ORIGINAL PAPER

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

Morphoclinical study of intracerebral hemorrhage with subarachnoid effusion

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Abstract

Aim. The study is an integrated assessment of clinical, imagistic and morphological parameters in severe intracerebral hemorrhages (ICH) complicated with subarachnoid effusion (SAE). *Materials and Methods*. The studied group had 37 cases of patients with ICH and SAE 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 and Glasgow score at admission) and morphological (the sites of the intraparenchymal hematoma and SAE, the size of the intraparenchymal hematoma, the presence of the mass effect, and the association of intraventricular effusion). The latter were assessed on CT films and during autopsy. *Results*. The presence of SAE as a complication of ICH showed a predilection for cold seasons, especially winter. From the 37 studied cases, 18 were men and 19 women. 51.3% of the patients were in the fourth and fifth life decade. Almost 73% of the patients had third stage arterial hypertension at admission, over 56% motor deficits and almost 49% Glasgow scores lower than 6. 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, perilesional edema and intraventricular extension (IVE) were constantly present. *Conclusions*. The association of SAE with other independent risk factors such as hypertension, low Glasgow scores, dimensions of hemorrhagic foci, presence of mass effect, perilesional edema and intraventricular extension (IVE) results in the death of patient despite any sustained therapeutical intervention.

Keywords: intracerebral hemorrhage, subarachnoid extension, morphoclinical parameters.

Introduction

Intracerebral hemorrhage (ICH) is one of the most devastating forms of stroke with substantial morbidity and mortality. It has a major impact on public health and ranks among the leading causes of death, resulting in enormous costs measured in both healthcare resources and lost productivity. Although the number of hospital admissions for intracerebral hemorrhage has increased worldwide during the last few years, mortality has not fallen.

Non-traumatic intracerebral hemorrhage (ICH) is an acute and spontaneous extravasation of blood into the brain parenchyma. Most commonly results from hypertensive damage to blood vessel walls, but it also may be due to a wide spectrum of disorders. Typical symptoms include focal neurologic deficits, often with abrupt onset of headache, nausea, and impairment of consciousness.

The extravasation of blood forms a roughly circular or oval mass that disrupts the tissue and grows in volume as the bleeding continues. Adjacent brain tissue is distorted and compressed. If the hemorrhage is large, midline structures are displaced to the opposite side and reticular activating and respiratory centers can be compromised, leading to coma and death [1].

Pressure from supratentorial hematomas and the accompanying edema may cause transtentorial brain herniation, compressing the brainstem and often causing secondary hemorrhages in the midbrain and pons, intraventricular rupture and extension or in rare cases, subarachnoid extension [2, 3].

The rupture into the adjacent ventricle is much more frequent than the direct rupture into the subarachnoidian space. The extension to both spaces is exceptional [4].

SAE was frequently found in cerebral amyloid angiopathy (CAA)-related ICH and it is the most reliable indicator that the hemorrhage is caused by CAA. ICH is most commonly lobar and therefore easily ruptures into the subarachnoid space. [5]

Materials and Methods

This study was an analysis of clinical and morphological data retrospectively collected from 37 cases with intracerebral hemorrhage (ICH) complicated with subarachnoid extension (SAE) who died during the

hospitalization in Emergency County Hospital of Craiova and were registered in the Pathology Department with a view to autopsy. 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 146 cases of IHC without SAE 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 19 cases, included the patients who survived more than 48 hours and were investigated by CT.

In these cases, the pathologist decided that the diagnostic was already well established by CT investigation. and the autopsy was unnecessary.

Group II, consisting of 18 cases, included patients with clinical suspicion of ICH but follow-up imaging was not obtained due to their moribund status or because despite the complex treatment, the patients died within the first 48 hours of hospitalization and the autopsy had been performed in order to establish the diagnostic.

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 hemorrhagic focus fixed in formalin for macroscopic evaluation and fragments of nervous tissue from the proximity of hemorrhagic 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.

The morphological data were: the site of the intracerebral hemorrhage; the site of the SAE; the size of the intracerebral hemorrhage; the presence of the mass effect; the presence of the perilesional edema and the presence of the subarachnoid effusion.

Results and Discussion

Clinical study

Season distribution

The ICH complicated with SE had a predilection for cold seasons. Comparing the distribution of cases with and without SAE we could observe that, in our group, the SAE complicated more frequently ICH during the winter whereas, in the spring, there were ICH extended less frequently (Table 1). This could probably be explained by the influence of atmospheric pressure changes.

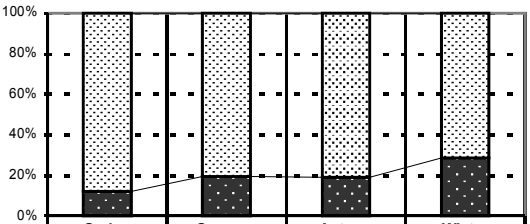
The sex of patients

The sex distribution indicated a slight predominance of the cerebral hemorrhagic stroke in male patients (78 *vs.* 68 cases) but SAE frequency was slightly higher in women (21.8% *vs.* 18.7%) (Table 2).

Studies to date have not determined whether these can be explained entirely by equal exposure to the known risk factors or whether there are additional factors, possibly genetic, which remain undiscovered.

