

SUBARACHNOID HEMORRHAGE: UNUSUAL SITUATIONS LEADING TO SAH AND UNDERLYING PRINCIPLES OF PHYSICS BEHIND ITS COMPLICATIONS

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ABSTRACT

Importance: Multiple authors have identified the most unusual novel associations as precipitant factors of subarachnoid hemorrhage and the knowledge of these and pathogenesis in background is necessary to suspect and therefore timely diagnose subarachnoid bleed and understand the mechanism of its subsequent complications. **Objective:** We herein describe unusual causes of subarachnoid bleed reported in various case reports with a comprehensive but elaborative review describing underlying pathogenesis and physiological mechanisms behind these precipitants and complications. **Evidence Review:** We sorted unusual causes of subarachnoid hemorrhage from literature review. By conducting meticulous scrutinization on search engines like Pubmed®, Medline®, Medline Plus®, PubMed Central®, MedNets®, Medbioworld®, Journal Watch® and Pakmedinet®; we found many novel associations using the key words: “Hemorrhagic stroke; subarachnoid hemorrhage; unusual precipitants; novel causes; pathogenesis; physical principles; aneurysms”. **Findings:** Novel associations of subarachnoid bleed include coagulopathies, lumbar puncture, degenerative vascular diseases, herpes encephalitis, sexual intercourse, bee sting, Conn’s syndrome and likewise many others. The basis of pathogenesis and its complications lies in understanding the complexity of relationship between the dynamics of intracranial pressure, volume and flow. **Conclusions and Relevance:** Understanding the physiology of exchange of force between different intracranial contents is the key to learn the mechanics of complicated brain injuries in SAH. Identifying the most unusual novel associations as precipitant factors of subarachnoid hemorrhage and the knowledge of these and the pathogenesis behind complications is necessary to suspect and therefore timely diagnose subarachnoid bleed. It may also help generate newer ideas for management in SAH.

INTRODUCTION

Among stroke subtypes of hemorrhagic nature, subarachnoid bleed contributes a significant number of cases. It is a serious but potentially treatable cause of neurological morbidity and mortality. Common etiological associations include intracranial arterial aneurysms, head injuries and arteriovenous malformations. Of these, aneurysms stand on the top in frequency.^{1,2} While many of these aneurysmal bleeds are spontaneous, many authors have described the most novel of associations as precipitants behind the rupture. The mechanism of autoregulation of central nervous system is unique in its self as being immune to a wide range of volume-pressure changes but of course, is bound by the rules of physics at one stage or another.^{3,4,5,6,7} The knowledge of these physical dynamics is the key to understand the pathogenesis of brain injury in different types of cranial insults, particularly vascular and the subsequent results of complications. By this review, we aim to describe unusual causes of subarachnoid hemorrhage (SAH)

with a comprehensive but elaborative review of its pathogenesis to understand the physiology behind these precipitants. We further explain the principles of physics lying behind the consequences of complications following SAH. This will help researchers better correlate the precipitants with dynamics of intracranial vascular system and thus innovate newer ideas for better management of subarachnoid hemorrhage.

REVIEW

An unusual case: [SAH with sneeze]⁸

We share one of our recent experiences with a patient; a 55 years old farmer who presented to our stroke unit with 2 days history of sudden onset, severe, generalized headache following forceful sneeze. A consultation with local general practitioner revealed normal blood pressure (120/80 mm Hg) and pulse (86/min, regular) but right sided weakness on the day of event almost instantaneously followed by neck ache,

vomiting and numbness and weakness of right half of body. Neither did he lose consciousness nor had fits or fever but had been irritable and aggressive since then. Clinical examination revealed supple neck with right sided pyramidal weakness and motor aphasia. 8His

Computed Tomography (CT) scan brain showed subarachnoid hemorrhage extending along the falx cerebri posteriorly and towards right duly reported by radiologist. Cerebrospinal fluid (CSF) examination confirmed the presence of xanthochromia suggestive of

