Morphoclinical study of intracerebral haemorrhage with intraventricular extension

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Abstract

Aims. The study is an integrated assessment of clinical, imagistic and morphological parameters in severe intracerebral haemorrhages (ICH) complicated with intraventricular extension (IVE). *Material and methods*. The studied group had 93 cases of patients with ICH and IVE who were hospitalized in the Emergency County Hospital of Craiova and died during hospitalization. The parameters evaluated were clinical (relation with the seasons, age, sex, arterial blood pressure, the motor deficit, degree of coma, Glasgow score at admission and medical care) and morphological (the sites of the intraparenchymal haematoma and IVE, the size of the intraparenchymal haematoma, the presence of the mass effect, perilesional oedema and subarachnoid effusion). The latter were assessed on CT films and during autopsy. *Results*. The presence of IVE as a complication of ICH showed a predilection for cold seasons, especially autumn. From the 93 studied cases 51 were men and 42, women. 52.6% of the patients were in the fifth and sixth life decade. Almost 80% of the patients had IIIrd stage arterial hypertension at admission, over 80% motor deficits and almost 60% Glasgow scores lower than 6. The ventricular effusion involved at least one of the lateral ventricles. The hematomas had huge dimensions as compared to hosting encephalic structures, in lobar sites involving more than one lobe. Other risk factors as mass effect and perilesional oedema were constantly present. *Conclusions*. The association of IVE with other independent risk factors such as hypertension, low Glasgow scores volume of intraventricular bleeding, dimensions of haemorrhagic foci, presence of mass effect and perilesional oedema results in the death of patient despite any sustained therapeutic intervention.

***Keywords*:** *intracerebral haemorrhage, intraventricular extension, morphoclinical parameters.*

Introduction

The intracerebral nontraumatic haemorrhage is a morphopathological entity which can be determined, related to or induced by a variety of pathological conditions having, as a common etiopathological base, certain anomalies of the encephalic vasculature structure and/or blood anomalies. Indifferently the composition of the triad: "etiological factor, promoting factor, trigger factor" is, the clinical manifestations of this vascular drama have to include: consciousness deterioration, almost always progressive neurological motor deficits with variable degrees of extent and severity, both having sudden onset on a clinical background, consisting of abruptly installed cephalgia, associated with central type emesis, signs of meningism and increased values of blood pressure. This precocious and progressive neurological deterioration and the high rate of mortality place this pathological entity among the major medical emergencies.

The intracerebral haemorrhage may remain relatively well-circumscribed within the cerebral matter or may rapidly and progressively enlarge associated with diffusion into the white matter, cerebral herniation, intraventricular rupture and extention or subarachnoidian extension [1, 2].

The rupture into the adjacent ventricle is much more frequent than the direct rupture into the subarachnoidian space and the extension to both spaces is exceptional [3].

The ventricular extension is seen in association with large haematomas profoundly localized [4] or in association with large lobar haematomas with frequent development to the medial areas and can be a strong predictor of death [5].

Material and methods

This study was an analysis of clinical and morphological data retrospectively collected from 93 cases with intracerebral haemorrhage (ICH) complicated with intraventricular extention (IVE) who died during the hospitalization in Emergency County Hospital of Craiova, and were registered in the Pathology Department with a view to autopsy between 2001 and 2003. The group was selected from a larger one, consisting of 183 cases with IHC registered in the Pathology Department records in the same period of time. The remaining 90 cases of IHC without IVE were considered as a reference group for comparing the results of data analysis coming from the studied group.

The studied group was subsequently divided into two groups:

▪ **Group I,** consisting of 54 cases, included patients with clinical diagnostic of IHC who had not been investigated by CT and were autopsied for establishing

the diagnostic. 50 of them died, despite the complex treatment, within the first 48 hours of hospitalization. The other 4, died after 48 hours, but CT examination could not be performed, the diagnosis of cerebral haemorrhagic stroke being confirmed only by lumbar puncture.

▪ **Group II**, consisting of 39 cases, included the patients who survived more than 48 hours and were investigated by CT. In these cases, the pathologist decided not to do the autopsy because the diagnostic was already established by CT investigation.

The studied material came from two data sources:

▪ Patient's medical records which included: medical records, CT films, autopsy protocols and histopathology records.

▪ Nervous tissue drawn during autopsy which included: fragments of nervous tissue including the haemorrhagic focus fixed in formalin for macroscopic evaluation and fragments of nervous tissue from the proximity of haemorrhagic lesions fixed in formalin and embedded in paraffin for histologic examination.

The clinical data taken into consideration were: relation with the year's seasons; sex of patients; age of patients; arterial blood pressure; the degree of coma – Glasgow score; the motor deficit and medical care.

The morphological data were: the site of the intraparenchymal haematoma; the site of the IVE; the size of the intraparenchymal haematoma; the presence of the mass effect; the presence of the perilesional oedema and the presence of the subarachnoid effusion.

