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Neurogenic Pulmonary Edema in Aneurysmal Subarachnoid Hemorrhage

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Abstract

Neurogenic pulmonary edema (NPE) is observed in cerebral injuries and has an impact on treatment results, being a predictor of fatal prognosis. In this study we retrospectively reviewed medical records of 250 consecutive patients with aneurysmal subarachnoid hemorrhage (SAH) for the frequency and treatment results of NPE. The following factors were taken under consideration: clinical status, aneurysm location, presence of NPE, intracranial pressure (ICP), and mortality. All patients had plain- and angio-computer tomography performed. NPE developed most frequently in case of the aneurysm located in the anterior communicating artery. The patients with grades I-III of SAH, according to the World Federation of Neurosurgeons staging, were immediately operated on, while those with poor grades IV and V had only an ICP sensor's implantation procedure performed. A hundred and eighty five patients (74.4 %) were admitted with grades I to III and 32 patients (12.8 %) were with grade IV and V each. NPE was not observed in SAH patients with grade I to III, but it developed in nine patients with grade IV and 11 patients with grade V. Of the 20 patients with NPE, 19 died. Of the 44 poor grade patients (grades IV-V) without NPE, 20 died. All poor grade patients had elevated ICP in a range of 24-56 mmHg. The patients with NPE had a greater ICP than those without NPE. Gender and age had no influence on the occurrence of NPE. We conclude that the development of neurogenic pulmonary edema in SAH patients with poor grades is a fatal prognostic as it about doubles the death rate to almost hundred percent.

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Keywords
Cerebral injury • Intracranial aneurysm • Intracranial pressure • Mortality • Pulmonary edema • Subarachnoid hemorrhage

1 Introduction

Neurogenic pulmonary edema (NPE) is a life threatening complication of central nervous system injuries (Mrozek et al. 2015; Davison et al. 2012; Maramattom et al. 2006). It develops mainly in cerebral injury, but may also constitute a sequela of spinal cord compression (Sedy et al. 2015). The most important role in NPE development plays increased intracranial pressure (Mrozek et al. 2015; Vespa and Bleck 2004). Intracranial hypertension activates the sympathetic nervous system, which affects the cardio-pulmonary system *via* release of catecholamines, leading eventually to NPE (Chen et al. 2014; Inamasu et al. 2012; Friedman et al. 2003). NPE can develop within minutes to hours after injury, but it can also present delayed forms that develop 12–24 h after cerebral injury (Piazza et al. 2011; Kahn et al. 2006). Aneurysmal subarachnoid hemorrhage (SAH) is one of the most common cause of NPE. The development of NPE is usually associated with poor grade patients, and the incidence of NPE in aneurysmal SAH ranges from 2 to 30 % (Mrozek et al. 2015; Veeravagu et al. 2014; Sato et al. 2012; Piazza et al. 2011; Wartenberg et al. 2006). In the present study we analyzed the occurrence of NPE in patients with aneurysmal subarachnoid hemorrhage and the influence of NPE on the results of treatment.

2 Methods

The study was accepted by the Ethics Board for Human Research of the Kazimierz Pulaski University of Technology and Humanities in Radom, Poland. We retrospectively analyzed the files of 250 patients admitted to neurosurgical wards with a diagnosis of aneurysmal SAH. Only were the patients admitted directly after SAH, with CT and angio-CT performed on admission, included into the study. The patients with large intracerebral hematomas, requiring prompt evacuation, were excluded from the analysis. The clinical condition on admission was assessed according to the modified WFNS grading scale (Sano et al. 2015; Rosen and Macdonald 2004). The patients with grades I-III were surgically treated within the first 3 days after admission. Poor grade patients underwent only the implantation of an intracranial pressure measurement device. All patients had chest X-ray performed on admission, which was repeated when pulmonary disturbances appeared. NPE was diagnosed on the basis of clinical criteria such as the auscultation of crackles and the presence of pink tracheal exudate, and radiographic criteria such as a sharp delineation of pulmonary markings, blurring or haziness of the perivascular outlines, and the loss of demarcation of hilar shadows. The patients with a suspicion of choking or with a history of a previous serious pulmonary disease were excluded from the analysis.

There were 140 men and 110 women, 25–69 years old, included into the analysis. One hundred and eighty six (74 %) of them were in I-III grade in WFNS scale, 32 (13 %) were in grade IV, and another 32 (13 %) in grade V. All 186 patients admitted in grade I to III were treated surgically by one of the authors of this article (ZK) within the first three days. Sixty four poor grade patients had only the implantation of an intracranial pressure (ICP) measurement device for continuous ICP monitoring. Poor grade patients who had improved were also surgically treated between the 8th and 20th day after aneurysmal SAH. The patients were treated microsurgically, no endovascular treatment was employed (Sandström et al. 2013).

Categorical data are presented as the number of patients. Numerical data of the intracranial

pressure are presented as means ± SD and their differences are compared with a *t*-test. A p-value of less than 0.05 defined statistical significance.