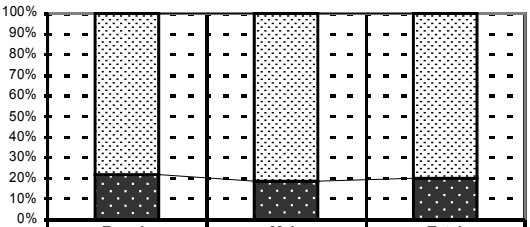
These data are concordant with other studies stating the same higher frequency of cerebral hemorrhagic stroke in men especially those older than 55 [6].

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



	Spring	Summer	Autumn	Winter
Without SAE	36	33	42	35
With SAE	5	8	10	14

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

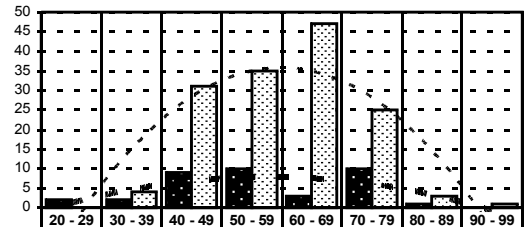


	Female	Male	Total
Without SAE	68	78	146
With SAE	19	18	37

The age of patients

Age is the greatest risk factor for ICH. Incidence rates increase dramatically among persons older than 55 years [6, 7]. The age distribution of our patients showed that ICH complicated with SAE prevailed in adults between 40 and 80 years, with a peak in the 5th, 6th and 8th decade of life. There is a gap between 60 and 69 years which appear to have no explanation (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 SAE	2	2	9	10	3	10	1	0
Without SAE	0	4	31	35	47	25	3	1

ICH is exceptionally rare between 24 and 40 years, its incidence in persons younger than 35 years being approximately 0.3/100 000 inhabitants [8, 9]. We found in our ICH group eight cases with hemorrhagic strokes occurring before the age of 40 years (4.4%), from which four had SAE associated as complication (10.8% from SAE group).

Arterial blood pressure

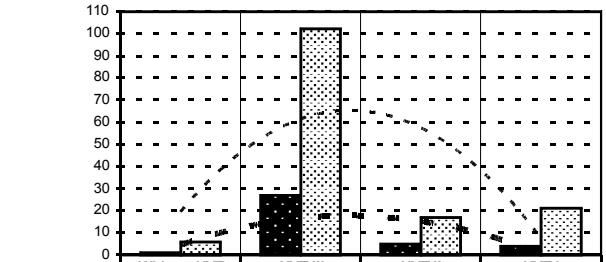
The incidence of spontaneous ICH is considerably higher in patients with hypertension in comparison with patients with normal blood pressure [10]. A history of

hypertension is usually found in 67.2% of patients with IHC and it is 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%) [11].

In our study, almost 73% of cases in SAE group had IIIrd stage hypertension at admission, with systolic values over 180 mmHg and diastolic values over 110 mm Hg. As we mentioned above, the blood pressure values were normal in seven cases whose ages were under 40 years.

We, therefore, considered that the cause of these severe hemorrhagic strokes in young people could be but malformations of intraparenchymal blood vessels.

Table 4 – ***Distribution depending on hypertension stages***

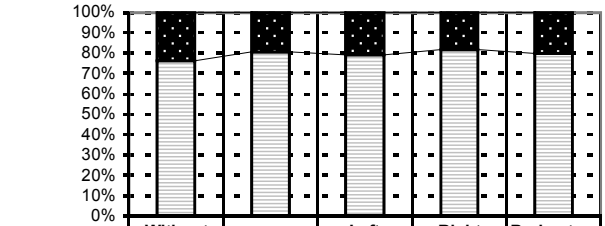


	Without HYT	HYT III	HYT II	HYT I
With SAE	1	27	5	4
Without SAE	6	102	17	21

Motor deficit

The motor deficit was observed at admission in 32 of studied SAE cases representing 86.4% of the group. Almost two thirds of these presented hemiplegia, with a slight predominance for the left part (11 cases *vs.* 10 cases), the remaining one third having signs of brain stem lesions, i.e., hyperextension and internal rotation of arms (Table 5).

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



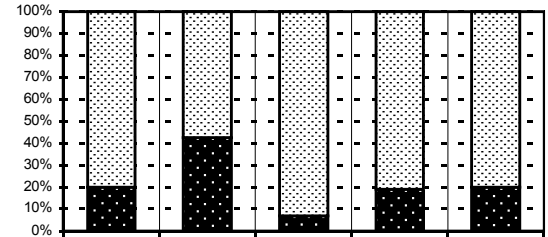
	Without MD	Hemiplegia	Left Hemiplegia	Right Hemiplegia	Brain stem signs
With SE	5	21	11	10	11
Without SE	16	87	42	45	44

Comparing the data with those of cases without SAE, no significant difference was observed between the two groups concerning the presence of different motor deficits, except a slight predominance of right hemiplegia in the group without SAE.

The degree of coma – Glasgow score

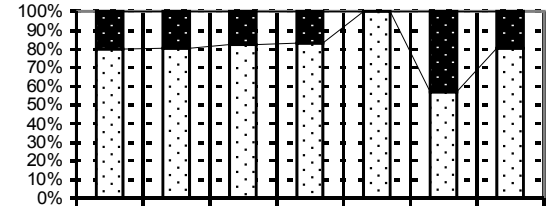
Half of cases with ICH presented even from the admission a deep coma (comas IIIrd or IVth degree) (Table 6) and 1/3 of the patients were conscious when they were brought into the hospital. In turn, only one third of patients with SAE were conscious, while 46% presented an advanced degree of consciousness alteration. The evaluation of Glasgow coma score revealed the same situation, with 46% of all 37 cases with SAE having a Glasgow score ≤5, emphasizing once again the severity of nervous tissue alterations enhanced also by the blood effraction into subarachnoid space (Table 7). There are studies indicating that these low scores are, like and moreover together with SAE, an independent factor associated with mortality in patients with intraparenchymal hematomas hospitalized [12].