Results and discussions

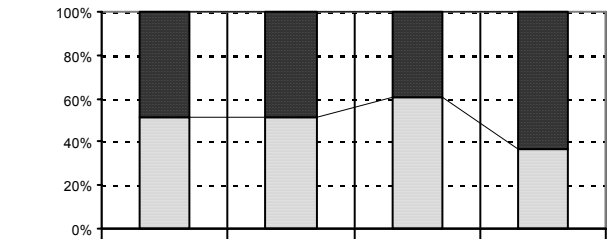
Clinical study

Season distribution

The ICH complicated with IVE had a predilection for cold seasons. Comparing the distribution of cases with and without IVE we could observe that, in our group, the IVE complicated more frequently ICH during the autumn whereas, in the summer, there was ICH extended less frequently in ventricular spaces (Table 1).

This could probably be explained by the influence of atmospheric pressure changes.

Table 1 – ***Season distribution of cases***



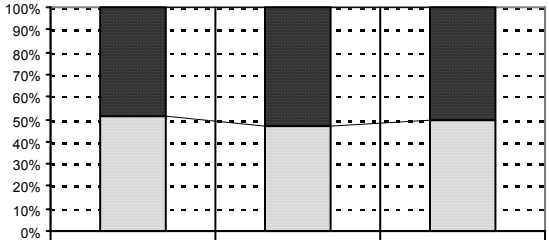
	Winter	Spring	Summer	Autumn
With IVE	24	20	16	33
Without IVE	25	21	25	19

The sex of patients

The sex distribution of investigated cases indicated a slight predominance of the cerebral haemorrhagic stroke in male patients (Table 2).

These data are concordant with other studies stating the same higher frequency in men, especially those older than 55 [6].

Table 2 – ***Sex distribution of cases***



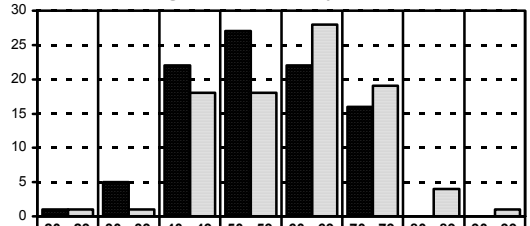
	Female	Male	Total
With IVE	42	51	93
Without IVE	45	45	90

The age of patients

The ICH incidence increases significantly with ageing, old age being one of the most important risk factors [6, 7].

The age distribution of our patients showed that ICH complicated with IVE prevailed in active adults, between 40 and 60 years, with a peak in the 6th decade of life, with an average age of 56.69 years and ranges between 29 and 79 years whereas the uncomplicated haemorrhagic stroke was more frequent after 60 years, with a peak in the 7th decade of life, with an average age of 64 years and limis of range between 22 and 96 years (Table 3).

Table 3 – ***Age distribution of cases***



	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79	80 - 89	90 - 99
With IVE	1	5	22	27	22	16	0	0
Without IVE	1	1	18	18	28	19	4	1

ICH is exceptionally rare between 24 and 40 years, its incidence in persons younger than 35 being approximately 0.3/100.000 inhabitants [8, 9].

We found in our ICH group eight cases with haemorrhagic strokes occurring before the age of 40 (4.4%), from which six had IVE associated as complication (6.4% form IVE group). The absence of high values of systolic blood pressure both to admission and in patients' history raised the suspicion of vascular malformation presence as etiological factor in these cases. The autopsy examination revealed only very large intraparenchymal haematomas associated with massive IVE. The high values of percentages representing the young patients compared with those from the literature could be explained by the fact that our study involved only cases with severe evolution, resulting in death within hospitalization.

Arterial blood pressure

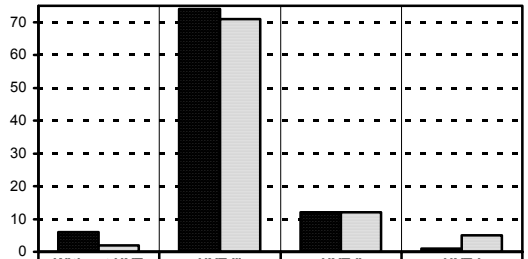
The incidence of spontaneous ICH is considerably higher in patients with hypertension in comparison with

patients with normal blood pressure [10].

A history of hypertension was found in 67.2% of patients with IHC and it was more frequent as compared to other cardiovascular risk factors such as a history of ischemic heart disease (17.2%), diabetes mellitus (18%) and cigarette smoking (13.1%) [5].

In our study, almost 80% of cases in IVE group were in third stage of hypertension at admission; with systolic values over 180 mmHg and diastolic values over 110 mm Hg. Nine of these cases had systolic values over 200 mmHg. The average value of the systolic arterial blood pressure in patients with IVE was 182.05 mmHg with limits between 70 and 280 mmHg.

Table 4 – ***Distribution according to hypertension stages***



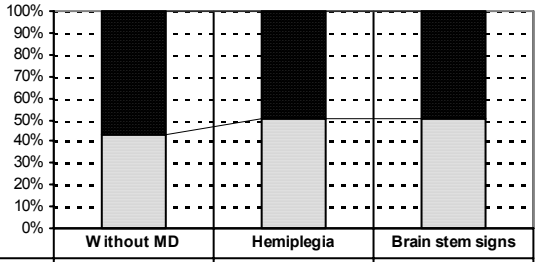
	Without HYT	HYT III	HYT II	HYT I
With IVE	6	74	12	1
Without IVE	2	71	12	5

As we mentioned above, the blood pressure values were normal in eight cases whose ages were under 40 years. We, therefore, considered that the cause of these severe haemorrhagic strokes in young people could be but malformations of intraparenchymal blood vessels.

