patients with haematoma occupying the medial zone was significantly low (GCS=6, P<.001).After multivariate analysis medial zone and midline shift were found to be significant predictors (Table 2). The regression analysis showed a good validation with an area under ROC curve (AUC) of 0.847.Cross tabulation of variables with zone is given in table 3.

Discussion

Ganglio capsular bleed has been a definite subset of stroke which has defied attempts to find an effective panacea. Heavy morbidity and high mortality associated with the condition warrants accurate prognostication .Volumes of literature have been published with this end in mind, but a big majority of them focus on the entire gamut of intracerebral haemorrhages or supratentorial haemorrhages from a larger perspective [12, 13]. We have observed that location and midline shift are two radiologic prognostic variables having significance. Several studies have come up with clinical, radiological and biochemical markers of prognosis[14,15,16].In the present study we have analysed radiological predictors only, as combining both radiological and clinical parameters in a single statistical model will lead to collinearity. Cerebellar and brainstem haemorrhages were also excluded in our study as they formed a separate cohort with respect to management and prognosis. A comprehensive literature review has been conducted by Al Mufti et al[17] on various radiological predictors wherein they have found that location, volume, hematoma expansion, spot sign, swirl sign, and perihaematomal oedema to be significant predictors. For a given volume the mortality and morbidity varied depending up on location of haematoma. Broderick et al [18] have described that volume of intracerebral haemorrhage and Glasgow Coma Scale score used in combination is a powerful and easy to use predictor of 30 days mortality in patients with primary spontaneous intracerebral haemorrhages. They have found that lethal volume of haemorrhage actually varies by location. When the volume exceeded 60ml the mortality of deep seated haemorrhages increased to 93% when compared to 71% for lobar haemorhages.ICH volumes of <30ml had a mortality of 23% for deep and 7% for lobar haematoma. In our series the mortality rate for medial zone was 73.5% and lateral zone was 10.5%.Shift of midline structures occurs due to the mass effect produced by the hematoma. In many studies shift of midline structures has not attained statistical significance. Fogelholm et al[19] has however demonstrated statistical significance for midline shift in their study. We found midline shift to be a significant predictor of mortality (P<.024).

Intraventricular haemorrhage has been associated with poor outcome across several studies [20.21.22.23].For patients with ICH and intraventricular haemorrhage the mortality ranges from 50% to 80%.Tuhrim et al [24] has confirmed IVH to be an independent risk factor for 30 day mortality after ICH. The number of ventricles containing blood and blood in the fourth ventricle add to the mortality. IVH will add mortality in two ways. It will make the patient prone to seizures. It will also obstruct the CSF pathways and add to hydrocephalus. This in turn will raise the ICP and produce secondary damage. Hallevi et al[25] have demonstrated that thalamic location was associated with IVH in 69.4% of cases while only 37.3% of lobar haemorrhages were associated with IVH. They also found that spontaneous decompression into ventricles did not translate to better clinical outcome. On univariate analysis we have found IVH to be a significant predictor of mortality, but in the multivariate model this did not acquire statistical significance (P=.135).

Ferro JM et al[26] has described the pathophysiology of damage in intracerebral haemorrhage to be triphasic.The first phase is of arterial rupture and hematoma formation, second phase is of hematoma expansion and third phase is of perihaematomal oedema. Haematoma expansion seldom occurs after first 48 hours.Thus the first two phases are often complete by first 48 hours. This accounts for the high mortality observed in the first 48 hours in several studies. In our series also 51.3% (N=19) of deaths occurred in first 48 hours. A definite subset of patients who would benefit from early surgery as identified in STICH phase 2 may be based on this pathophysiologcal profile. Hydrocephalus is often an accompaniment of capsulo ganglionic bleed with medial locations. Small thalamic haemorrhages can cause aqueduct obstruction and predispose to hydrocephalus. Ventriculostomy is usually done in many of such patients, but outcome did not differ significantly in those patients treated with ventriculostomy[27].Thus hydrocephalus is an independent predictor of mortality after ICH.

Our study give deep insights in to the pathophysiologcal mechanisms of poor outcome in patients with gangliocapsular bleed. On univariate analysis the location, volume, MLS, IVH and hydrocephalus were found to have significant correlation with outcome .When these predictors were put into multivariate regression model volume, IVH and hydrocephalus did not attain statistical significance. The medial location was associated with a high incidence of hydrocephalus (56%, N=19) and IVH (67.6%, N=23) in our series. The medial location of haematoma is associated with a high mortality rate of 73.5% in our series when compared to 30.8% mortality of the series as a whole. The anatomical substrate of this location is the cause of the significantly bad outcome. This area corresponds to the head of caudate nucleus, internal capsule, putamen and the major portion of the thalamus. When there was IVH, the volume of haematoma could not be correctly

Table 1: Multivariate analysis.