Table 6 – ***Distribution depending on coma degree***



	Without coma	I dg	II-nd dg	III-d dg	IV-th dg
Without SAE	53	8	14	47	24
With SAE	13	6	1	11	6

Table 7 – ***Distribution depending on Glasgow score***



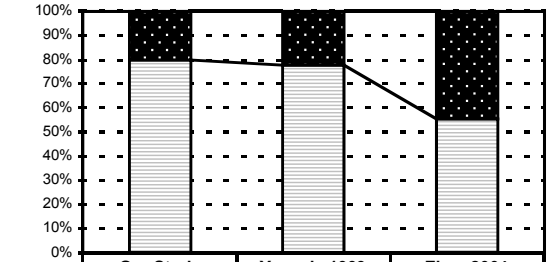
	GCS 3	GCS 4	GCS 5	GCS 6	GCS 7	GCS 8	GCS>8
With SE	6	8	3	1	0	6	13
Without SE	24	33	14	5	9	8	53

Morphological study

SAE as a complication of IHC

As we mentioned above, subarachnoid extension is a rare complication of IHC. Extension of an intracerebral bleeding into the subarachnoid spaces is less frequent compared with IVE. Thus, the study group included only of 37 cases with SAE in patients who died during hospitalization and were registered in the Department of Pathology, representing 20% of all cases (Table 8).

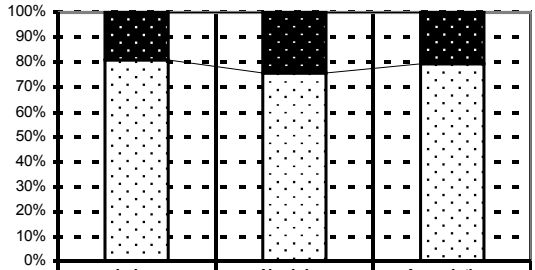
Table 8 – ***The incidence of SAE in IHC – comparison with Yamada and Zhan's study***



	Our Study	Yamada 1993	Zhan 2004
With SAE	37	23	37
Without SAE	146	81	46

Comparing our data with those from other studies, we saw that our observations are in concordance with those presented by other authors [13], excepting Zhan's study [5], which reports a higher percentage of IHC complicated with SAE (Table 9).

Table 9 – *Distribution and frequency of ICH complicated with SAE depending on site*



	Lobar	Nonlobar	Associations
With SAE	23	7	7
Without SAE	97	22	27

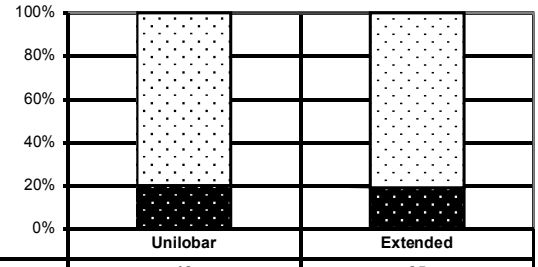
Site of the intraparenchymal hematoma

The site of the intraparenchymal haematomas was discovered either by CT, for Group I or by autopsy, for Group II. Almost 2/3 of cases with ICH complicated with SAE wee situated in cerebral lobes. The other third of cases were either non-lobar or associations of two or three hemorrhagic foci with different location. Non-lobar hemorrhages had a slighter frequency than the lobar ones and the associations (24.1% *vs.* 19.2% and 20.6 respectively) (Table 9).

Lobar hematomas

Most of ICH complicated with SAE were extended to more than one lobe (20 of 23 cases – 87%). In only three cases, the hematoma was restricted only to one lobe (Figure 1). In one case, hematoma arose in frontal lobe, in the other two cases being located in parietal lobe. The frequency of SAE presence was almost the same in both unilobar and extended groups (Table 10).

Table 10 – *Distribution and frequency of ICH complicated with SAE in lobar sites*



	Unilobar	Extended
Without SAE	12	85
With SAE	3	20

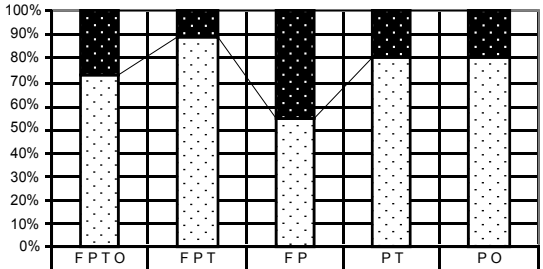
All extended ICH included either as starting area or as extending area the parietal lobe. Hematomas involving parietal and temporal lobes were the most numerous, representing almost 1/3 of extended lesions (Figure 2).

They were followed by frontal-parietal lesions (Figure 3) and by the group of hematomas with the largest extension, from frontal area until occipital area (Figure 4). Instead, the highest frequency of SAE was observed in frontal-parietal hematomas – 45%, followed by large hematomas – 26.7% (Table 11).

