Study of Incidence and Factors: Risk and Preventive, of Chronic Subdural Hematoma/hygroma in Clipped Patients of Unruptured Intracranial Aneurysms – An Institutional Experience

Abstract

Introduction: One of the underreported complications of clipping of unruptured aneurysm is chronic subdural hematoma/hygroma (CSDH). It can cause sudden deterioration and might need emergency evacuation. Recently, very few papers have studied its incidence and predisposing factors. We are reporting our institutional experience of it along with the study of its risk factors and possible pathogenesis. Methodology: Totally 91 postoperative patients of unruptured aneurysms were retrospectively analyzed. Totally 21 patients had CSDH who were operated. In rest seventy patients, there was no CSDH. Results: Male sex, old age, anticoagulant use, presence of pneumocephalus and dead space were significantly associated with occurrence of CSDH, whereas arachnoidoplasty significantly protected against it. There was no significant relation of CSDH with Gorei-san use. Conclusions: We recommend arachnoidoplasty should be carried out in all patients of clipping of unruptured aneurysm. Male patients or/and patients with dead space with pneumocephalus must be given extra attention like avoiding any dead space in postoperative period, doing arachnoidoplasty and regular follow up till 1st year.

Keywords: Arachnoidoplasty, chronic subdural hematoma/hygroma, clipping, pneumocephalus, unruptured aneurysm

Introduction

In the last few years, unruptured intracranial aneurysms have been detected more frequently due to good screening methods.[1] The numbers of patients who are undergoing clipping of unruptured aneurysms, have increased significantly. The surgery is easy due to fewer adhesions, no brain edema and good plane of dissection. The morbidity and mortality are also less due to well-preserved patients. One of the side effects, which have been, especially reported in clipping of unruptured aneurysm, is chronic subdural hematoma/hygroma (CSDH).[2,3] It can cause morbidity and mortality both. Very few studies are there, which have reported its incidence, risk factors and methods to prevent it in clipped unruptured aneurysm.[2-5] We did an institutional study to find its incidence, predisposing risk factors, methods which can prevent it.

Methodology

This was a retrospective comparative study, which included operated patients between 2014 and 2015. Patients of unruptured aneurysms treated by clipping at our institute, of any age/sex, who were followed up for 1 year, were enrolled in this study after informed consent. We took approval from the Institutional Ethical Committee. Totally 100 patients were operated, of which, 91 patients were enrolled who met all inclusion criteria. Patient’s details were taken from our data collection center. Two groups were formed – patients who developed symptomatic CSDH for which they were operated (Group I) and patients who either developed small asymptomatic CSDH, managed conservatively or no CSDH at all (Group II). The demographic profile of patients such as age/sex, aneurysm site, use of Kampo medicine (Gorei-san which is suspected to prevent CSDH), anticoagulant use (pre- or post-operatively), the presence of pneumocephalus, arachnoidoplasty were analyzed and compared in all patients of both groups. Tables 1 and 2 show the details of Group I and II, respectively. The Bar Chart 1 depicts the...
distribution (percentage wise) of all analyzed factors in both groups.

**Illustrative case (Group I)**

First [3rd patient in Table 1 and Figure 1a-d] A female aged 76 years, operated for the left middle cerebral artery (MCA) aneurysm [Figure 1a] without arachnoidoplasty. She was given Gorei-san in the postoperative period and was on tablet aspirin for long time. She was having complaint of headache in the postoperative period. Computed tomography (CT) [Figure 1c] head was done, which detected large left hemispheric CSDH. She underwent burr hole evacuation under sedation, after informed consent. Gorei-san was given after evacuation and follow up CT head [Figure 1d] revealed no recurrence. She recovered without deficit.