Variable	P Value	OR (Odds Ratio)	95% CI†
Demographic s and risk factors	.008	3.086	1.340-7.062
Age(≥65 years)	.468	0.743	0.333-1.659
Sex	.004	3.987	1.575-10.090
Hypertension	.113	2.085	0.840-5.177
Diabetes	.202	1.825	0.723-4.606
Alcohol	.850	0.960	0.630-1.463
Smoking			
Clinical variable GCS (≤8 vs >8)	<.001	0.065	0.024-0.174
Radiological variable	<.001	.012	0.003-0.043
Zone (Medial vs Lateral)	<.001	27.614	5.868-129.948
Midline shift (MLS) (<6mm & >6mm)	<.001	30.569	10.518-88.850
IVH‡	<.001	13.307	5.274-33.574
Hydrocephalus	<.001	15.25	5.586-41.652
Volume			

Dependent variable : Mortality.
†95 % CI: 95 percent Confidence Interval.
‡IVH : Intraventricular haemorrhage.
MLS, Zone of haematoma are significant predictors of outcome(P < .05).

Table 2: Multivariate Logistic Regression Analysis.

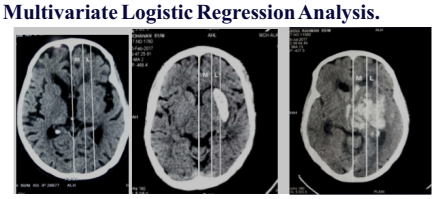

Figure 1: A B C
A showing medial **(M)** and lateral **(L)** zones in normal CT. B showing haematoma in lateral zone. **C** showing haematoma in medial and lateral zones.

Radiological Variable	P value	Odds ratio	95% CI
Zone (Medial vs Lateral)	<.001	.020	0.003-.120
MLS	<.001	19.451	1.479-255.782
IVH	0.135	4.631	0.820-34.585
Hydrocephalus	0.176	4.032	0.527-30.852
Volume	0.278	2.659	0.455-15.536

Dependent variable: Mortality

Table 3 .Cross Tabulation of Variables with Zone.

Variable	Medial zone (N=34)	Lateral zone (N=86)	P value
Deaths	73.5% (N=25)	10.5% (N=9)	<.001
Hydrocephalus	56% (N=19)	22% (N=19)	<.001
IVH	67.61% (N=23)	21% (N=18)	<.001

assessed using the ellipsoid method. This is because haematoma spread may be uneven and also that development of hydrocephalus may occur by expansion. Hallevi et al have described the IVH score to rapidly estimate IVH volume. Flemming et al have identified 40 ml as critical volume predicting poor outcome. Many studies gave a good cut off at 30ml. Hallevi et al have described that spontaneous decompression of haematoma in to ventricles need not necessarily translate to a good outcome. Thalamic ICH have a high chance of rupture into the ventricles. Thus in a medially located haematoma due to the high incidence of IVH, hydrocephalus and damage to critical structures the mortality is high even for a small sized haematoma.

To suggest an appropriate treatment modality for this condition, the exact pathophysiology must be understood. The cause of neurophysiologic worsening following ICH is still unclear. This could be due to mass effect, toxins of blood products, ischemia surrounding the haematoma, damage produced at the ictus, development of hydrocephalus, seizures etc. An unfortunate misinterpretation of STICH phase one trial was that many people argued that there was no need to operate on patients with spontaneous intracerebral haemorrhage [(28)].This problem occurred due to the fact that people considered the entire spectrum of supratentorial haemorrhage as one single cohort. Thus many patients who could have benefited by surgery might have gone to the conservative group. This was in fact one of the proximate cause to undertake phase two trials. Our study clearly demonstrates this difference in natural history viewed from a radiological perspective. The present phase two trial have excluded basal ganglio-thalamic haemorrhages and lobar haemorrhages with extensions to these areas. This is to identify a definite cohort of patients with lobar haemorrhages for whom surgical therapy would be beneficial. Surgical treatment of IVH is also in the evolving phase. The IVH can produce chemical meningitis, block the ventricular pathways and thus removing the blood early through minimally invasive methods seems to be intuitive. Khan NR et al [(29)] have conducted a meta analysis and systematic review of literature to assess the role of intraventricular fibrinolysis (IVF) in the treatment of IVH. They concluded that IVF for IVH is safe intervention and can be used as an effective strategy for reducing mortality and improving functional outcome. CLEAR phase three trial have demonstrated that in patients with IVH in whom a external ventricular drain is put, irrigation with alteplase did not substantially improve functional outcome at three months,compared with irrigation with saline [(30)]. Minimally invasive surgery in form of endoscopic surgery and stereotactic aspiration have been tried and have been found to be effective procedures with low morbidity and mortality rates [(31)].

Thus gangliocapsular bleed is a definite subset of supratentorial haematomas having its own natural history and prognostic variables. Caution must be exercised while applying the prognostic factors applicable to supratentorial haemorrhage as a whole, to this cohort. Plain CT of brain taken in first 24 hours of ictus can be used for prognostication of these patients. Medial location of haematoma and MLS were significant radiological predictors in our study. Our study is not however without limitations. The single institutional nature and relative small number of patients are major limitations.

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