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Evaluation of Nontraumatic Aneurysmal Subarachnoid Hemorrhage - A Retrospective Cross-sectional Analysis

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Abstract

Introduction: Primary (nontraumatic) subarachnoid hemorrhage (SAH) is an important complication of intracranial aneurysms. Multiple intracranial aneurysms are discovered in 15% to 35% of patients with aneurysm who present with subarachnoid hemorrhage (SAH). Increased age and female sex have an increased incidence of SAH patients with multiple aneurysms.

Objective: This study was undertaken to analyse and evaluate the frequency and risk factors of nontraumatic aneurysmal subarachnoid hemorrhage using conventional CT angiography.

Materials and Methods: The present study was a 2-year cross-sectional study, conducted on 350 patients with primary SAH, admitted in the wards and intensive care units of S.C.B Medical College and Ashwini hospital, Cuttack, Odisha, India during the period from January 2016 to December 2017.

Results: In this retrospective cross sectional study we analysed 87 patients presented with spontaneous subarachnoid hemorrhage. Intracranial aneurysms are more common in female sex and in older age group. In male patients the aneurysms are more commonly seen on left side while in female patients it is seen more commonly on right side but overall it is observed more commonly on right side. Among the male patients aneurysms are more commonly located at Anterior communicating artery while in female patients it is more commonly detected at Posterior communicating artery.

Conclusion: Subarachnoid hemorrhage is a grave complication of intracranial aneurysm. Female sex by itself is also associated with an increased incidence of multiple aneurysms. Eary CT angiographic study can locate exact location and size of aneurysm so that early intervention can be given. It appears likely that morphological risk stratification of intracranial aneurysms must at some point involve greater predictive power than that available with aneurysm size alone.

Keywords: Subarachnoid hemorrhage, intracranial aneurysms, CT angiography.

Introduction

The pathophysiology of aneurysmal subarachnoid hemorrhage (aSAH) is still unclear, and the overall rates of morbidity and mortality for patients with aSAH remain high despite improved diagnostic techniques and management strategies. Established risk factors for poor outcome after aSAH include increasing age, hypertension, smoking, excess alcohol consumption, poor clinical condition at admission, and certain aneurysm characteristics (posterior circulation [PC] aneurysms and

large aneurysms).[1,2] Female sex is also thought to confer an increased risk for poor outcome.[3,4] Subarachnoid hemorrhage from ruptured intracranial aneurysms (IAs) is associated with significant morbidity (eg, hydrocephalus, seizures, vasospasm, and stroke) and mortality.[5] As a result, IA treatment is often performed as a prophylactic measure before rupture. However, IA treatments, including both surgical clipping and endovascular coiling, are associated with substantial risks of their own.[6] Three percent of the general population harbors an intracranial aneurysm and the number of incidentally discovered unruptured intracranial aneurysms is rising with the increasing quality and availability of non-invasive imaging techniques.[7,8] Only a minority of aneurysms rupture, but when this happens, it is usually a disabling or fatal occurrence.[9] The precise pathophysiological mechanism of aneurismal rupture is not completely understood. It is important to identify risk factors for aneurysmal rupture in order to tailor treatment of intracranial aneurysms. Female gender and an age above 60 years are factors associated with an increased risk of rupture, as are an aneurysm size of more than 5 mm and location of the aneurysm on the posterior circulation.[10] Multiple intracranial aneurysms are discovered in 15% to 35% of patients with aneurysm who present with subarachnoid hemorrhage (SAH).[11] Population-based studies have indicated that increased age and female sex are significantly associated with SAH.[12] However, the correlation between increased age and female sex and the incidence of SAH patients with multiple aneurysms remains controversial because few population-based studies have compared the proportion of SAH patients with a single aneurysm and that of patients with multiple aneurysms. Among SAH patients, the frequency of aneurysm occurrence at each site is not always compatible between patients with a single aneurysm and those with multiple aneurysms.Whether the prognosis for SAH patients with multiple aneurysms is less favorable than that for SAH patients with a single aneurysm is also not well established.[13]

Objectives

This study aimed to compare the sex differences in patients with aSAH in terms of predisposing factors, admission-related factors, aneurysm characteristics.