Second [9th patient in Table 1 and Figure 2a-d] A gentleman, aged 71 years, operated for anterior communicating (ACOM) aneurysm [Figure 2d] clipping by inter hemispheric approach, without arachnoidoplasty. He received Gorei-san in postoperative period, And no aspirin. He presented with headache, forgetfulness, and urinary incontinence in follow up after 5 months. CT head [Figure 2b] was suggestive of large left side CSDH. It was evacuated by burr hole under sedation after informed consent.
consent. Gorei-san was given in postoperative period. Postoperative CT head [Figure 2c] was clear.

Illustrative case (Group II)

First [23rd patient in Table 2 and Figure 3a-c] A lady, aged 61 years, operated for right MCA aneurysm [Figure 3a] clipping without arachnoidoplasty. She was given Gorei-san in postoperative period. There was no history of aspirin intake. Postoperative CT head [Figure 3b] showed dead space with pneumocephalus. There were no symptoms. Follow up CT head at 1 month showed no dead space/ pneumocephalus and patient was asymptomatic.

Second [7th patient in Table 2 and Figure 4a-c] A lady, 80 years, operated for the right internal carotid artery-posterior communicating (ICA) [Figure 4a] junction aneurysm clipping without arachnoidoplasty. She was given Gorei-san in postoperative period. There was no history of aspirin intake. Postoperative CT head showed no dead space with pneumocephalus [Figure 4b]. There were no symptoms. In follow up after 6 months, patient was asymptomatic and CT head [Figure 4c] was normal.

Results

The incidence of symptomatic CSDH was 23% in our study. The mean postoperative duration of the occurrence of CSDH was 2.62 months in Group I. The age was calculated as mean age and compared by using two-sample independent t-test. There was significant difference \( P = 0.015 \) between Group I (mean age = 69.48 ± 6.35 years) and Group II (mean age = 64.66 ± 11.32 years). Group I had higher age group patients.

Rest of the data were quantitative data, which was compared by using Chi-square/Fisher/Mantel–Haenszel Chi-square/Yates corrected Chi-square test to know \( P \) value \((P < 0.05 \) significant\). Odds ratio (OR) was calculated to know the association between factors. We used OpenEpi, version 3 software (Emory University, Atlanta, Georgia) to do statistical analysis. The male patients were significantly more common in Group I (11/21, 52.4%) than the Group II (10/70, 14.3%). The use of anticoagulants (pre- or post-operative) was significantly \((P = 0.044)\) associated with CSDH formation (Group I – 3/21 and Group II – 2/70). The occurrence of dead space with pneumocephalus was significantly \((P = 0.00001)\) more common in Group I (19/21, 90.5%) than Group II (27/70, 38.6%). Use of Kampo medicine (Gorei-san) did not significantly reduce the CSDH (Group I – 17/21 and Group II – 48/70). The arachnoidoplasty (after clipping) was associated with significant \((P = 0.019)\) reduction in CSDH formation (Group I – 4/21 and Group II – 31/70). Table 3 shows final results of both groups along with \( P \) value and OR.

Discussion

According to various studies, the incidence of CSDH in unruptured aneurysms clipping is between 2% and 20%.[2-6] In our study, the incidence was 23%, which was almost similar to previous studies that considered both hematoma and hygroma. The findings were confirmed.

Various studies have shown that higher age group patients are more prone to develop CSDH.[2-5] In this study, CSDH was significantly more common in older age group.

According to Kanat et al. study, male sex is more prone to develop CSDH due to more cerebral atrophy.[7] In females, the estrogen has a protective action on capillaries, which is absent in males.[2] In case of unruptured aneurysm clipping also, studies have confirmed this finding.[2,4] We also found the same observation.
Table 2: Clinical/demographic/intraoperative/radiological profile of Group II