Non-lobar hematomas

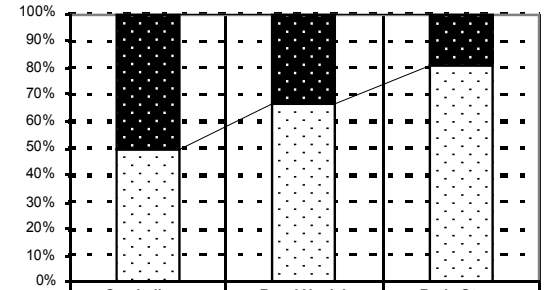
SAE complicated seven of the 21 hematomas with non-lobar location, meaning 1/3 of them (Table 12). The most numerous cases were those with brain stem hematomas (four of seven cases – Figure 6), but the highest frequency of SAE was observed in cerebellar hematomas (Figure 5).

Table 11 – *Extended lobar IHC – anatomical site distribution*



	FPTO	FPT	FP	PT	PO
With SAE	4	3	5	7	1
Without SAE	11	24	6	29	4

Table 12 – *Distribution and frequency of ICH complicated with SAE in non-lobar sites*

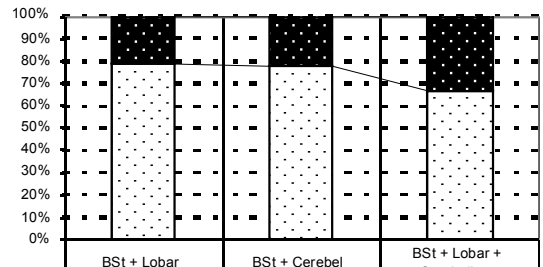


	Cerebellum	Basal Nuclei	Brain Stem
With SAE	2	1	4
Without SAE	2	2	17

Associations of hemorrhagic foci

The presence of more than one hematoma complicated with SAE was observed in only seven of the 27 cases with multiple hemorrhagic lesions. In all cases, one of the hematomas was observed in the brainstem (BSt) and it was usually associated with a lobar lesion. Cerebellum was the third site affected in this group of cases (Table 13).

Table 13 – *Distribution and frequency of ICH complicated with SAE in associations of hemorrhagic lesions*



	BSt + Lobar	BSt + Cerebel	BSt + Lobar + Cerebellum
With SAE	4	2	1
Without SAE	15	7	2

These data are concordant with other studies [5, 13], the presence of SAE being almost the same despite the fact that most of our cerebral hemorrhagic foci were very large, involving at least two lobes and, therefore, being very difficult to identify the site of original bleeding (Table 14).

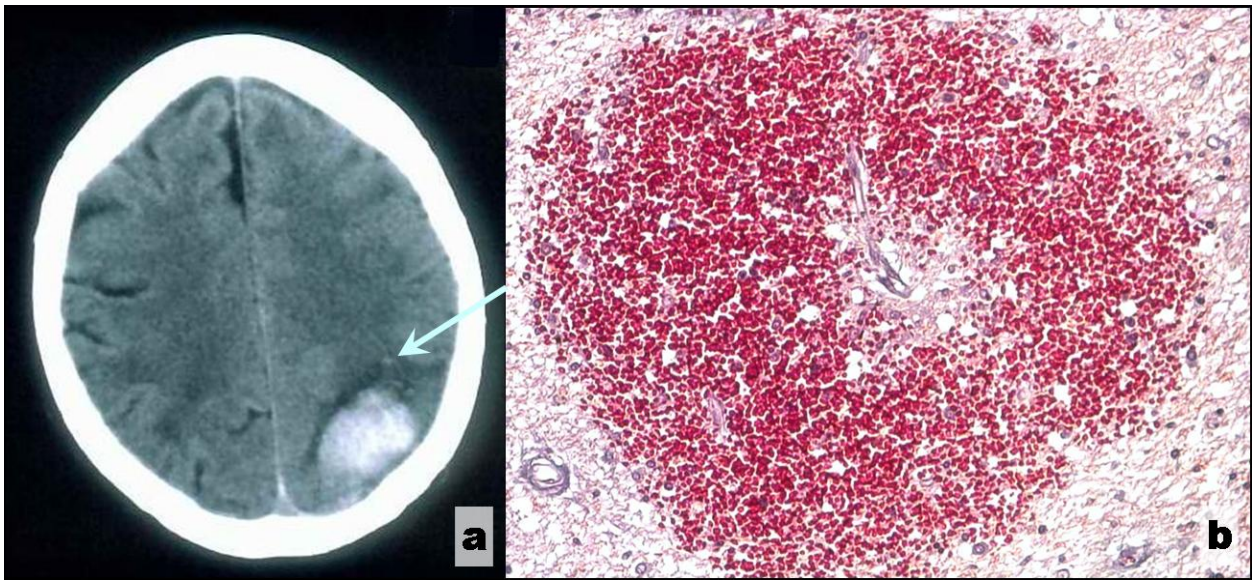


Figure 1 – ***Right side unilobar parietal hematoma: (a) CT aspect; (b) Satellite microhemorrhage.***

Figure 2 – ***Right side extended temporal-parietal hematoma: (a) CT aspect; (b) Necropsy gross aspect.***