Motor deficit

The motor deficit was observed at admission in 81 of studied IVE cases representing 87% of the group. Two thirds of these presented hemiplegia, with a slight predominance for the right part (28 cases vs. 26 cases), the remaining one third having signs of brain stem lesions, i.e., hyperextension and internal rotation of arms (Table 5). Comparing the data with those of cases without IVE, no significant difference was observed between the two groups concerning the presence of different motor deficits.

Table 5 – ***Distribution according to motor deficit***

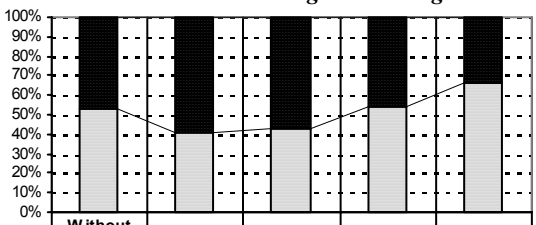


	Without MD	Hemiplegia	Brain stem signs
With IVE	12	54	27
Without IVE	9	54	27

The degree of coma – Glasgow score

Half of cases with IVE presented even from the admission a deep coma (comas of IIIrd or IVth degree) (Table 6) but 1/3 of the patients were conscious when they were brought into the hospital.

Table 6 – ***Distribution according to coma degree***

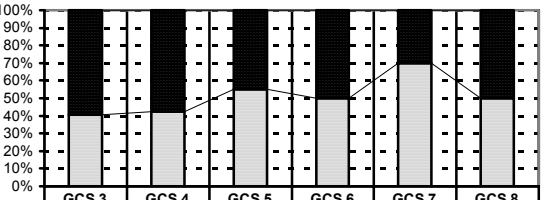


	Without Coma	IV-th dg	III-d dg	II-nd dg	I dg
With IVE	31	19	27	12	4
Without IVE	35	13	20	14	8

In turn, only one third of patients without IVE had an advanced degree of consciousness alteration.

The evaluation of Glasgow coma score revealed the same situation, with 59% of all 93 cases having a Glasgow score ≤ 5 emphasizing once again the severity of nervous tissue alterations enhanced also by the blood effraction into ventricular spaces (Table 7).

Table 7 – ***Distribution according to Glasgow score***



	GCS 3	GCS 4	GCS 5	GCS 6	GCS 7	GCS 8
With IVE	19	27	9	3	3	1
Without IVE	13	20	11	3	7	1

There are studies indicating that these low scores are, like and moreover together with IVE, an independent factor associated with mortality in patients with intraparenchymal haematomas hospitalized [11].

Medical care

The medical care for reducing the intracranial pressure and for optimizing the pressure of the cerebral perfusion consisted in the administration of diuretics (Mannitol 20% and Furosemid) associated or not with corticosteroids (Betametasone or Dexametasone), with magnesium sulfate, glucoses 20% and controlled hyperventilation (IPPV ventilation mode).

In addition to this, the patients were placed so that their head and trunk form a 15–30 degrees angle with the surface of the bed and with head in a neutral position in order to facilitate the venous jugular drainage. No techniques for mechanical reduction of the volume of the cephalorahidian liquid were used.

Anticonvulsants (Diazepam, Midazolam or Phenobarbital) were used in order to prevent the increase of the intracranial pressure. The convulsions resisting to benzodiazepines administration were treated with neuromuscular blocking agents (Pancuronium or Vecuronium) after intubation and ventilation.

The control of hyperthermia (in order to decrease the neuronal metabolism) was achieved by: external refrigeration, cold saline and glucose solutions, gastric wash with cold solutions, sedation and mechanical ventilation.

The cerebral perfusion pressure manipulation was acquired by control of the arterial systemic pressure and by reduction of the intracranial pressure (control of the

cerebral oedema). In order to normalize the values of the blood pressure we used i.v. beta-blockers (Propanolol, Metoprolol), inhibitors of the angiotensine conversion enzyme (Enalapril) and loop diuretics (Furosemid). Haemostatic treatment, neurotropic therapy and parenteral nutrition were used in all the studied cases.

Despite the complex treatment applied, all the patients with haemorrhagic strokes complicated with IVE from our group died either in the first 48 hours (Group I – 54 cases) or in the next days of hospitalisation (Group II – 39 cases). It could be noticed that almost 60% form the studied group died in the first two days from the admission.

Morphological study

IVE as a complication of IHC

As we mentioned above, the study group was made only of 93 cases where IVE complicated an IHC in patients who died during hospitalization and were registered in the Department of Pathology (Table 8).

