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ORIGINAL COMMUNICATION

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Cognitive and emotional consequences of perimesencephalic subarachnoid hemorrhage

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Abstract Little is known about the long-term cognitive-functional outcome of patients with perimesencephalic subarachnoid haemorrhage (PM SAH). We investigated the neurological, cognitive and emotional consequences of perimesencephalic subarachnoid haemorrhage in eighteen PM SAH patients admitted between November 1990 and July 1997 to the Neurology/Neurosurgery services of a University Hospital. The follow-up study consisted of a face-to-face interview, a neurological examination, an headache questionnaire, a neuropsychological evaluation (Mini-Mental State and a complementary battery to assess specific cognitive domains), the Hamilton Depression Rating Scale (HDRS) and the Blessed Dementia Scale. Thirteen patients performed below the 10th percentile in at least one cognitive domain. Six patients scored more than 12 points on the HDRS. Mini-Mental State and HDRS scores were moderately correlated (r= 0.55). Only three patients left their previous occupation. Minor cognitive deficits and high scores on a depression scale were frequent findings in this cohort of PM SAH patients. Reassurance and treatment of depressive symptoms could be important to improve the long-term outcome of PM SAH patients.

Key Words Subarachnoid haemorrhage · Perimesencephalic haemorrhage · Cognition · Depression

Introduction

Perimesencephalic subarachnoid haemorrhage (PM SAH) accounts for 10% of all Subarachnoid Haemorrhages (SAH) [21]. In PM SAH bleeding is located around the mesencephalon, acute prognosis is excellent, there is no risk of rebleeding [21, 22, 26] and the quality of life does not seem to be reduced [5]. However, in long-term follow-up [6], some PM SAH patients felt unwell, complained of a variety of headaches and experienced depressive symptoms or failed to reassume their previous activities and jobs.

Because there is insufficient information concerning the cognitive and emotional consequences of PM SAH, we investigated neurological complaints, cognitive and emotional functions in a cohort of PM SAH.

Patients and methods

Patients

From a prospective registry of all SAH patients admitted to Santa Maria Hospital Neurology/Neurosurgery services we selected those discharged between 1990 and 1997 with a diagnosis of PM SAH. These patients fulfilled the following criteria: 1) CT scans showing the centre of the haemorrhage located in front of the brainstem, mainly in the interpeduncular cistern, with or without extension to the ambient, chiasmatic or horizontal part of the Sylvian cisterns, no intraventricular blood except what could be accounted for sedimentation effects and no extension to the interhemispheric fissure [21, 22]; 2) CT scanning performed within 72 hours of the first clinical symptoms; 3) no detectable aneurysm on four-vessel angiography. Between November 1996 and July 1997 these patients received a letter inviting them to come to our institution for a neurological and neuropsychological evaluation.

Methods

Demographic and clinical information concerning the acute phase of PM SAH including complications during hospital stay (rebleeding, vasospasm, hydrocephalus, delayed intracerebral ischaemia) were retrieved from the data encoded in the registry. A neurological examination was performed and a face-to-face interview was conducted to obtain information concerning current professional status and any illness leading to hospital admission or disability. All patients, except one who requested to be observed in her village, were evaluated at our institution by the same neurologists (P. C., J. F.) and the same psychologist (S. M.) who was blind to all clinical data.

Neuropsychological evaluation included the Mini-Mental State [9] (MMS) and a complementary battery as described in Table 1 [7, 8, 11, 13, 19, 25, 28, 29]. Cognitive domains assessed were attention, orientation, verbal fluency, visual-motor initiative, abstract reasoning, verbal and visual memory, visuo-spatial and constructional abilities, associative learning and calculation. From the NINDS-AIREN proposed cognitive instruments for the evaluation of vascular dementia [20] we selected those that had been previously validated in the Portuguese population [11, 13]. MMS normative values took into consideration educational levels: severe impairment was considered when scores were below 16, for people who never went to school; below 23, for patients who had at least one year of school; below 28, for those who had more than 11 years of education [10]. Concerning the complementary neuropsychological battery, patients were classified as having impairment in a particular test when they scored below the 10^{th} percentile of the normal controls for their age and education level range. The Hamilton Depression Rating Scale (HDRS) [14] was used to assess the severity of depressive symptoms. A HDRS score of _13 was used as the cut-off between normal and depressed subjects [2]. We used the Blessed Dementia Scale (BDS) [3] to evaluate the impact of cognitive impairment on daily-life activities. Functional impairment was considered when patients scored > 4 on that scale. Dementia was defined according to the NINDS-AIREN criteria for Vascular Dementia [20] and to DSM-IV criteria for dementia not otherwise specified [1].