| Age | Gender | Location       | Goreisan | Plasty | Deadspace | Aspirin |
|-----|--------|----------------|----------|--------|-----------|---------|
| 67  | Female | Left ICA-Oph   | No       | No     | Yes       | No      |
| 74  | Female | ACOM           | No       | No     | Yes       | No      |
| 71  | Male   | Left-ICA       | No       | No     | Yes       | No      |
| 69  | Female | DACA           | No       | No     | No        | No      |
| 78  | Female | Right ICA-PCOM | Yes      | Yes    | Yes       | Yes     |
| 80  | Female | ACOM           | Yes      | No     | No        | No      |
| 80  | Female | Right-ICA-PCOM | Yes      | No     | No        | No      |
| 76  | Female | ACOM           | Yes      | No     | No        | No      |
| 82  | Female | ACOM right-MCA left-MCA | Yes | Yes | No | No |
| 73  | Female | ACOM           | Yes      | Yes    | No        | No      |
| 67  | Female | Right-ICA-PCOM | Yes      | Yes    | No        | No      |
| 76  | Female | Right-MCA      | Yes      | No     | Yes       | No      |
| 68  | Male   | BA-left SCA right-MCA | Yes | No | Yes | No |
| 65  | Female | Left ICA-ACH   | Yes      | Yes    | No        | No      |
| 64  | Female | ICA            | Yes      | No     | No        | No      |
| 77  | Male   | Right MCA      | Yes      | Yes    | No        | No      |
| 67  | Male   | ACOM           | Yes      | No     | Yes       | No      |
| 49  | Female | Left MCA       | Yes      | No     | No        | No      |
| 61  | Female | Left ICA-PC    | No       | No     | Yes       | No      |
| 65  | Female | ACOM           | Yes      | No     | Yes       | No      |
| 71  | Female | Left ICA-PC    | Yes      | Yes    | Yes       | No      |
| 64  | Female | Left MCA       | Yes      | No     | No        | No      |
| 61  | Female | Right MCA      | Yes      | No     | Yes       | No      |
| 42  | Female | Left MCA       | Yes      | Yes    | Yes       | No      |
| 53  | Female | Left MCA       | Yes      | No     | Yes       | No      |
| 39  | Female | Right ICA Oph  | No       | No     | Yes       | No      |
| 66  | Male   | Left MCA       | Yes      | Yes    | No        | No      |
| 61  | Female | Left ICA       | Yes      | Yes    | No        | No      |
| 47  | Female | Left MCA       | Yes      | Yes    | No        | No      |
| 36  | Female | Left ICA       | Yes      | Yes    | Yes       | No      |
| 63  | Female | Left ICA-PC    | Yes      | Yes    | Yes       | No      |
| 56  | Female | Left ICA       | Yes      | Yes    | No        | No      |
| 47  | Female | Left ICA       | Yes      | No     | Yes       | No      |
| 73  | Female | Right MCA      | Yes      | No     | No        | No      |
| 57  | Female | Left ICA Oph   | Yes      | Yes    | No        | No      |
| 73  | Female | Left ICA-PC    | Yes      | Yes    | Yes       | No      |
| 80  | Male   | Left MCA       | Yes      | No     | Yes       | No      |
| 64  | Female | Left ICA       | Yes      | No     | Yes       | No      |
| 75  | Female | Left ICA-ACH   | Yes      | Yes    | No        | No      |
| 78  | Female | Right MCA      | No       | No     | Yes       | No      |
| 67  | Female | Right MCA      | Yes      | Yes    | No        | No      |
| 48  | Female | Right MCA      | Yes      | No     | No        | No      |
| 63  | Female | Right ICA-ACH  | Yes      | Yes    | No        | No      |
| 54  | Female | BA top         | No       | No     | No        | No      |
| 77  | Male   | Left MCA       | Yes      | No     | No        | No      |
| 61  | Male   | BA top and ACOM | Yes     | No     | Yes       | No      |
| 71  | Female | Right ICA-PC   | Yes      | Yes    | No        | No      |
| 69  | Female | Right MCA      | Yes      | Yes    | Yes       | No      |
| 76  | Male   | ACOM           | Yes      | Yes    | No        | No      |
| 59  | Female | Right MCA      | Yes      | Yes    | Yes       | No      |
| 44  | Female | Right MCA      | Yes      | No     | No        | No      |
| 36  | Female | Right ICA Oph  | Yes      | No     | Yes       | No      |
| 62  | Female | Right MCA      | Yes      | Yes    | No        | No      |
| 55  | Female | Left ICA-PC    | Yes      | Yes    | No        | No      |