Materials and Methods

The present study was a 2-year cross-sectional study, conducted in the medical and neuromedical department of S.C.B Medical College and Ashwini hospital, Cuttack, Odisha, India on patients presented with acute subarachnoid hemorrhage during the period of January 2016 to December 2017 after obtaining an informed written consent. 100 patients with primary (nontraumatic) subarachnoid hemorrhage admitted in the wards and intensive care units of a tertiary care hospital and who have undergone CT imaging were evaluated with following inclusion and exclusion criteria.

Inclusion Criteria

1. Patients with age ≥20 and < 90 years

2. Patients with spontaneous subarachnoid hemorrhage of nontraumatic origin detected on CT imaging study.

(a) Who have presented with history of acute severe headache, altered sensorium, slurring of speech, acute hemiparesis, and accelerated hypertension—suggestive of acute cerebrovascular stroke

Exclusion Criteria

1. Patients aged < 20 and > 90 years of age

2. Patients with history of trauma

3. Patients with nonaneurysmal SAH

3. Patient with ischemic stroke and venous thrombosis

All raw data were collected.

Among 100 patients with SAH who were 20 to 89 years of age, 2-dimensional digital subtraction cerebral angiography was performed in 92 patients. Cerebral angiography was not performed in 8 patients because of

their poor condition. Presence of intracranial aneurysms were confirmed in 87 patients and further studied , rest 5 cases were excluded as no intracranial aneurysms were detected in them. The presence of aneurysms was confirmed by conventional angiography using CT angiography or MR angiography. Using patient notes and radiological images, we compared the differences between male and female patients in terms of the following: 1) predisposing risk factors (age, hypertension, smoking, alcohol consumption, and family history of aneurysms/stroke), 2) admission-related factors (World Federation of Neurosurgical Societies [WFNS] grade and admission delay), 3) characteristics of ruptured aneurysms (side, size, location, and multiplicity).

World Federation of Neurological Surgeons Grading System for Subarachnoid Hemorrhage - (WFNS) scale

WFNS Grade	Glasgow Coma Score	Motor Deficit
1	15	absent
2	13 - 14	absent
3	13 - 14	present
4	7 - 12	present or absent
5	3 - 6	present or absent

The clinical grading system proposed by the World Federation of Neurologic Surgeons is intended to be a simple, reliable and clinically valid way to grade a patient with subarachnoid hemorrhage. This system offers less inter observer variability than some of the earlier classification systems.

Interpretation:

• Maximum score of 15 has the best prognosis

• Minimum score of 3 has the worst prognosis

• Scores of 8 or above have a good chance for recovery

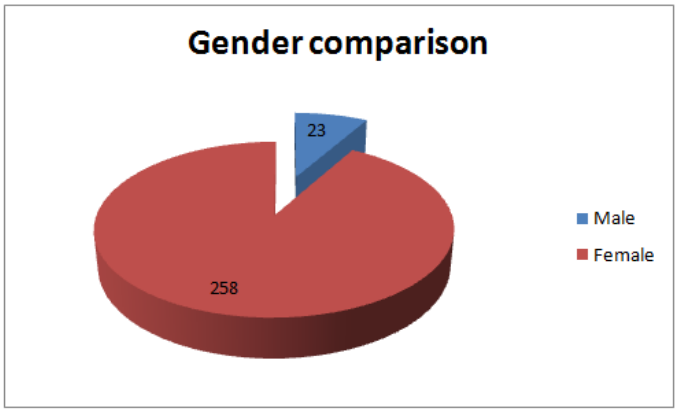
• Scores of 3-5 are potentially fatal, especially if accompanied by fixed pupils or absent oculovestibular responses

Aneurysms were classified as being in 1 of 4 locations: anterior cerebral artery (ACA), internal carotid artery (ICA), middle cerebral artery (MCA), and Posterior circulation (PC) but are also sub-classified according to their exact locations like Anterior communicating artery (ACoM), Posterior communicating artery, Basilar artery, Posterior inferior cerebellar artery, Distal ACA or Pericallosal artery, Vertebral artery, A1 segment of ACA, Posterior cerebral artery, Anterior choroidal artery and Superior cerebellar artery.