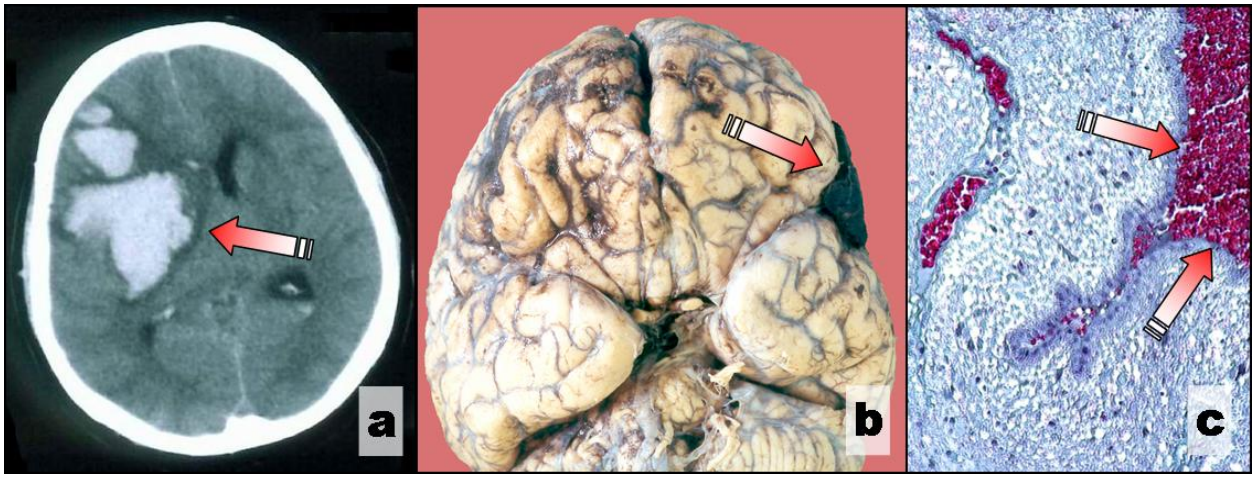


Figure 3 – ***Left side extended frontal-parietal hematoma: (a) CT aspect; (b) Necropsy gross aspect; (c) Hemorrhage extension in the subarachnoid space.***