Table 8 – ***The incidence of IVE in IHC died cases***

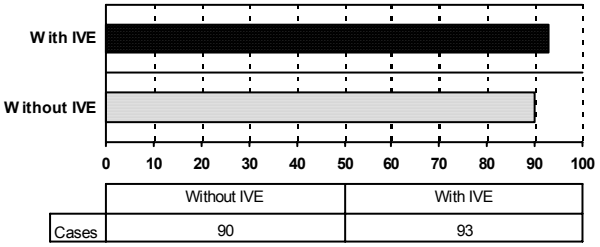
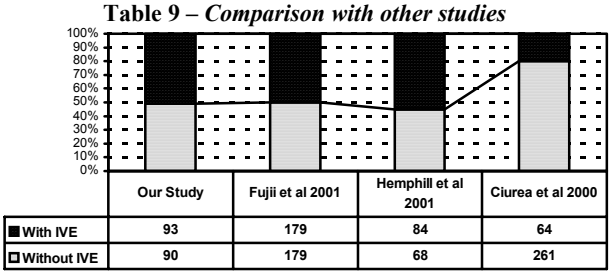


Table 9 – ***Comparison with other studies***



	Our Study	Fujii et al 2001	Hemphill et al 2001	Ciurea et al 2000
■ With IVE	93	179	84	64
□ Without IVE	90	179	68	261

Comparing our data with those from other studies, we saw that our observations are in concordance with those presented by other authors [12, 13], excepting another Romanian study [14], which reports a very low percentage of IHC complicated with IVE (Table 9).

Site of the intraparenchymal haematoma

The site of the intraparenchymal haematomas was discovered either by autopsy, for Group I (including also the four patients which could not have a CT examination) or by CT, for Group 2.

The analysis of the intraparenchymal haematomas sites proved that the most frequent site was the lobar site (Figure 2), usually involving more than one cerebral lobe (Figure 3), followed by multiple site location (deep and lobar associations or deep, lobar and extralobar associations) and by the non lobar sites (cerebellum – Figure 4, brain stem and basal ganglia – Figure 5) (Table 10).

Our data are different from other studies [12] (Table 10) although the presence of IVE is almost the same and that because most of our cerebral haemorrhagic foci were very large, involving at least two lobes and it was very difficult to identify the origin site of bleeding.

Table 10 – ***Comparison with Fujii's study***

Site	Fujii *et al.* 2001		Our Study	
	IHC	*+IVE*	*IHC*	*+IVE*
Supratentorial	**279**	**144**	**123**	**64**
Basal ganglia	***253***	***133***		
Putamen	159	63	***3***	***2***
Caudatus	4	3		
Talamus	90	67		
Lobar (Subcortical)	***26***	***11***	***120***	***62***
Infratentorial	**79**	**35**	**26**	**9**
Brain stem	***45***	***17***	***22***	***7***
Cerebellum	***34***	***18***	***4***	***2***
Multiple site involvement	**0**	**0**	**34**	**20**
T O T A L	*358*	*179*	*183*	*93*
Incidence	***100***	***50%***	***100***	***50.8%***

Site of IVE

Intraventricular extension of the haematoma can be a strong predictor of death, being one of the factors independently associated with in-hospital mortality [5, 11].

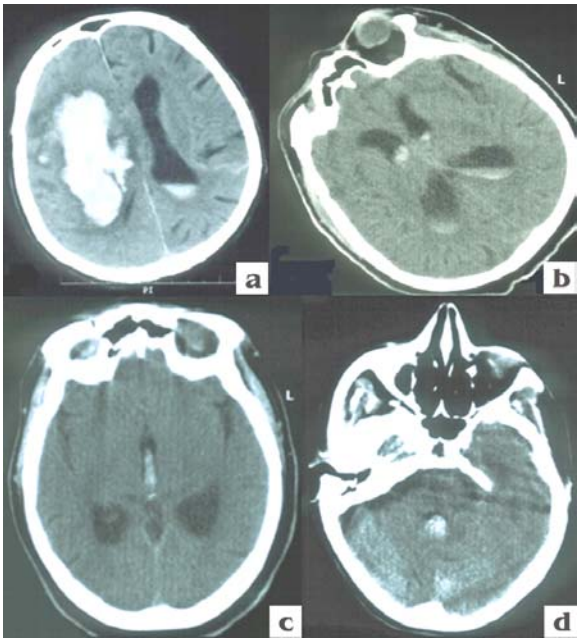


Figure 1 – ***Sites of ventricular extention: a) lateral ventricles; b) bilateral; c) IIIrd ventricle; d) IVth ventricle***

The severity of IVE was classified into the following two groups: **mild**, meaning massive haematoma in one ventricle (one of the lateral ventricles, third ventricle, and fourth ventricle); and **severe**, massive haematoma in two or more than two of the four ventricles.