Contd...
The aneurysms located in depth, for example, ACOM artery or ICA, are more common to develop CSDH formation than MCA aneurysm clipping. Lee et al. gave the explanation that the more cisternal dissection and hence, more cerebrospinal fluid (CSF) loss in the case of depth aneurysms (anterior cerebral artery [ACA] and ICA) than surface aneurysms (MCA) might be the cause of increased CSDH formation. In our study, MCA aneurysm was the most common in both groups and there was no statistical significant difference in aneurysm distribution. The possible reason could be much more common incidence of MCA aneurysm in our aneurysmal patients.

Kampo medicine, which includes Gorei-san, is a Japanese herbal medicine that has been used to treat CSDH formation and recurrence. Various studies on the use of Kampo medicine in CSDH occurrence and recurrence have showed both promising and nonpromising results. The possible mechanism of prevention of CSDH is via inhibitory effect on aquaporin-4. Gorei-san ingredients like poria, polypus, Atractylodes, lanceae rhizoma inhibit aquaporin-4 and thus decrease subdural collection.

Table 2: Contd...

| Age | Gender | Location | Gorei-san | Plasty | Deadspace | Aspirin |
|-----|--------|----------|-----------|--------|-----------|---------|
| 72  | Female | Left VA PICA | Yes | No | No | No |
| 73  | Female | Left MCA | Yes | Yes | No | No |
| 58  | Female | Left ICA | Yes | Yes | No | No |
| 78  | Female | Right MCA | Yes | No | No | No |
| 47  | Female | Right MCA | Yes | Yes | No | No |
| 56  | Male | Left ICA ACH | Yes | Yes | No | No |
| 75  | Female | Left MCA | Yes | Yes | No | No |
| 59  | Female | Left MCA | No | No | No | No |
| 76  | Female | Right MCA | No | No | No | No |
| 65  | Female | Left ICA-PC | No | No | No | No |
| 64  | Female | Right MCA | No | No | No | No |
| 79  | Female | Right MCA | No | No | Yes | No |
| 68  | Female | Left ICA Oph | No | No | Yes | No |
| 67  | Female | Right VA-PICA | Yes | Yes | No | No |
| 68  | Female | Right MCA | Yes | No | No | No |
| 64  | Female | Left ICA | No | No | No | No |

ICA – Internal carotid artery; PC – Posterior communicating artery; Oph – Ophthalmic segment; MCA – Middle cerebral artery; ACOM – Anterior communicating artery; ACH – Anterior choroidal artery; VA – Vertebral artery, BA – Basilar artery; DACA – Distal anterior cerebral artery; PICA – Posterior inferior cerebellar artery; SCA – Superior cerebellar artery; PCOM – Posterior communicating artery

Table 3: Data analysis of all factors and P value in both groups

| Factors | Group I (%) | Group II (%) | P   | OR  |
|---------|-------------|--------------|-----|-----|
| Mean age (years) | 69.5 | 64.66 | <0.015 | -  |
| Male:Female | 11:10 | 10:60 | <0.0004 | 6.6 |
| Gorei-san use | 17/21 | 48/70 | >0.143 | 0.5865 |
| Anticoagulant | 3/21 | 2/70 | >0.044 | 5.667 |
| Dead space | 19/21 | 27/70 | <0.00001 | 15.13 |
| Arachnoidoplasty | 4/21 | 31/70 | <0.019 | 0.296 |