Results

Twenty-two patients fulfilled the criteria for PM SAH. Concerning acute complications, three patients had hydrocephalus on their admission CT but none required ventricular shunting or lumbar punctures. One patient had vasospasm during angiography, but none rebleed or had delayed cerebral ischaemia. One patient was lost for follow-up, one died of an unrelated cause, and two refused to come to the follow-up visit. When contacted by telephone they denied any neurological or neuropsychological complaints. Therefore, we examined eighteen patients (nine women and nine men), with ages ranging from 34 to 71 years (mean, 54 years; sd = 8.4). Time lapse between PM SAH and evaluation varied from 3 months (two patients) to 6 years (mean 39 months; sd = 24.6). None of these patients reported neurological, cognitive or psychiatric disturbances prior to PM SAH.

Neuropsychological evaluation

Table 2 shows the clinical and socio-demographic characteristics of the PM SAH patients. Table 3 shows the results

Table 1 Cognitive domains evaluated and tests used

Tests	Cognitive domains
Mini-Mental State [9, 13]	Screening test used to evaluate general cognitive function (orientation, verbal memory, calculation, language, writing and visuo-spatial abilities).
Letter Cancellation [11]	Simple test of vigilance consisting of a series of random letters among which a target letter appears with greater than a random frequency. Patients are asked to mark the single-target letter.
Word Fluency Test [11]	Test used to assess verbal fluency: patients are asked to recall names of food products, during 1 minute.
Alternating Sequences [7]: visual, motor	Tests used to assess frontal lobe dysfunction. Visual form: patients are asked to reproduce a stimulus figure and then to continue the alternating sequence. Motor form: we used a reciprocal co-ordination test. Patient place both hands on the desk, one with the fingers extended palm down, other in a fist, then are asked to rapidly alternate the position of both hands.
Proverb Interpretation [11]	Three well known proverbs used to assess abstract reasoning.
Raven's Progressive Matrices [19]	Used to assess non-verbal intelligence.
Wechsler Memory Scale [28]	Test to assess verbal and visual memory. Paired associate is also used to assess new learning ability.
Clock drawing [25]	Used to assess visual neglect and constructional abilities. In the clock drawing patient are asked to draw a picture of a clock with the numbers and hands on it.
WAIS Block Designs Subtest [29]	
Simple arithmetic operations [8]	Simple operations of addition, subtraction and multiplication used to assess calculation function.
Temporal, spatial and personal orientation test [11]	A simple test with questions concerning temporal, spatial and personal orientation.
WAIS Information subtest modified [11]	Used to assess remote memory.

of the neuropsychological evaluation. Five patients had no cognitive impairment and scored less than 13 on the HDRS. Only one of these patients, a 59-year-old farmer, had not returned to her previous activity and was retired. Thirteen (72 %) patients showed impairment in at least one cognitive domain. Six (33 %) of them scored ≥ 13 on the HDRS. Only one patient, who has cognitive impairment had left her previous activity. One patient was classified as severely impaired as she scored 16 in the MMS and demonstrated impairment in four cognitive domains: attention, executive functions (verbal fluency and motor initiative), memory and orientation. Her HDRS score was 24. She did not return to her previous activity as a factory worker. However, according to her husband, she was able to care for herself and her social and occupational behaviour were not impaired. Therefore, she did not fulfil the NINDS-AIREN or DSM IV criteria for dementia.