Table 11 – ***Degree of intraventricular extension***

Degree of extention	Fujii *et al.* 2001	Our Study
Mild IVE	**113**	**55**
Unilateral (ventricle I or II)	113	52
Ventricle IV		3
Severe	**66**	**38**
Bilateral (ventricle I + II)	66	13
Associations (two or three ventricles)		9
Massive (ventricles I, II, III and IV)		16
T O T A L	***179***	***93***

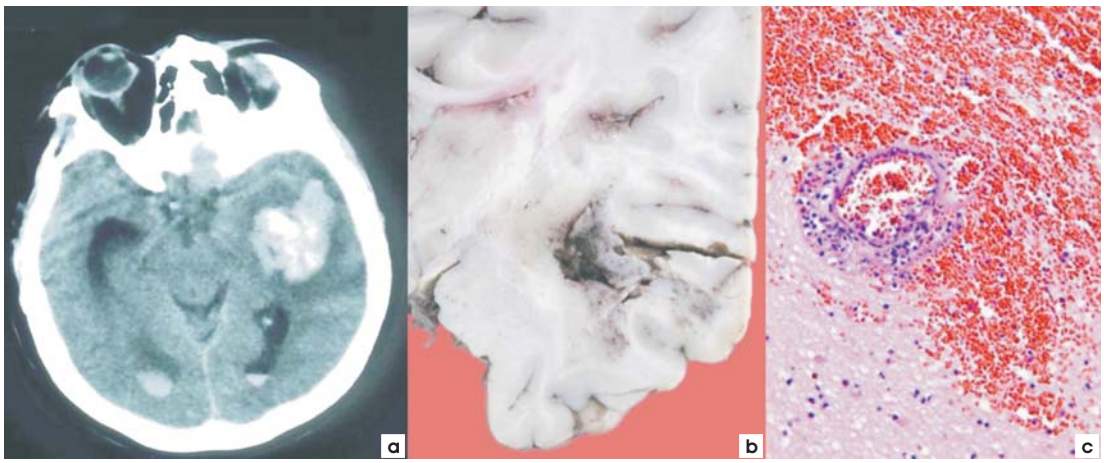


Figure 2 – ***Deep left temporal haematoma: (a) CT image; (b) Pitres section on necroptic sample fixed in formalin; (c) Microscopic aspect of the haematoma boundary; arteriola with altered wall***

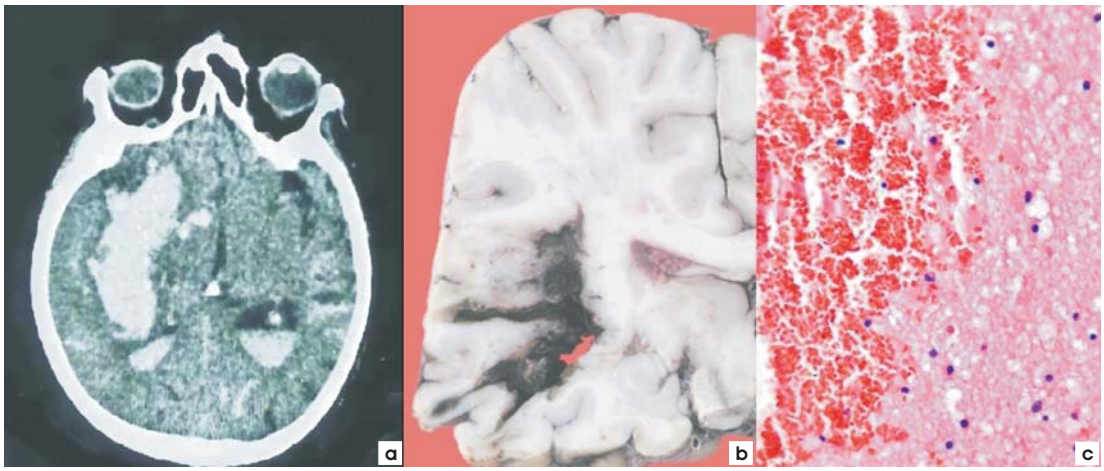


Figure 3 – ***Deep right temporo-parietal haematoma: (a) CT image; (b) Pitres section on necroptic sample fixed in formalin; (c) Microscopic aspect: neuronal debris within haemorrhagic focus; oedema in the white matter***