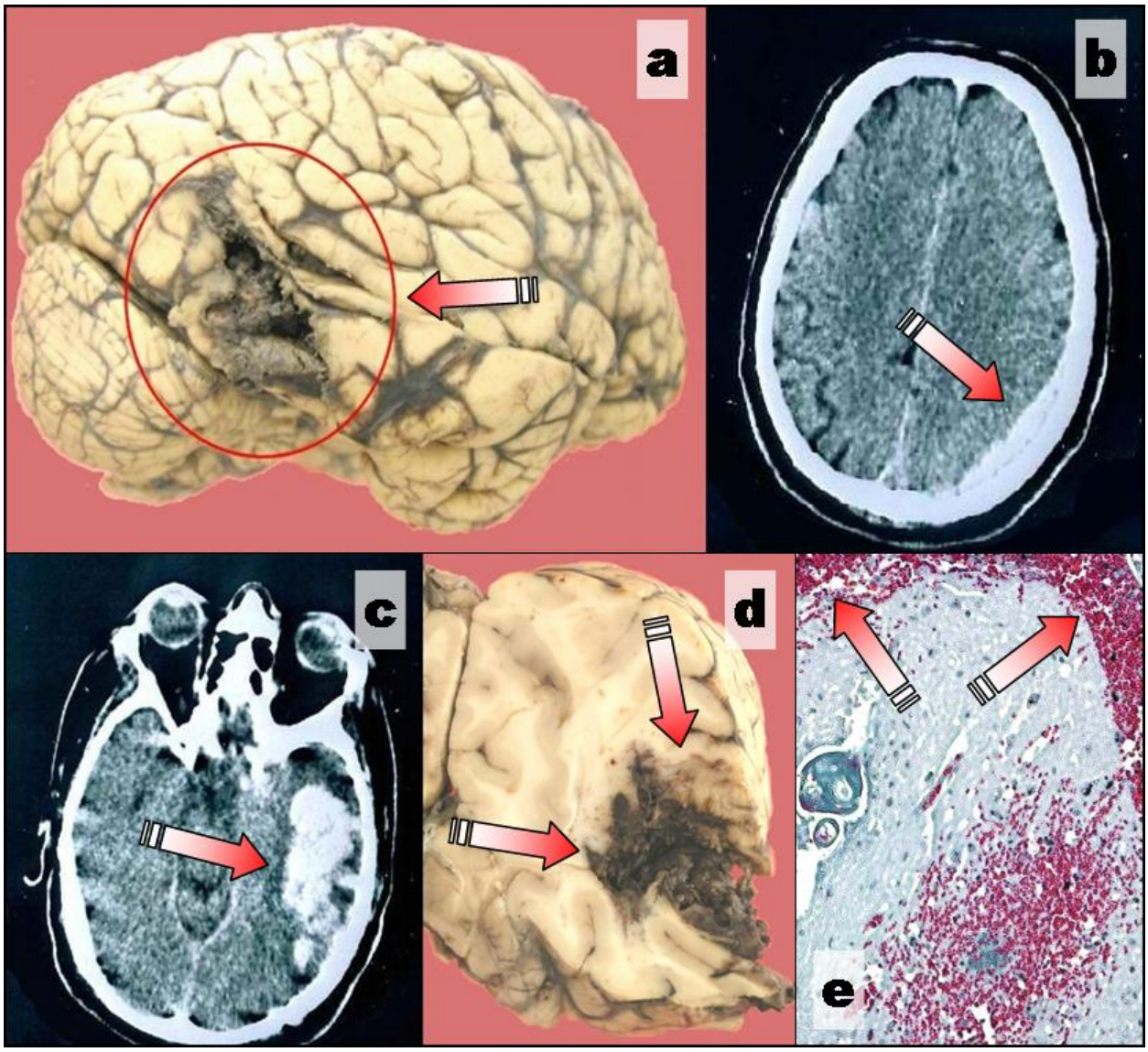


Figure 4 – ***Right side frontal-temporal-parietal-occipital hematoma: (a) Effraction at temporal lobe level; (b) Parietal-occipital effusion; (c) CT aspect; (d) Necropsy gross aspect on Pitres section; (d) Hemorrhage extension in the subarachnoid space.***

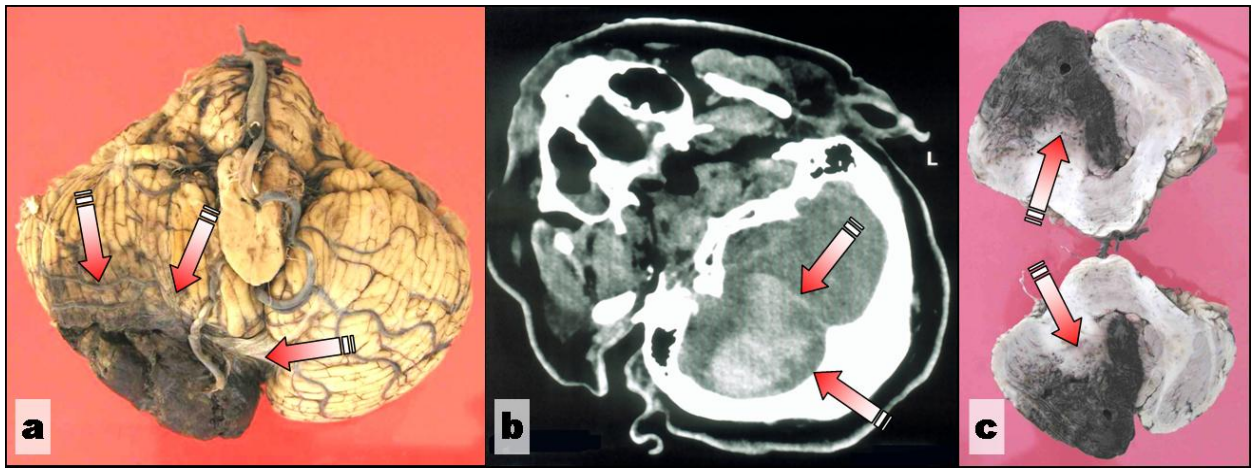


Figure 5 – ***Right side cerebellar hematoma: (a) Necropsy gross aspect – caudal view; (b) CT aspect; (c) Necropsy gross aspect on transverse section.***