Results

In this study of 100 cases, 13 cases were excluded based on exclusion criteria and rest 87 cases were included and analysed. Among the 87 patients, 23 (26.4%) are male and 64 (73.6%) are female. (Graph 1)

Graph 1 – Gender wise Distribution of cases



42 (48.3%) patients are <55 yr of age and 45 (51.7%) are >55 yr of age. Among the male patients 14 (60.8%) are <55 yr of age , 9 (39.2%) are >55 yr of age and among females 28 (43.7%) are <55 yr af age , 36 (56.2%) are >55 yr of age. (Table 1)

Table 1 – Distribution of cases according to age

Age	Total , n=87, (%)	Male ,n=23, (%)	Female,n=64, (%)
<55 yr	42 (48.3)	14 (60.8)	28 (43.7)
>55 yr	45 (51.7)	9 (39.2)	36 (56.2)

The size of the aneurysm was <6mm in 61 (70.1%), 6-10mm in 18 (20.7%), 11-20mm in 7 (8.0%) and >20mm in 1(1.2%) cases. (Table 2)

Table 2 – Distribution of cases according to size of aneurysm

Size of Aneurysm	n (87)	%
<6mm	61	70.1
6-10mm	18	20.7
11-20mm	7	8.0
>20mm	1	1.2

The aneurysms are left sided in 35 (40.2%), right sided in 41 (47.1%), bilateral in 6 (6.8%) and midline in 5 (5.7%) cases. In male patients the aneurysms are more commonly seen on left side in 11 (47.8%) than right side in 9 (39.1%) followed by midline in 2 (8.7%) and bilateral in 1 (4.3%) cases while in female patients it is seen more commonly on right side in 31 (48.7%) than left side in 24 (37.5%) cases followed by bilateral in 6 (9.4%), midline in 3 (4.7%) cases but overall it is observed more commonly on right side. Overall more number of intracranial aneurysms are located at Anterior communicating artery in 23 (26.4%) cases followed by at Posterior communicating artery 21 (24.1%), M1 segment of MCA 20 (22.9%), ICA (proximal/bifurcation) 6 (6.8%), Basilar artery 6 (6.8%), Posterior inferior cerebellar artery 4 (4.6%), Distal ACA 3 (3.4%), Vertebral artery 1 (1.1%), A1 segment of ACA 1 (1.1%), Posterior cerebral artery 1 (1.1%) and Anterior choroidal artery 1 (1.1%) cases. Among the male patients aneurysms are more commonly located at Anterior communicating artery in 10 (43.5%) followed by M1 segment of MCA in 5 (21.7%) cases while in female patients it is more commonly detected at Posterior communicating artery in 18 (28.1%) followed by M1 segment of MCA in 15 (23.4%) and in Anterior communicating artery in 13 (20.3%) cases. (Graph 2, Table 3)

Graph 2 – distribution of cases according to site if intracranial aneurysm

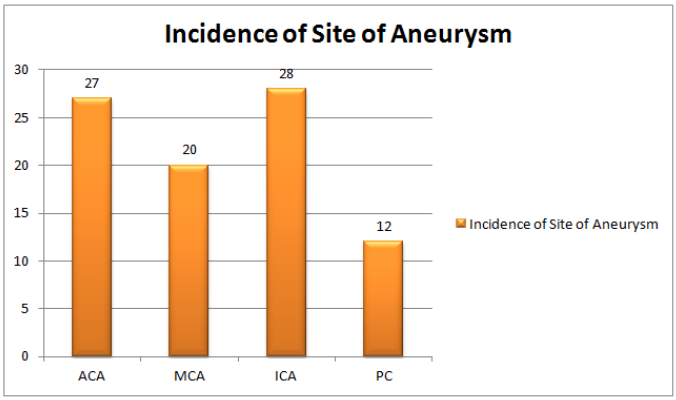


Table 3 – Sex differences in aneurysm characteristics.