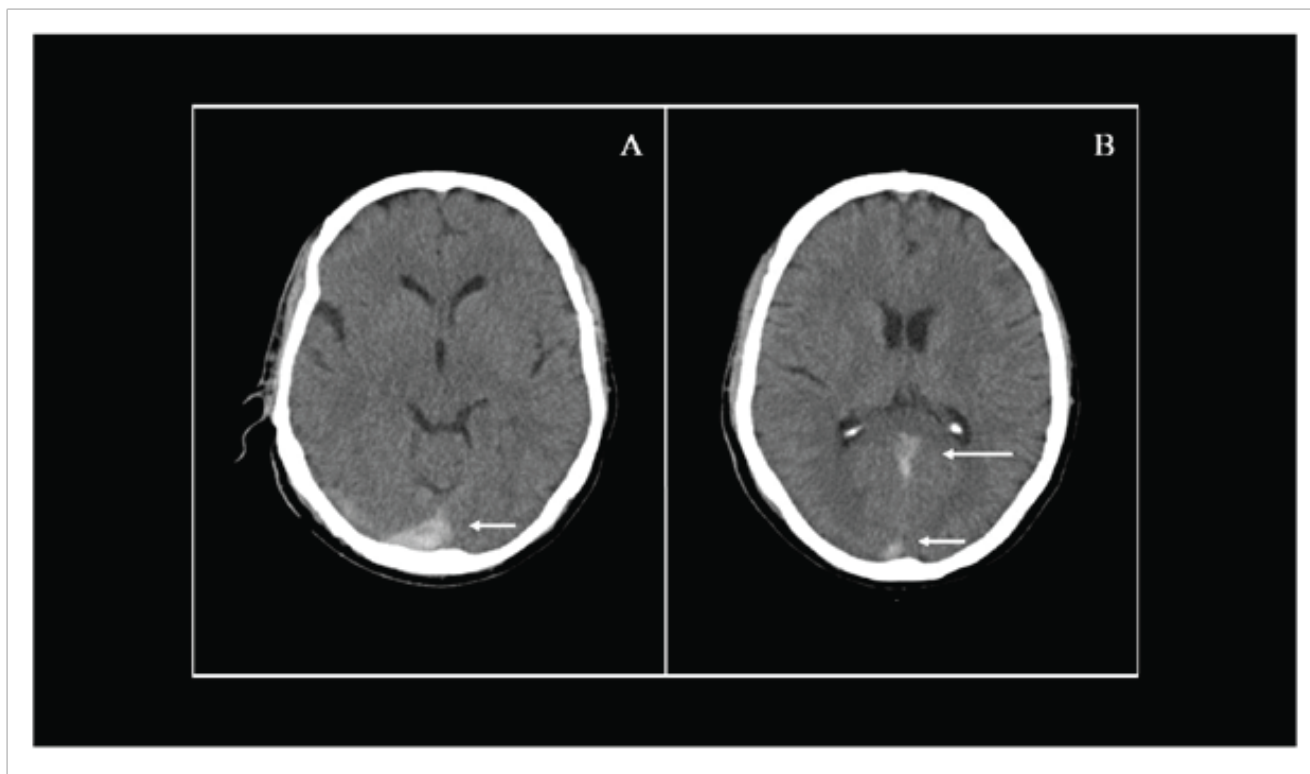


Figure 1: CT scan brain showing subarachnoid hemorrhage. A: hyperdensity involving the posterior most portion of falx cerebri and extending to right (white arrow); B: hyperdensity extending along falx cerebri posteriorly (white arrow long) and marginally to the right (white arrow short).⁸

subarachnoid hemorrhage. CT Angiography (CTA) revealed aneurysm of posterior communicating artery. The patient was managed conservatively using analgesics, antiemetics, nimodipine and follow-up rehabilitation program as he did not consent for neurosurgical intervention. The patient made an uneventful recovery with complete resolution of neurological deficit.⁸