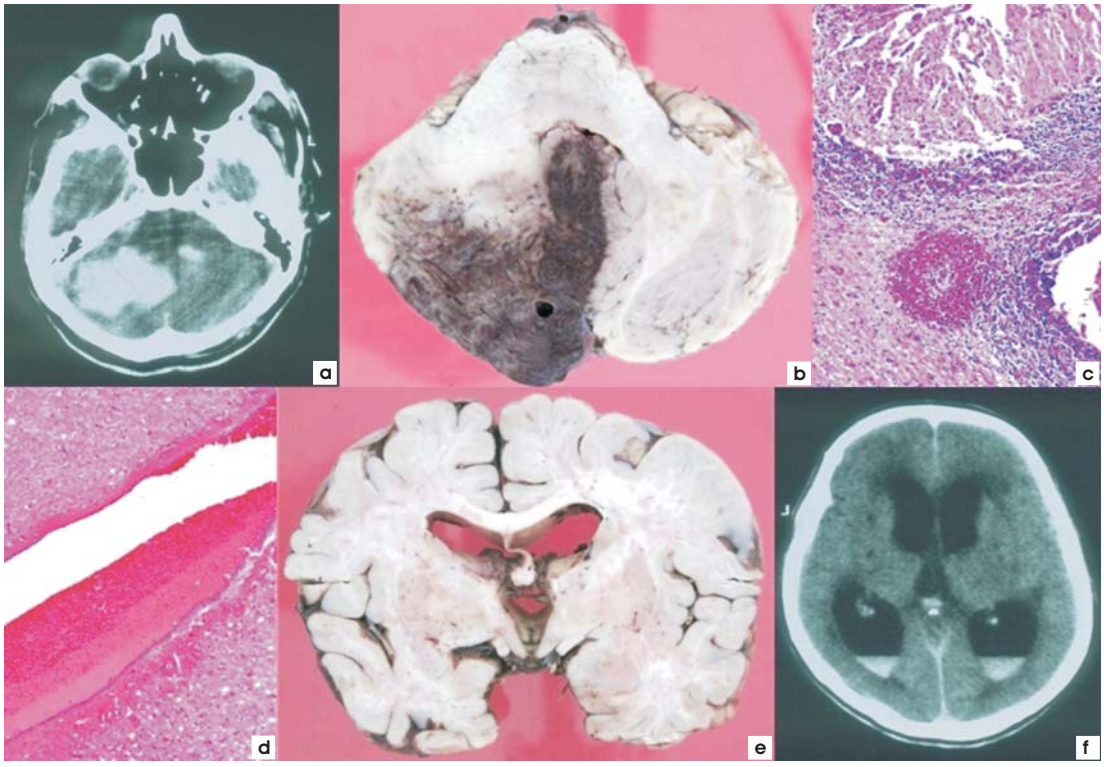


Figure 4 – ***Large right cerebellar hematoma: (a) CT image; (b) Pitres section on necroptic sample fixed in formalin; (c) Microhaemorrhage in the white matter; (d), (f) Blood effusion in the ventricles; (e), (f) Enlargement of ventricular spaces***

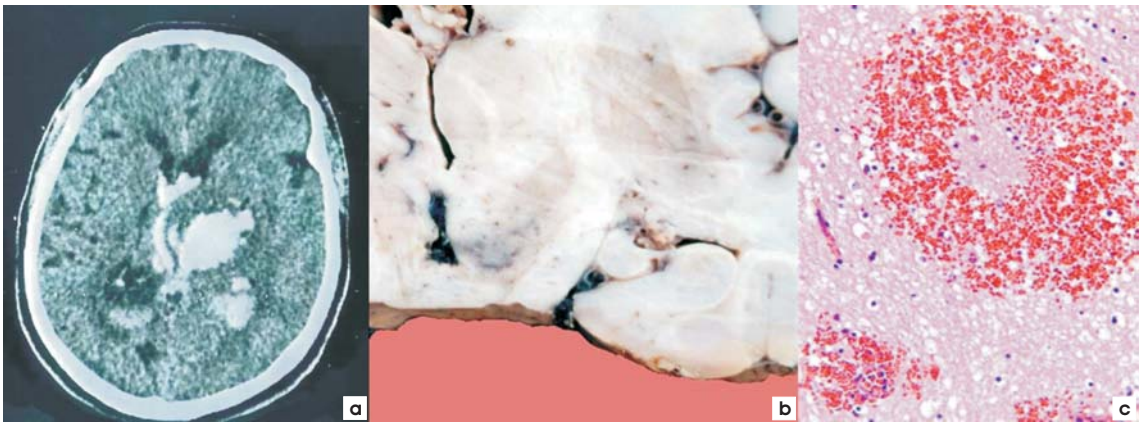


Figure 5 – ***Deep hematoma in left basal ganglia with ventricular extention: (a) CT image; (b) Pitres section – presence of blood in III[rd] ventricle; (c) microscopy – satelite microhaemorrhage; arteriola with altered wall***

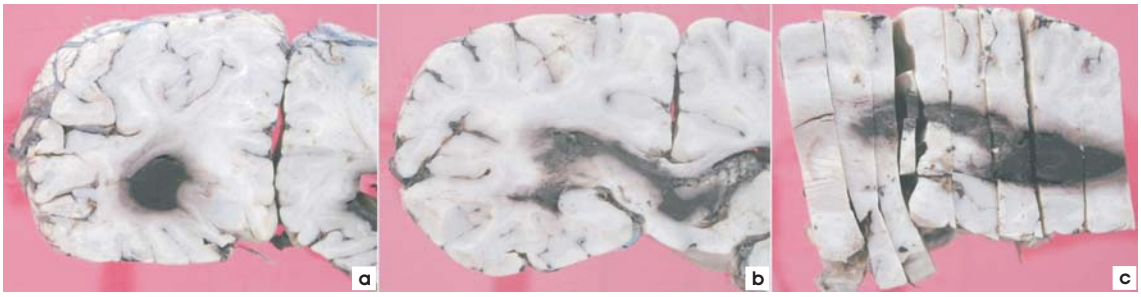


Figure 6 – ***Deep hematoma in right basal ganglia with extention in lateral an III[rd] ventricles: (a) frontal section – blood in I[st] ventricle; (b) frontal section – hematoma and blood in I[st] and III[rd] ventricles; (c) right parasagittal section***