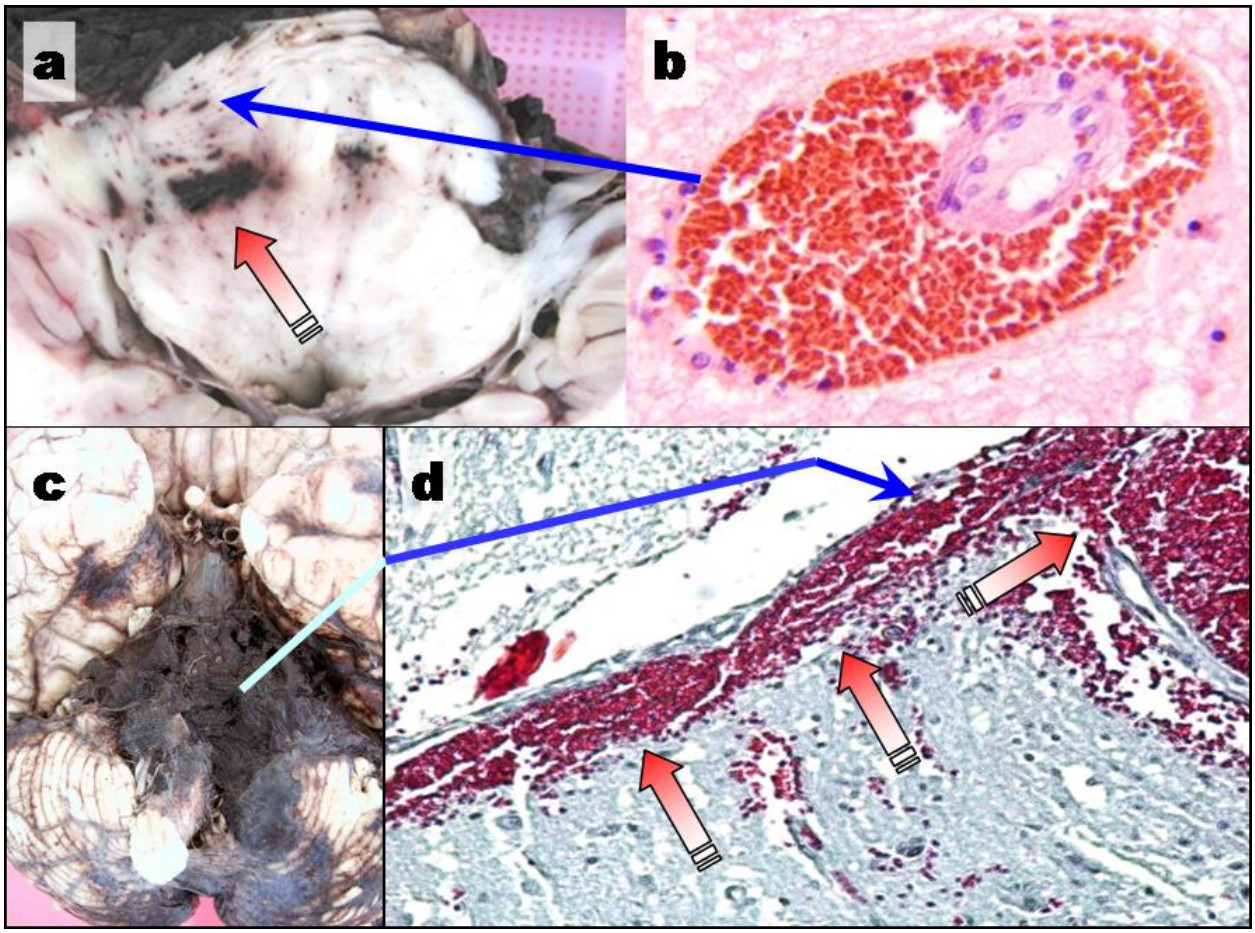


Figure 6 – ***Left side brain stem hematoma: (a) Necropsy gross aspect – cranial view; (b) Satellite microhemorrhage; (c) and (d) Hemorrhage extension in the subarachnoid space.***

Table 14 – ***Comparison with Yamada and Zhan's study***

Site	Yamada *et al.*, 1993		Zhan *et al.*, 2004		Our study	
	No SAE	With SAE	No SAE	With SAE	No SAE	With SAE
Supratentorial	95	17	74	35	123	24
Basal ganglia	66	0	17	2	3	1
Lobar (subcortical)	*29*	*17*	*57*	*33*	*120*	*23*
Infratentorial	19	6	9	2	26	6
Brainstem	*5*	*1*	*0*	*0*	*22*	*4*
Cerebellum	*14*	*5*	*9*	*2*	*4*	*2*
T O T A L	*104*	*23*	*83*	*37*	*183*	*37*
Incidence		*22%*		*44.5%*		*20.2%*

Dimensions of intraparenchymal hematomas

Another factor independently associated with in-hospital mortality is the volume of hematoma [12]. Some investigators found that 38% of the patients show an increase in intraparenchymal hematoma volume higher than 33% in the first 24 hours after the onset of the symptoms [14].

The extension of hematoma is associated with the alteration of the neurological status [14, 15] and the mortality rate is influenced by the hematoma volume, approximately 85% from the patients with hematomas bigger than 50 cm^3 dying [17]. This extension is attributed to continuous bleeding at the level of the primary source, as well as to mechanical injury of adjacent vessels [18].

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

Thus, the anterior–posterior (A–P) diameter had, in 42% of lobar hematomas complicated with SAE (including also the five lobar hematomas associated with other hemorrhagic lesions), values ranging between 3 and 5 cm (Figure 7a). It should be noticed also that 46% of cases had an A–P diameter over 7 cm. Although slightly more than 50% of cases had transverse (T) and longitudinal (L) diameter between 2 and 4.9 cm (Figure 7b), almost 40% of cases had values of the same diameters over 6 cm (Table 15).

Table 15 – ***Dimensions of lobar hematomas***

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

Brainstem hematomas were also large, as compared with organ's dimensions. Almost all of the 11 cases with a brainstem hematoma (including also the seven hematomas associated with other hemorrhagic lesions) had more than 2 cm in all diameters (Table 16 and Figure 7c).

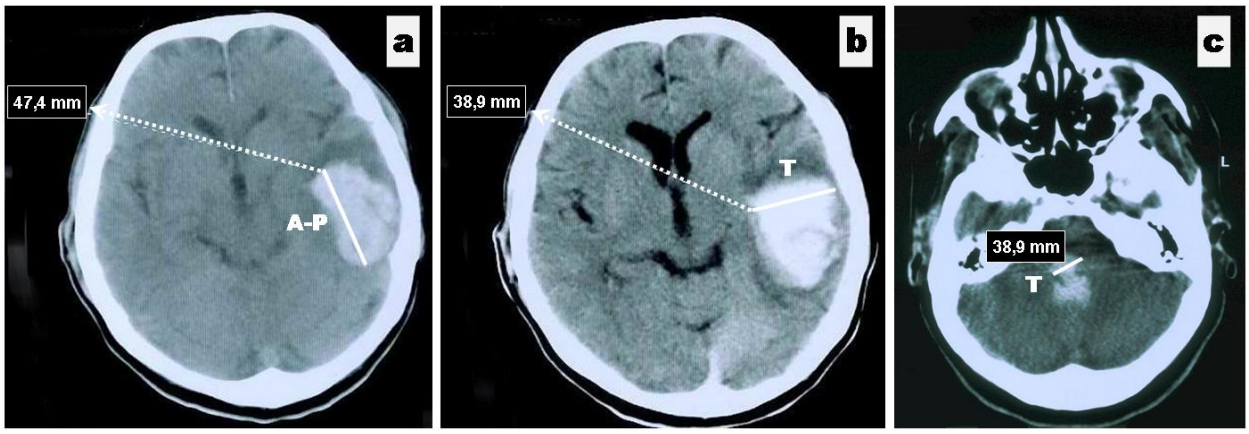


Figure 7 – ***Measurements of IHC dimensions: (a) and (b) Right side temporal hematoma antero-posterior diameter and transverse diameter; (c) Brain stem hematoma transverse diameter.***

Table 16 – ***Dimensions of brain stem hematomas***

Dimension [cm]	Diameter		
	L	T	A-P
0.1–0.9	0	1	1
1–1.9	3	3	3
2–2.9	6	2	3
3–3.5	2	5	4

Finally, the five cases with cerebellar hematomas and SAE 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.