Aneurysm characteristic			n=87, (%)	Male, n=23, (%)	Female=64, (%)
Aneurysm side	Left		35 (40.2)	11 (47.8)	24 (37.5)
	Right		41 (47.1)	9 (39.1)	31 (48.4)
	Bilateral		6 (6.8)	1 (4.3)	6 (9.4)
	Midline		5 (5.7)	2 (8.7)	3 (4.7)
Multiplicity	Yes		10 (11.5)	2 (20%)	8 (80%)
	No		77 (88.5)	21 (27.3%)	56 (72.7%)
Aneurysam location	ACA n=27	A1 segment	1 (1.1)	Nil	1 (1.5)
		Anterior communicating artery	23 (26.4)	10 (43.5)	13 (20.3)
		Distal ACA	3 (3.4)	1 (4.3)	2 (3.1)
	MCA n=20	M1 segment	20 (22.9)	5 (21.7)	15 (23.4)
	ICA n=28	Anterior choroidal artery	1 (1.1)	Nil	1 (1.5)
		ICA (proximal/bifurcation)	6 (6.8)	2 (8.7)	4 (6.2)
		Posterior communicating artery	21 (24.1)	3 (13.1)	18 (28.1)
	PC n=12	Basilar artery	6 (6.8)	2 (8.7)	4 (6.2)
		Posterior cerebral artery	1 (1.1)	1 (4.3)	Nil
		Posterior inferior cerebellar artery	4 (4.6)	1 (4.3)	3 (4.7)
		Vertebral artery	1 (1.1)	1 (4.3)	Nil

In majority of cases aneurysms are single in nature 77 (88.5%), but in 10 (11.5%) cases multiple (dual site) aneurysms are observed. (Table 4)

Table 4 – Distribution of cases according to multiplicity of aneurysm

Multiplicity	Male	Female
Yes,10	2 (20%)	8 (80%)
No, 77	21 (27.3%)	56 (72.7%)

Among 10 cases with multiple (dual) aneurysm 8 (80%) are female and 2 (20%) are male. Multiple aneurysms are more commonly located at ICA in 4 (40%), followed by MCA in 3 (30%), ACoA in 2 (20%) and BA in 1 (10.7%) cases. In female patients, multiple aneurysms are commonly located at ICA in 4 (50%) cases but in male patients it is equally detected at ACoM and MCA each in 1 (50%) cases. (Table 5)

Table 5 – Sex differences of cases showing single vs multiple aneurysm.

Site of aneurysm n=87	Single aneurysm	Single aneurysm n=77 (%)		Multiple aneurysm	Multiple aneurysm n=10 (%)	
	n=77 (88.5)	Male 21 (27.5)	Female 56 (72.5)	n=10 (11.5)	Male 2 (17.8)	Female 8 (82.2)
ACoA, n=23	21 (27.3)	9 (42.8)	12 (21.4)	2 (20)	1 (50)	1 (1.3)
ICA n=28	24 (31.2)	5 (23.8)	19 (33.9)	4 (40)	Nil	4 (50)
MCA n=20	17 (22.1)	4 (19.1)	13 (23.2)	3 (30)	1 (50)	2 (25)
Distal ACA, n=3	3 (3.8)	1 (4.8)	2 (3.6)	Nil	Nil	Nil
BA, N=6	5 (6.5)	2 (9.5)	3 (5.3)	1 (10)	Nil	1 (1.3)
Others , n=7	7 (9.1)	Nil	7 (12.5)	Nil	nil	Nil

We found hypertension as the single most common risk factor association for intracranial aneurysms seen in 33 (37.9%) cases. Other risk factor observed are diabetes in 23 (26.4%), smoking in 19 (21.8%), alcohol use in 18 (20.7%), h/o cancer in 8 (9.2%) and h/o anticoagulants use in 5 (5.7%) cases. The most common risk factor association in male is smoking seen in 18 (78.2%) while in females it is hypertension seen in 21 (32.8%) cases. (Table 6)

Table 6 – Distribution of cases showing Predisposing factors.