Aneurysm location

| Total aneurysms | 21 | 75 |
| ACOM | 5 (23.8) | 9 (12) |
| ICA (PCOM, ACH, Oph, bifurcation, cavernous) | 3 (14.3) | 27 (36) |
| Total depth aneurysms (ICA + ACOM complex) | 8 (38.1) | 36 (48) | 0.218 | 0.667 |
| MCA | 13 (61.9) | 33 (44) | 0.079 | 2.068 |
| BA | 0 | 3 (4) |
| VA | 0 | 2 (2.7) |
| SCA | 0 | 1 (1.3) |
| Multiple | 0 | 3 |

ACOM – Anterior communicating artery; ICA – Internal carotid artery; PCOM – Posterior communicating artery; ACH – Anterior choroidal artery; Oph – Ophthalmic; MCA – Middle cerebral artery; BA – Basilar artery; VA – Vertebral artery; SCA – Superior cerebellar artery; OR – Odds ratio

The aneurysms located in depth, for example, ACOM artery or ICA, are more common to develop CSDH formation than MCA aneurysm clipping. Lee et al. gave the explanation that the more cisternal dissection and hence, more cerebrospinal fluid (CSF) loss in the case of depth aneurysms (anterior cerebral artery [ACA] and ICA) than surface aneurysms (MCA) might be the cause of increased CSDH formation. In our study, MCA aneurysm was the most common in both groups and there was no statistical significant difference in aneurysm distribution. The possible reason could be much more common incidence of MCA aneurysm in our aneurysmal patients.
The possible mechanism is prevention of CSF leak in subdural space by repairing torn arachnoid. However, the presence of pneumocephalus has not been studied by any searched study on PubMed. We found postoperative dead space and pneumocephalus (CT brain) in all patients, who developed postoperative CSDH. The finding was very significantly \( (P < 0.0001) \) associated with the occurrence of CSDH. The possible hypothesis could be the empty space and air. Postsurgery, arachnoid is torn and it leads to direct contact of brain cortex and CSF with subdural space. The air has almost no pressure and brain is injured due to retraction/manipulation. It leads to continuous oozing of capillaries and CSF in empty subdural space. It might not happen if arachnoid remains intact and fluid like saline is filled, to remove air. However in absence of protective factors, this leaked fluid and CSF, full of inflammatory cells and cytokines, lead to CSDH formation. As this is only a possible hypothesis, it needs to be confirmed by further studies. Yagi \textit{et al.} have proposed that arachnoid tear causing CSF leak in subdural space and then subdural fluid collection.\[14\]

The use of anticoagulants leading to CSDH has been very well established.\[13\] In our study, use of anticoagulants (aspirin) was significantly associated with occurrence of CSDH. The role of arachnoidoplasty in prevention of CSDH is recently been documented by a few studies.\[14,15\] The possible mechanism is prevention of CSF leak in subdural space by repairing torn arachnoid.\[14,15\] It is usually carried out by using fibrin glue. Lee \textit{et al.} study showed that there was no statistically significant reduction in CSDH formation after doing it. They gave the reason that it might be due to spontaneous dissolution of glue over time and then leak again. In our study, we found that the arachnoidoplasty significantly reduced CSDH in postclipping patients. Other than prevention of CSF leak, we think that it also acts through reducing the subdural space by increasing CSF + brain volume covered by arachnoid.

Our study has a few limitations also. It was a retrospective, nonrandomized study. Our patient number is 91, which is lesser than the other reports.

Conclusions

It can be concluded that incidence of CSDH formation is quite high in postoperative patients of unruptured aneurysm clipped patients. To reduce its occurrence, we should do arachnoidoplasty and avoid postoperative pneumocephalus/dead space by filling subdural space with saline. The male sex, patients using anticoagulants and depth aneurysms (ACA/ICA) must be strictly followed up with CT brain, after taking necessary precautions to prevent CSDH formation. Role of Kampo medicine is still not clear and it should be confirmed by a large scale prospective randomize study.

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Conflicts of interest

There are no conflicts of interest.

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