Visual memory was the most commonly affected cognitive domain as 7 (39 %) patients showed scores below the 10^{th} percentile of normal controls in this test. Abstract reasoning was the second most commonly affected domain (33 % of patients had scores below the 10^{th} percentile). Six (33 %) out of eight patients with memory deficits scored ≥ 13 in the HDRS, contrasting with those who had no cognitive deficits or had impairment in other non-memory cognitive domains (55 %) (Fischer exact test, p = 0001). The correlation between MMS and HDRS scores was moderate (r= 0.55), but there was no significant difference in MMS scores between subjects who scored ≥ 13 (mean=25.3; sd=5) or < 13 (mean=27.6; sd=2.6) on the HDRS (t=1.04; p=0.33; df = 6.4). There was no relation between age, gender or length of follow-up and the intensity of depressive symptoms.

Discussion

In the long follow-up of this sample of PM SAH subjects, no patient rebleed, was physically disabled or demented and only 17 % retired after the PM SAH. Nevertheless 72 % of the patients showed neuropsychological deficits and depressive symptoms were present in 33 % of the patients. Concerning case selection and ascertainment, we utilised a strict definition of PM SAH and excluded patients with PM SAH whose CT was obtained after 72 hours from onset. We could trace all patients who were admitted to our hospital and the large majority came to the follow-up examination. However, the delay between the follow-up and the event was heterogeneous. Because PM SAH has a low incidence and our study was performed in a single institution, we could only collect a small sample. For the neuropsychological evaluation both MMS, as a global mental status measure,and a neuropsycological battery were used to allow a more detailed assessment of memory, attention, orientation, executive functions and constructional ability. More complex tests that assess executive functions could not be used, because there is a lack of normative data for the Portuguese population and because performance on these tests is strongly influenced by education level, which was highly variable in our sample. Quality of life was not

Table 2 Clinical and sociodemographic characteristics of PM SAH patients

Patient no.	Sex	Age (years)	Complications during hospitalization	Years of education	Hunt and Hess score on admission	Length of follow-up (months)	Professional Status
1	M	51	None	4	1	54	Active
2	F	60	None	0	2	62	Active
3	M	55	Hydrocephalus	4	1	58	Active
4	F	55	None	7	1	75	Retired before PM SAH
5	F	58	None	4	3	61	Retired
6	M	44	None	5	2	70	Active
7	M	61	None	2	2	38	Active
8	F	53	Hydrocephalus	4	1	39	Active
9	F	46	None	11	2	20	Active
10	F	50	None	6	2	21	Active
11	M	54	None	4	2	9	Active
12	F	53	None	3	2	50	Retired
13	M	66	Hydrocephalus Vasospasm during angiography	4	2	50	Retired before PM SAH
14	M	34	None	6	2	4	Active
15	F	71	None	4	2	3	Retired before PM SAH
16	F	59	None	0	2	63	Retired
17	M	48	None	4	2	24	Active
18	M	51	None	11	2	3	Active

Table 3 Neuropsychological results of PM SAH patients (*WMS* Wechsler Memory Scale, *WAIS* Wechsler Adult Intelligence Scale, *RPM* Raven's Progressive Matrices, *BDS* Blessed Dementia Scale)