Predisposing factors	n=87, (%)	Male, n=23, (%)	Female=64, (%)
Hypertension (>160/90)	33 (37.9)	12 (52.2)	21 (32.8)
Smoking	19 (21.8)	18 (78.2)	1 (1.5)
Alcohol	18 (20.7)	16 (69.6)	2 (3.1)
F/H/O Stroke or Aneurysm	3 (3.4)	2 (8.7)	1 (1.5)
H/O Cancer	8 (9.2)	2 (8.7)	6 (9.4)
Diabetes	23 (26.4)	9 (39.1)	14 (21.9)
Anticoagulants	5 (5.7)	2 (8.7)	3 (4.7)

The proportion of cases with good WFNS grading (1 and 2) in male patients are 13 (56.5%), 4 (17.4%) and in females are 36 (56.2%), 13 (20.3%) respectively. (Table 7)

Table 7 – Distribution of cases according to WFNS grading

WFNS grading	Male, n=23, (%)	Female=64, (%)
1	13 (56.5)	36 (56.2)
2	4 (17.4)	13 (20.3)
3	1 (4.3)	6 (9.4)
4	3 (13.1)	5 (7.8)
5	2 (8.7)	4 (6.3)

Discussion

In this present study we have analysed 87 patients presented with nontraumatic spontaneous subarachnoid hemorrhage. We observed intracranial aneurysms are more common in females seen in 64 (73.6%) cases in compare to males seen in 23 (26.4%) cases. Similar to us Alhafidz Hamdan et al[14] observed aneurysms more common in women than men in the ratio of 1.2:1 to 3.5:1in various age group. They also observed the ratios of women to men were constant at approximately 1.2:1 from the 3rd and 4th decades of life but increased to approximately 1.7:1 in the 5th decade, 2.2:1 in the 6th decade, and 3.5:1 in later decades combined. The female patients were significantly older than the male patients (mean age 56.6 vs 51.9 years, respectively), with a higher proportion of women aged ≥ 55 years (56.2% vs 40.4%, respectively).

We studied 42 (48.3%) patients are <55 yr of age and 179 45 (51.7%) are >55 yr of age. Among the male patients aneurysms are more common in <55 yr of age group 14 (60.8%) while in female patients these are seen more commonly after 55 yr age 36 (56.2%). Similarly Alhafidz Hamdan et al[14] studied female patients were significantly older than the male patients (mean age 56.6 vs 51.9), with a higher proportion of women aged ≥ 55 years (56.2% vs 40.4%). There is an established increase in aSAH incidence in women in the literature, with studies demonstrating female-to-male ratios ranging from 1.2:1 to 3.1:1.[15,16] The increased incidence of aSAH in women has been shown to peak during the 5th and 6th decades of life, which correlates with the postmenopausal decline in

estrogen level. Because estrogen promotes normal vascular endothelial function[17] reductions in its levels may weaken vascular wall integrity,[18] leading to increased risk of aneurysm formation.

In this study we observed most of the aneurysms are of <6mm size seen in 61 (70.1%) cases followed by, 6-10mm in 18 (20.7%), 11-20mm in 7 (8.0%) and >20mm in 1(1.2%) cases. In accordance to us Gabriel J.E. Rinkel et al[19] studied aneurysms of <6mm size in 72%, 6-10mm in 21%, 11-20mm in 6.5% and >20mm in 0.8% cases. Monique H. M. Vlak et al[20] found 60.0% of ruptured aneurysms were >5 mm and 9.6% were >10 mm.

We observed aneurysms are more common on right side than left side {41 (47.1%) vs 35 (40.2%)}, bilateral in 6 (6.8%) and midline in 5 (5.7%) cases. In male patients the aneurysms are more commonly seen on left side in 11 (47.8%), while in females it is seen more commonly on right side in 31 (48.7%). Incidence of bilateral aneurysms are more in females than males {6 (9.4%) vs 1 (4.3%)} while midline cases are more common in males than females {2 (8.7%) vs 3 (4.7%)}. Similarly Alhafidz Hamdan et al[14] have also observed that in male patients aneurysms are more on left side (48.2%) and in female pastients on right side (48.4%). Bilateral aneurysms are more in female patients (6.8% vs 2.6%).