Novel associations

In the light of above, we sorted unusual causes of subarachnoid hemorrhage from literature review. By conducting meticulous scrutinization on search engines like Pubmed®, Medline®, Medline Plus®, PubMed Central®, MedNets®, Medbioworld®, Journal Watch® and Pakmedinet®; we found many novel associations. These included associations with coagulopathies (either pharmacologically-induced or resulting from systemic diseases), lumbar puncture for diagnostic or anesthesiological purposes, traumatic

injuries, aortic coarctation, degenerative vascular diseases, herpes encephalitis, aneurysmal rupture following sexual intercourse, venous hypertension, cortical venous thrombosis, bee sting, epidural blood patch, takayasu arteritis, brucella meningitis, cranial arterial dissections, contrast agent neurotoxicity, Wegner's granulomatosis, dengue fever, polyarteritis nodosa, moyamoya and Conn's syndrome. Cases secondary to cough or sneeze have rarely been reported and one presenting at our unit is perhaps the only few of the internationally reported cases. In all of the above including its complications, the most plausible explanation is described by the volume-pressure relationship either within the vascular system or between the brain parenchyma, CSF and intracranial space as suggested by the Monro-Kellie doctrine hypothesis.^{8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29}

Intracranial volume–pressure and flow relationships: Simple principles of physics The dynamics of fluid flow through a tube is described by Poiseuille's law, i-e-,

$$Q = \frac{\pi(P_i - P_o)r^4}{8\eta l}$$

Where Q = flow, $P_i - P_o$ = pressure gradient from the inlet (i) of the tube to the outlet (o), r = radius of the tube, l = length of the tube, η = viscosity of the fluid The velocity (v) and flow (Q) are related to one another by the cross-sectional area (A) of the tube:

$$v = \frac{Q}{A}$$

Similarly, in fluid mechanics, hydraulic resistance, R, may be defined as the ratio of the pressure drop, $P_i - P_o$, to flow, Q; i-e-,

$$R = \frac{P_i - P_o}{Q} = \frac{8\eta l}{r^4}$$

The physics of fluid flow through rigid tubes provides a basis for understanding the flow of blood through blood vessels, even though the blood vessels are not rigid tubules (i.e., they are distensible) and blood is not a simple homogeneous fluid. Changes in vascular resistance occur when the caliber of vessels changes. The most important factor that leads to a change in vessel caliber is contraction of the circular smooth muscle cells in the vessel wall. Changes in internal pressure also alter the caliber of blood vessels and therefore alter the resistance to blood flow through these vessels. Blood vessels are elastic tubes. Hence, the greater the transmural pressure (i.e., the difference between internal and external pressure) across the wall of a vessel, the greater the caliber of the vessel and the less its hydraulic resistance.^{30, 31, 32, 33, 34} This explains why the relation between volume and pressure within the cranium is non-linear. The dynamics within an aneurismal structure i-e-, an arterial configuration, can be understood by acknowledging the existence of these similar principles within the human body. Fig^{2, 3}

Off-balance proportion of force and resistance and SAH

The described precipitants of SAH either cause weakening of the wall of artery/ aneurysm or primarily affect the pressure-volume curve almost instantaneously such that the normal autoregulatory forces get short of time to accommodate to such rapid physical changes. For example, of the precipitants reported by various authors; degenerative vascular diseases, herpes encephalitis, venous hypertension and takayasu arteritis

might result into SAH via following the former while lumbar puncture, sexual intercourse, cough and sneeze might do so via latter.^{8, 9, 10, 14, 16, 17, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43} It is the off-balance of these natural forces that causes a breach in the integrity of arterial wall and seepage of blood. Fig⁴