We can conclude that most of studied hematomas had large dimensions, which could explain their extension to the subarachnoid space.

Mass effect

Brott T *et al.* stated that the significant mortality of intraparenchymal hematomas is, in most cases, due to mass effect [14].

The presence of mass effect was assessed only in Group I. The compression produced by the usually large hemorrhagic foci on neighboring encephalic structures was revealed by CT examination in 10 of the 19 cases with SAE, representing more than 50% of Group I cases (Figure 8 a and c – red arrows).

Perilesional edema

An area of perilesional edema appears immediately around the recent intraparenchymal hematoma [19]. It extends by approximately 75% in the first 24 hours after the onset [20], it usually persists for up to five days [21] and it can be seen even two weeks after a cerebral stroke [22]. Although the significant morbidity of ICH is mostly due to mass effect, SAE or/and IVE, the deterioration of the clinical status subsequent to hemorrhagic recurrences and/or to the presence of the perihaematomal edema is frequently registered [14].

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 8, a and b).

Intraventricular extension

Finally, the severity of studied hematomas was also argued by the presence of the simultaneous extension of the hemorrhagic focus to the intraventricular spaces in 2/3 of the cases with SAE (Figure 8c, blue arrow) while in cases without SAE the absence of IVE was slightly higher than its presence (Table 17).

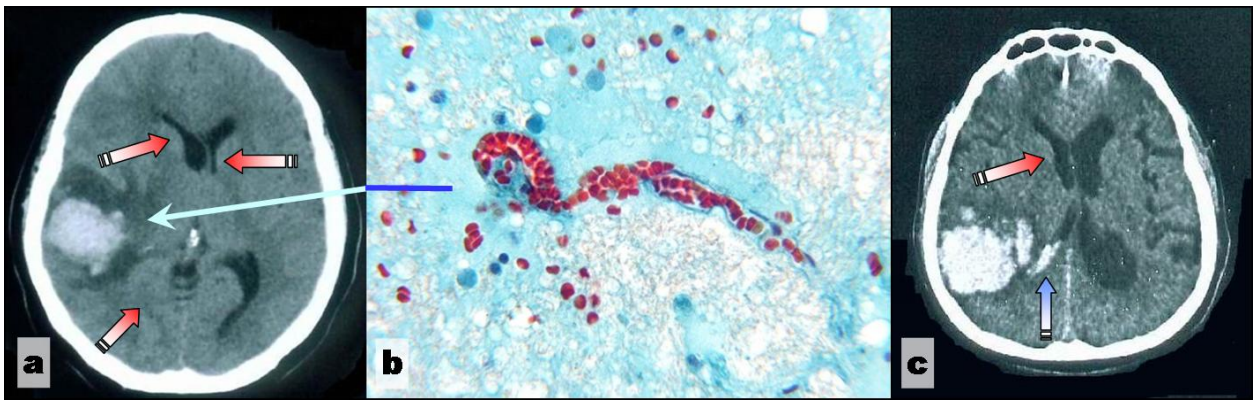
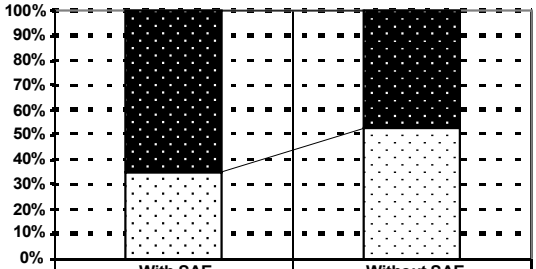


Figure 8 – ***(a) Left side temporal hematoma: "Mass effect" on ventricle II and perilesional edema; (b) Perilesional edema – microscopic aspect; (c) Left side parietal occipital hematoma / "Mass effect" and intraventricular effusion in ventricle II.***

Table 17 – ***Presence of intraventricular effusion***



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

Conclusions

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

Hemorrhagic stroke complicated with SAE showed an evident relationship with cold seasons and especially winter. SAE is almost equally present in both sexes, but more frequently before 60 years and over 70 years.

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

The typical features of ICH complicated with SAE included lobar site, mainly the lobar superficial areas, lobule shaped hematoma, frequently multiplicity of hemorrhage and secondary IVH.

The severity of hematomas complicated with SAE was also sustained by the huge dimensions of hemorrhagic foci as compared to the dimensions of different encephalic structures where they developed and by the constant presence of mass effect perilesional edema and intraventricular extension.

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

Acknowledgements

The study was part of the Research Project CNCSIS Code No. 958/2007 [GR26(4)/2007, continued with GR64(4)/2008].

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Received: November 20th, 2010 *Accepted: December 20th, 2010*