We observed the most common site of intracranial aneurysm is Anterior communicating artery 23 (26.4%) followed by Posterior communicating artery 21 (24.1%), M1 segment of MCA 20 (22.9%), ICA (proximal/bifurcation) 6 (6.8%), Basilar artery 6 (6.8%), Posterior inferior cerebellar artery 4 (4.6%), Distal ACA 3 (3.4%), Vertebral artery 1 (1.1%), A1 segment of ACA 1 (1.1%), Posterior cerebral artery 1 (1.1%) and Anterior choroidal artery 1 (1.1%) cases. Among the male patients aneurysms are more commonly studied at Anterior communicating artery in 10 (43.5%) cases followed by M1 segment of MCA in 5 (21.7%) cases while in female patients it is more commonly detected at Posterior communicating artery in 18 (28.1%) followed by M1 segment of MCA in 15 (23.4%) and in Anterior communicating artery in 13 (20.3%) cases. Similar to us Alhafidz Hamdan et al[14] observed the predominant aneurysm location in men was anterior communicating artery (42.3%) but in women they were more similarly distributed in 3 most common areas (anterior communicating artery [26.3%], MCA [22.5%], and posterior communicating artery [27.3%]). In both sexes, PC aneurysms contributed less than one-sixth of the total aneurysms. Lindner SH et al[15] have also observed women have more ICA aneurysms and men have more ACA aneurysms. Makio Kaminogo et al [23] have observed that in SAH patients with a single aneurysm, the most common site of aneurysm in men was the anterior communicating artery (ACoA; 41.2%); in women, it was the internal carotid artery (ICA; 32.0%). The influence of estrogen and its postmenopausal decline does not explain the fact that women have more ICA aneurysms and men have more ACA aneurysms. Instead, a hemodynamic mechanism may be responsible for such sex-linked variations in the anatomy of and flow dynamics across the circle of Willis have been demonstrated. Horikoshi et al[21] who studied 131 patients with cerebral aneurysms using MR angiography, demonstrated that anterior communicating artery aneurysms are significantly related to Type A anatomy (no visualization of a unilateral A1 segment), which is more common in men, whereas ICA aneurysms are associated with Type P anatomy (presence of a fetal type of posterior cerebral artery that was continuously delineated from the ICA through the posterior communicating artery), which is more common in women. Lindekleiv et al[22] in a study using computational fluid dynamics, showed that compared with men, women have disproportionately smaller vessel diameters, greater blood flow velocities,

and higher wall shear stress at ICA bifurcations, which increases the risk of aneurysm formation.

We observed that in majority of cases 77 (88.5%) aneurysms are single in nature and multiple (dual site) aneurysms seen in 10 (11.5%) cases. Among 10 cases with multiple (dual) aneurysm 8 (80%) are female and 2 (20%) are male. Multiple aneurysms are more commonly located at ICA in 4 (40%), followed by MCA in 3 (30%), ACoA in 2 (20%) and BA in 1 (10.7%) cases. In female patients, multiple aneurysms are commonly located at ICA in 4 (50%) cases but in male patients it is equally detected at ACoM and MCA each in 1 (50%) cases. Similar to us Alhafidz Hamdan et al[14] observed multiple aneurysms more in femsales in compare to males (11.5% vs 5.2%). Makio Kaminogo et al [23] have also observed that the proportion of multiple aneurysms among patients with SAH was higher in women than in men for all age categories by 5.2% to 15.2% except in the 80- to 89-year-old group. The overall frequency of multiple aneurysms was 20.2% in women, which was significantly higher than the 12.4% in men. They also studied that with respect to SAH in cases of multiple aneurysms, the most common site of ruptured aneurysm in women was ICA, but in men it was middle cerebral artery (MCA). A ruptured ACoA aneurysm was encountered less frequently in male patients with multiple aneurysms than in those with a single aneurysm.

We found hypertension as the single most common risk factor association for intracranial aneurysms seen in 33 (37.9%) cases. Other risk factor observed are diabetes in 23 (26.4%), smoking in 19 (21.8%), alcohol use in 18 (20.7%), h/o cancer in 8 (9.2%) and h/o anticoagulants use in 5 (5.7%) cases. But the most common risk factor associated with male patients is smoking seen in 18 (78.2%) while in females it is hypertension seen in 21 (32.8%) cases. In contrast to our study Alhafidz Hamdan et al[14] observed smoking as the most common risk factor associated with aneurysm both in males and females. Feigin VL et al [24] in their meta-analysis concluded that environmental factors such as smoking, excess alcohol consumption, and hypertension are the main risk factors for aSAH.