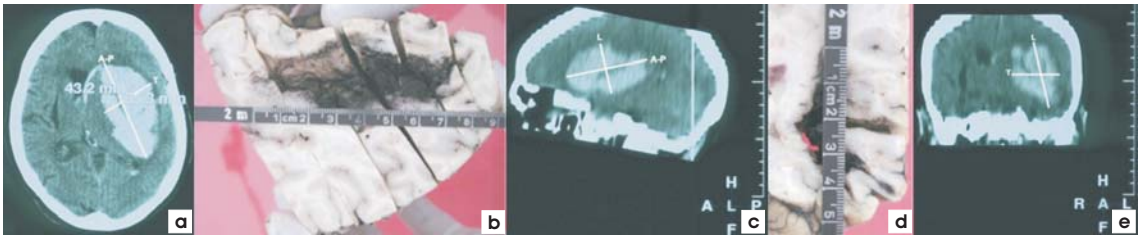


Figure 7 – ***Large left basal ganglia hematoma with extension in white matter of temporal and parietal lobes***

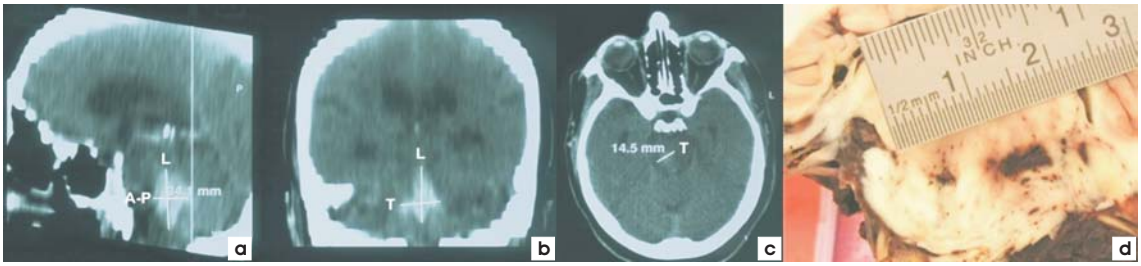


Figure 8 – ***Large brain stem hematoma: (a), (b), (c) CT images; (d) necroptic aspect***

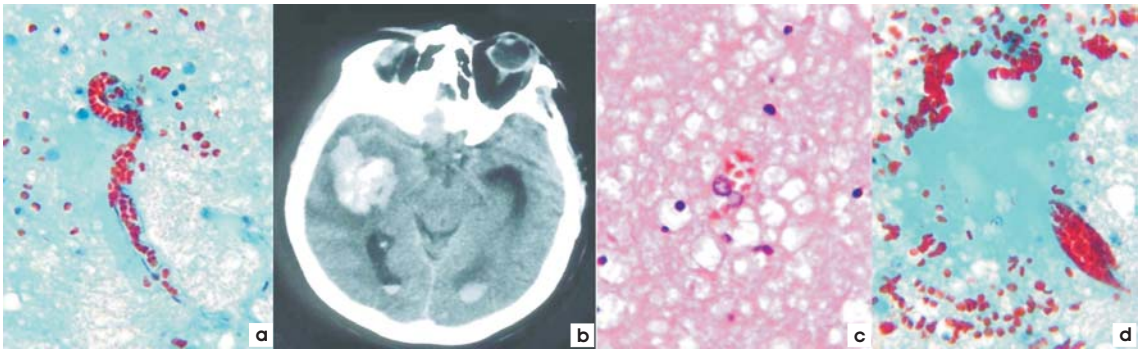


Figure 9 – ***Large right temporal hematoma. with extention in lateral ventricles. Well defined perilesional oedema: (a), (c), (d) microscopic aspects of perilesional oedema; (b) CT image***

Thus, in our study, IVE involved one ventricle in 59% of cases and two or more ventricles in 41% of cases (Figure 6).

Anyway, most of the univentricular involvements concerned one of the lateral ventricles, with a slight predominance on IInd ventricle (27 vs. 25 cases).

The results are similar to Fujii's study where IVE was mild in 63.12%, and severe in 36.88% of cases [12].

Dimensions of intraparenchymal haematomas

Another factor independently associated with in-hospital mortality is the volume of haematoma [11].

Some investigators found that 38% of the patients show an increase in intraparenchymal haematoma volume higher than 33% in the first 24 hours after the onset of the symptoms [15].

The extension of haematoma is associated with the alteration of the neurological status [15–17] and the mortality rate is influenced by the haematoma volume, approximately 85% from the patients with haematomas bigger than 50 cm^3 dying [18].

This extension is attributed to continuous bleeding at the level of the primary source, as well as to mechanical injury of adjacent vessels [19].

In our study, the dimensions of intraparenchymal haematomas were established either by CT examination (Group II) or during necroptic examination (Group I). Therefore, none of the cases had a dynamic assessment of the haemorrhagic focus (by several CT examinations or by CT and necropsy examinations).

Thus, the anterior-posterior diameter had, in 63% of lobar haematomas, values ranging between 4 cm and 6.9 cm. It should be noticed also that 1/3 of cases (i.e., 23) had an A–P diameter over 7 cm (Figure 7).