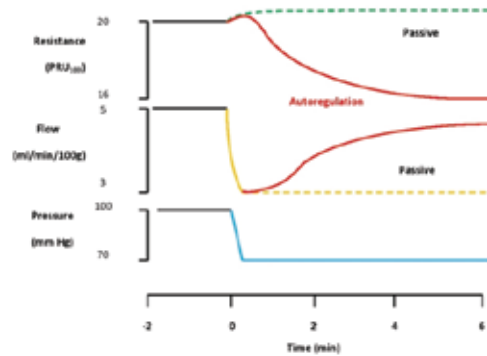


Figure 2: Intracranial volume-pressure relationship and physiological autoregulation changes with flow, resistance and pressure changes

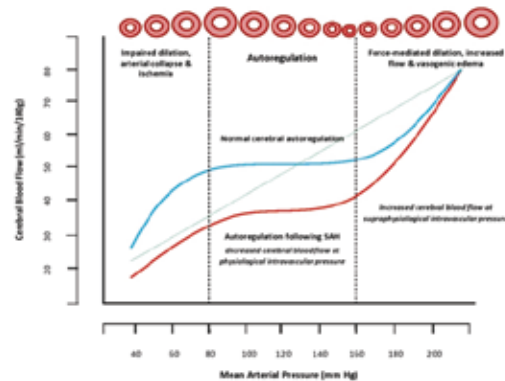


Figure 3: Intracranial cerebral blood flow and autoregulation

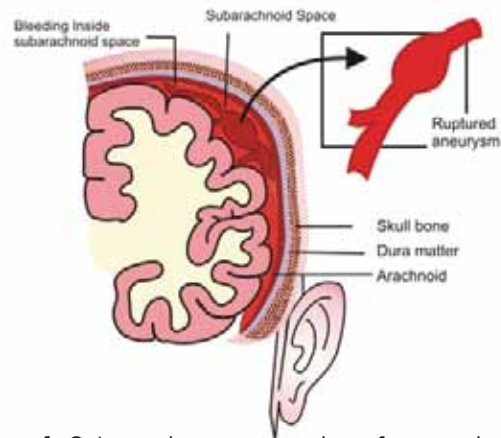


Figure 4: Schematic representation of anatomical relations in subarachnoid hemorrhage depicting the relationship of location of aneurysm in reference to leptomeninges, subarachnoid space and brain parenchyma

Complications in SAH: A basic principle of neurophysiology

The Monro-Kellie hypothesis states that the sum of intracranial volumes of blood, brain, CSF and other components (primary tumours, abscesses, hematoma, secondaries, tuberculomas) is constant. Skull is considered as a confined, enclosed and inelastic reservoir filled with the most fragile but vital organ systems. An increase in the volume of any one of the intracranial contents must be offset by a decrease in one or more of the others or be associated with a rise in intracranial pressure (ICP). Intracranial blood (especially in the venous compartment) and CSF are the two components whose volume can adapt most easily to accommodate an increase in the volume of intracranial contents. The relationship of elasticity and compliance provides an index of compensatory reserve and contents of cranium do not allow any foreign object to interfere beyond this narrow window of compensatory expansion. Once these compensatory mechanisms get exhausted, further increases in volume results in large rises in ICP. ^{4, 5, 6, 7, 34, 35, 36, 37, 38}

Intracranial pressure and compensatory brain shifts.

The cranial vault is divided into compartments by the dural reflections of the falx cerebri and tentorium cerebelli. Raised ICP frequently results in pressure gradients between compartments and a shift of brain structures between these compartments. Many of the clinical counterparts of raised ICP are the consequence of such shifts rather than the absolute level of ICP. The margin of permissible compromise is still very small and any alien pressure jeopardizes the functional capacity nearly always and the life of patient at times. Fig² Brain shifts may be supratentorial or infratentorial. ^{5, 6, 7, 34, 35}

Supratentorial:

Uncal (transtentorial), Central, Cingulate (subfalcine), Transcalvarial

Infratentorial:

Upward (Cerebellar/ transtentorial), Tonsillar (Downward cerebellar)

It is pertinent to mention that brain shifts (like lateral transtentorial herniation without a rise in ICP with temporal lobe haematomas) may not always lead to raised ICP and it is therefore important not to place uncritical reliance on ICP levels in the management of such patients. ^{1, 2, 3, 5, 6, 7, 34, 35, 36, 37}