We observed more number of cases with WFNS grading (1 and 2), in male patients {13 (56.5%), 4 (17.4%)} and in females {36 (56.2%), 13 (20.3%)} respectively. So good WFNS grading are seen in 73.9% and 76.5% of cases of male and female patients respectively. Alhafidz Hamdan et al[14] had also observed the proportion of women with good WFNS grades (1 and 2) at admission was similar to that of men (76.3% vs 74.3%, respectively).

Conclusion

Both single aneurysm or multiple aneurysms are more common in female sex and age >50 years. Aneurysms are more commonly located at Anterior communicating artery in males while at Posterior communicating artery in females. Bilateral presentation is more common in females. In cases of multiple aneurysm, the ACoA aneurysm is most prone to hemorrhage. Predicting risk of rupture of intracranial aneurysms continues to be a topic of much debate. It appears likely that morphological risk stratification of intracranial aneurysms must at some point involve greater predictive power than that available with aneurysm size alone.

Abbreviations

1. aSAH – aneurysmal subarachnoid hemorrhage
2. ACA – Anterior cerebral artery
3. MCA – Middle cerebral artery
4. IC – Internal carotid artery
5. PC – Posterior circulation
6. ACoM - Anterior communicating artery

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LIST OF IMAGES

Figure 1a - ACoM aneurysm

Figure 1b - ACoM aneurysm presented with SAH

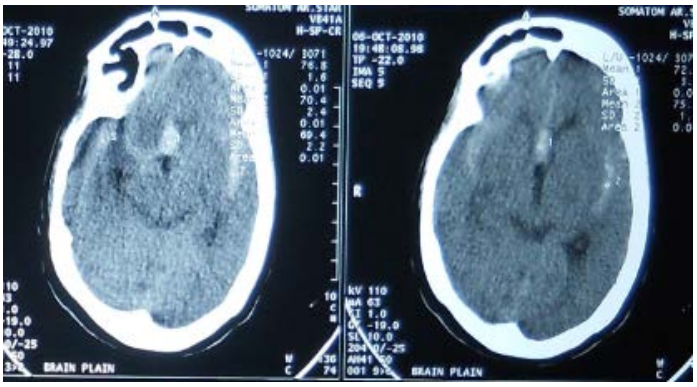

Figure 2a - Aneurysm of right MCA

Figure 2b Aneurysm of right MCA with SAH

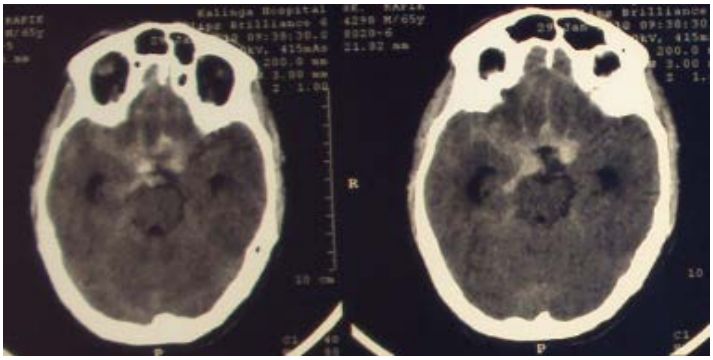

Figure 3 - Thrombosed aneurysm of ACA presented with SAH and ACA territory infarct

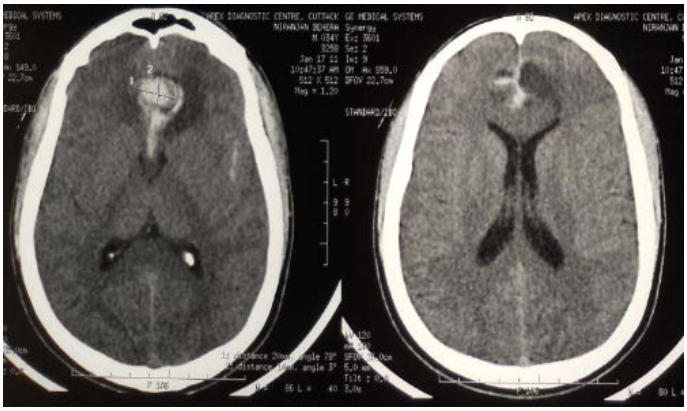

Figure 4 – Aneurysm at the junction of Anterior cerebral artery and Middle cerebral artery

Figure 5 – Aneurysm at Anterior communicating artery