Table 12 – ***Dimensions of lobar haematomas***

Dimension [cm]	Diameter		
	A–P	*L*	*T*
1–1.9	0	1	2
2–2.9	0	10	10
3–3.9	13	16	16
4–4.9	13	10	10
5–5.9	10	5	3
6–6.9	3	13	13
7–7.9	10	2	3
8–8.9	1	0	0
9–9.9	2	0	0
>10	10	5	5

Also, almost 1/3 of cases had a transverse diameter and a longitudinal diameter over 6 cm (Table 12).

We can conclude that most of studied haematomas had large dimensions, thus explaining their extention to one of the ventricular spaces.

Brain stem haematomas (27 cases) were also large; comparing their diameters with organ's dimensions almost all having more than 2 cm in all diameters (Table 13 and Figure 8).

Finally, the five cerrebelar haematomas were also large ones, with A–P diameter between 4 and 6 cm, T diameter between 1 and 6 cm, and L diameter between 3 and 5 cm.

Table 13 – ***Dimensions of brain stem haematomas***

Dimension [cm]	Diameter		
	L	*T*	*A–P*
1–1.9	0	4	5
2–2.9	6	12	12
>3	11	11	11
>4	10	–	–

Mass effect

Brott T. *et al.* stated that the significant mortality of intraparenchymal haematomas is, in most cases, due to mass effect and IVE [15].

The presence of mass effect was assessed only in Group II. The compression produced by the usually large haemorrhagic foci on neighboring encephalic structures was revealed by CT examination in 21 of cases representing more than one half of Group II cases.

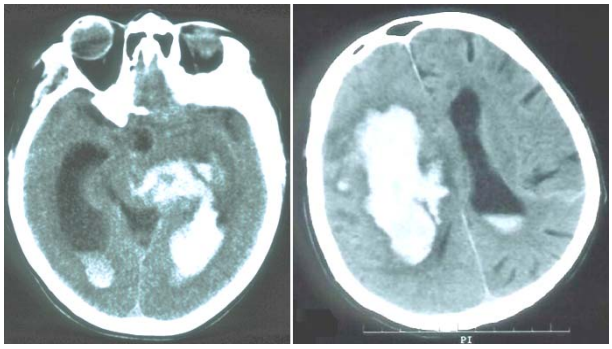


Figure 11 – ***Mass effect. Left: Left basal ganglia haematoma with compression on third ventricle and extention to lateral ventricles. Right: Large right fronto-parietal haematoma collapsing the Ist ventricle and extension to IInd ventricle***

Perilesional oedema

An area of perilesional oedema appears immediately around the recent intraparenchymal haematoma [20].

It extends by approximately 75% in the first 24 hours after the onset [21], it usually persists for up to five days [22] and it can be seen even two weeks after a cerebral stroke [23].

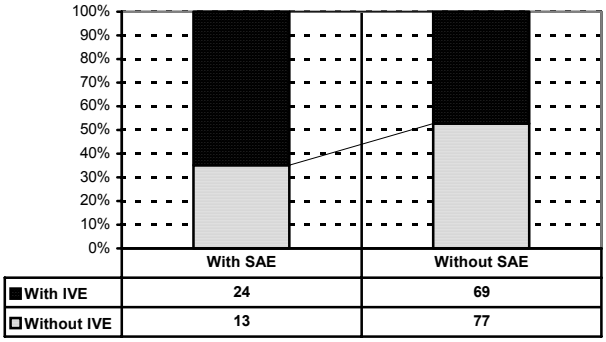
Although the significant morbidity of ICH is mostly due to mass effect and IVE, the deterioration of the clinical status subsequent to haemorrhagic recurrences and/or to the presence of the perihaematomal oedema is frequently registered [15].

Therefore, we could identify in both our groups, either by microscopic examination of the nervous tissue drawn during autopsy or by CT examination the constant presence of diffuse or perilesional edema (Figure 9).

Subarachnoid efusion

Finally, the severity of studied haematomas was also argued by the presence in a quarter of the 93 cases of a simultaneous extension of the haemorrhagic focus to the subarachnoid spaces (Table 14).

Table 14 – *Presence of subarahnoid effusion (SAE)*



	With SAE	Without SAE
■With IVE	24	69
□Without IVE	13	77

Comparing the data with those of ICH cases without IVE, it could be noticed that two thirds of all SAE cases had also IVE.

Conclusions

The results of our study allow us to draw some interesting concluding remarks:

Haemorrhagic stroke complicated with IVE showed an evident relationship with cold seasons and especially autumn. IVE is almost equally present in both sexes, but more frequently before 60 years.

Hypertension, motor deficits, usually of plegic type and deep degrees of coma, with low Glasgow scores were almost unfailing from our observations.

The severity of haematomas complicated with IVE was also sustained by the volume of intraventricular bleeding, occupying at least one of the lateral ventricles, by the huge dimensions of haemorrhagic foci as compared to the dimensions of different encephalic structures where they developed and by the constant presence of mass effect and perilesional oedema.

Finally, our data suggest that the association of IVE with other independent risk factors results in the death of patient, despite any sustained therapeutical intervention and enhances the IVE role of strong predictor of death.

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