3 Results

None of the 186 patients admitted in grade I-III developed NPE. All these patients were operated on within 72 h; 90 % of them within the first 24 h after admission. Seven patients (3.8 %) died after surgery due to a cerebral vasospasm. For comparison, 39 (60.9 %) of the 64 poor grade patients died. NPE was diagnosed in 20 (31.3 %) of the poor grade patients, which makes 8.0 % of all 250 patients analyzed in this study. Clinical and radiological symptoms of NPE appeared in up to 12 h after admission. Of the 20 patients with NPE 19 died, all within the first seven days after aneurysmal SAH. The NPE patients had higher ICP values (mean 45.0 ± 7.2 mmHg) than the patients without this pulmonary complication (mean 26.0 ± 4.2 mmHg); the difference between the two groups was significant ($p < 0.001$). In general, the higher the ICP the more cases of NPE were noted (Table 1). Of the 44 poor grade patients who did not develop NPE, 17 (38.6 %) died within the first week. All the remaining 27 patients in this group, who survived the first week, were operated on 10 to 21 days after aneurysmal SAH and three of them died after surgery.

The most frequent location of an aneurysm was the middle cerebral artery (36.0 %), followed by the internal carotid artery (31.5 %), and the anterior communicating artery (29.0)%. Eight patients had a different aneurysm location, four in the anterior cerebral artery and another four at the tip of the basilar artery. NPE developed in 13 (59.1 %) of the 22 poor grade patients with the anterior communicating artery aneurysms, in two (50.0 %) with the basilar artery aneurysms, and in five (12.8 %) of the 39 patients with another location of aneurysms. Thus, NPE developed most frequently in SAH resulting from a rupture of the anterior communicating artery aneurysm. Table 2 delineates the location of aneurysms in relation to clinical grading. We failed to substantiate the presence of an association between the development of NPE and gender or age of patients.

4 Discussion

Neurogenic pulmonary edema is the most common extracerebral complication of subarachnoid hemorrhage and its development is a predictor of bad treatment outcome (Mrozek et al. 2015; Davison et al. 2012; Maramattom et al. 2006). NPE usually develops during the first 12–24 h after aneurysmal SAH, mainly in poor grade patients (Veeravagu et al. 2014; Piazza et al. 2011; Wartenberg et al. 2006). The present findings are in line with the reports outlined above, as we did not notice NPE in any of better-grade patients. Of the poor-grade patients, grade IV and V, NPE developed in 31.3 % of patients within several hours after brain hemorrhagic injury. NPE developed in patients with significantly increased ICP, above 30 mmHg, irrespective of patient gender or age. Aneurysmal SAH produces a massive sympathetic nervous system activation which enhances catecholamine concentration in extracerebral tissues. Except for the effects of catecholamines on the endothelium, which provoke cerebral vasospasm and

Table 1 Intracranial pressure (ICP) and the development of neurogenic pulmonary edema (NPE) in poor-grade patients

ICP (mmHg)	<21	21–30	31–40	41–50	>50	
Number of poor grade patient						Total
Grade IV	0	19	4 (2)	3 (2)	6 (5)	32 (9)
Grade V	0	15	6 (3)	4 (3)	7 (5)	32 (11)
Total	0	34	10 (5)	7 (5)	13 (10)	64 (20)

The number of patients with NPE in parenthesis

Table 2 Location of aneurysms in relation to clinical grading

Patient's grading according to modified WFNS scale	I–III	IV	V	Total
Aneurysm location				
ACoA	51	10 (6)	12 (7)	73 (13)
MCA	66	11 (1)	13 (2)	90 (3)
ICA	64	10 (1)	5 (1)	79 (2)
ACA	4	0	0	4
BA	1	1 (1)	2 (1)	4 (2)
Total	186	32 (9)	32	250 (20)

The number of patients with neurogenic pulmonary edema (NPE) in parenthesis
ACoA anterior communicating artery, *MCA* middle cerebral artery, *ICA* internal carotid artery, *ACA* anterior cerebral artery, *BA* basilar artery

consequently a secondary ischemic cerebral injury, NPE increases the formation of toxic cytokines, resulting in pulmonary edema or myocardial myocytolysis (Chen et al. 2014; Cinotti et al. 2014; Fontes et al. 2003). Lung dysfunction can also be a result of disturbed hypothalamo-pituitary adrenal axis (Davison et al. 2012; Inamasu et al. 2012; Friedman et al. 2003). In the present study, NPE appeared mainly in patients with the anterior communicating artery aneurysms. The lesion location nearby the hypothalamus and pituitary gland, and a direct irritation of these structures by hemorrhage can play an important role in the NPE development (Kahn et al. 2006). It seems, however, that increased intracranial pressure plays the most essential role in the occurrence of NPE (Mrozek et al. 2015; Sato et al. 2012; Piazza et al. 2011; Ochiai et al. 2001). Pulmonary disturbance, leading notably to decreased oxygen delivery to tissues, causes hypoxic brain injury that amplifies intracranial pressure increase. The vicious cycle created leads to a worsening of symptoms of brainstem insufficiency and is conducive to fatal treatment results. The present findings show that NPE develops in the first 12 h after brain hemorrhagic injury and almost all patients with NPE die in the first week after the injury.

5 Conclusions

Neurogenic pulmonary edema developed in 8.0 % of patients with aneurysmal SAH. In patients in clinical grades 1–3, pulmonary edema was unobserved. Pulmonary edema appeared explicitly in poor grade patients, grade IV and V, with the prevalence of 31.3 % (20 out of 64 patients). Patients with neurogenic pulmonary edema had a significantly worse result of treatment outcome, only 1 in 20 survived, which makes up a 5 % survival rate, while from the 44 poor grade patients who did not develop pulmonary edema mortality rate amounted to 45.5 % (20 patients died). The main predictors of neurogenic pulmonary edema after aneurysmal SAH are poor grade of the patient, enhanced intracranial pressure, and a location of the aneurysm in the anterior communicating artery.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

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