Intracranial blood pressure and cerebral blood flow mechanics

ICP and arterial blood pressure interact to affect cerebral blood flow, particularly in circumstances where cerebrovascular autoregulation has been impaired. Under normal circumstances, cerebral blood flow is maintained constant over a range of cerebral perfusion pressures by cerebrovascular autoregulation while maintaining a specific narrow range of mean arterial pressure (MAP). If autoregulation gets impaired, changes in blood pressure or ICP can have direct effects on cerebral blood flow. Even if it remains intact, changes in ICP and blood pressure may alter intracranial blood volume as a result of dilatation or constriction of cerebral blood vessels while volume-pressure changes and brain shifts are taking place. This in turn influences ICP. Fig 3 Subsequently, vitals centers in the brain and brainstem get compromised putting the functional capacity of patient at ultimate risk and death if not physiologically or therapeutically controlled. ^{1, 2, 4, 5, 6, 7, 34, 35, 36, 37, 38}

Intricate reciprocity of raised intracranial pressure with SAH

The combination of headache, papilloedema, and vomiting is generally considered indicative of raised ICP, although there is no consistent relation between the severity of symptoms and the degree of hypertension. Pressure headaches are often described as throbbing or bursting and are exacerbated by any factors that further increase ICP such as coughing, sneezing, recumbency or exertion. ^{6, 7, 35, 36, 37, 38, 39} Classically the headache of raised ICP is worse in the morning. This has been attributed to a rise in ICP during the night as a consequence of recumbency, a rise in PCO₂ during sleep caused by respiratory depression and probably a decrease in CSF absorption. Papilloedema is a reliable sign of raised ICP but can require several days of raised pressure to develop. Fundal haemorrhages can develop in response to acute and severe rises in ICP as in subarachnoid haemorrhage. Longstanding raised ICP however may fail to cause papilloedema if the subarachnoid sleeve around the optic nerve does not communicate with the subarachnoid space. Vomiting tends to be a late feature, usually occurs after waking, and frequently accompanies morning headache. ^{7, 35, 36, 37} A progressive deterioration in conscious level usually accompanies rising ICP almost in a linear fashion and is probably a consequence of caudal displacement of the diencephalon and midbrain. Other signs often seen in association with raised ICP such as pupillary dilatation, bilateral ptosis, impaired upgaze, extension to pain and

respiratory irregularity, are related to tentorial or tonsillar herniation rather than the absolute level of ICP. Changes in blood pressure, pulse, and respiratory pattern are usually late signs of raised ICP in clinical practice. These signs are related to brain stem distortion or ischaemia.^{2, 5, 6, 7, 35, 36, 37, 38, 39, 40, 41}

Molecular intrigues of cerebral injury in SAH

Despite intense research efforts in the field, current knowledge about the understanding of the molecular intrigues in post-SAH brain injury is very limited. A number of studies have recently indicated that apoptosis may be a major player in the pathogenesis of secondary brain injury after SAH. Apoptosis is the term given to programmed cell death, which has been widely connected to a number of intracranial pathologies including stroke, Alzheimer's disease and SAH. Experimental data suggest that apoptotic cascades occur very early after the initial insult and may be related directly to physiologic sequel commonly associated with SAH. Identification of these cascades presents a number of potential therapeutic opportunities that may ameliorate secondary brain injury after SAH in near future.

CONCLUSION

Subarachnoid hemorrhage is a serious but potentially treatable cause of neurological morbidity. Understanding the physiology of exchange of force between different intracranial contents is the key to learn the mechanics of complicated brain injuries in SAH. Identifying the most unusual novel associations as precipitant factors of subarachnoid hemorrhage and the knowledge of these and the pathogenesis behind complications is necessary to suspect and therefore timely diagnose subarachnoid bleed. It may also help generate newer ideas for management in SAH.

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