Patient no.	Affected cognitive domains	Percentile	Test used	HDRS	MMS	Dementia Scale
1	Verbal fluency	< 10	Word fluency	11	26	1.5
	Abstract reasoning	< 10	Proverb Interpretation			
2	Calculation	< 10	Arithmetic operations	9	26	5
3	Abstract reasoning	< 10	Proverb interpretation	19	26	4.5
	Immediate memory	< 10	WMS digit span			
4	–	–	–	9	30	2.5
5	Verbal fluency	< 10	Word fluency	17	24	4
	Motor initiative	< 10	Alternating sequences			
	Immediate memory	< 10	WMS digit span			
	Learning ability	< 10	WMS Paired associate			
	Visual memory	< 10	WMS visual memory subtest			
6	Visual memory	< 10	WMS visual memory subtest	16	29	4
	Verbal fluency	< 10	Word fluency			
	Constructional ability	< 10	WAIS block design			
7	Verbal fluency	< 10	Word fluency	3	29	1.5
8	–	–	–	11	30	0
9	Immediate memory	< 10	WMS digit span	14	29	3.5
		< 10	WMS immediate story recall			
	Visual memory	< 10	WMS visual memory subtest			
	Orientation	< 10	Temporal, spatial, personal orientation test			
10	Immediate memory	< 10	WMS digit span	16	28	3.5
	Learning ability	< 10	Paired associate			
	Visual memory	< 10	WMS visual memory subtest			
	Orientation	< 10	Temporal, spatial, personal orientation test			
	Abstract reasoning	< 10	Proverb interpretation and RPM			
11	Abstract reasoning	< 10	Proverb interpretation	9	29	1.5
12	Attention	< 10	Letter cancellation	24	16	4
	Verbal fluency and	< 10	Word fluency			
	Motor initiative	< 10	Alternate sequences			
	Immediate and	< 10	WMS digit span and immediate story recall			
	Remote memory	< 10	WAIS information subtest			
	Learning ability	< 10	WMS Paired associate			
	Visual memory	< 10	WMS visual memory subtest			
	Orientation	< 10	Temporal, spatial, personal orientation test			
13	Immediate memory	< 10	WMS digit span	6	28	0
	Visual memory	< 10	WMS visual memory subtest			
	Abstract reasoning	< 10	Proverb interpretation			
14	–	–	–	5	30	0.5
15	Visual memory	< 10	WMS visual memory subtest	3	26	0
	Motor Initiative	< 10	Alternate sequences			
16	Abstract reasoning	< 10	RPM	10	21	3
17	–	–	–	11	28	3.5
18	–	–	–	8	28	2

evaluated because of lack of normative data in Portugal for subjects under 65 years. Brilstra et al. [5] performed a follow-up study of 25 patients, six months to six years following PM SAH. Quality of life, as measured by the Sickness Impact Profile, was not reduced. However, neuropsychological functions, depressive symptoms and headaches were not evaluated in their study.

Some studies showed similar cognitive deficits in pa-

tients with aneurysmal SAH and patients with SAH of unknown origin [15, 17]. Hutter et al [15] demonstrated a relationship between severity of bleeding and cognitive deficit. These authors reported a"diffuse" cognitive damage pattern in patients with SAH of unknown cause, in contrast with"focal" cognitive deficits in aneurysmal SAH patients. In this study we found cognitive deficits in 72 % of our PM SAH sample. Half of these patients showed impairment in visual memory. The pathophysiology of the subtle neuropsychological deficits that were disclosed in 2/3 of PM SAH patients is probably similar to those found in other forms of non-aneurysmal SAH, i. e. related to the effects of subarachnoid blood [12], except that no detectable vasospasm or infarcts occur and there is a smaller amount of blood in the CSF [24].

In our series, 46 % of cognitive impaired patients, especially those who had memory deficits, had depressive symptoms. Depressive symptoms after PM SAH can be: a) a direct consequence of the brain damage caused by the haemorrhage, and therefore be classified as a mood disorder secondary to PM SAH with depressive features [1]; b) related to persisting symptoms (e. g. headache, mild memory troubles) and difficulty in reassuming previous life style and occupation, fear of a new episode, and in this case, be classified as an adjustment disorder with depressive mood [1]; c) related to psychosocial stress occurring during the follow up or other mechanisms not related to PM SAH or its consequences; d) a reactivation of undiagnosed primary mood disorder, in particular a disthymic one. The design of our study, concerning the variable delay between the acute event and the follow-up, does not allow distinction between these mechanisms. Depression can influence cognitive performance, while in other cases depression appears to be the consequence of cognitive impairment [23]. Some studies have reported a relation between depression and mild memory deficits [18, 27]. However, no significant difference between depressed and non-depressed stroke patients concerning several aspects of memory function was found in another study [4]. Among patients with left-sided stroke, significantly greater cognitive impairment in orientation, language, visuoperceptual and visuoconstructional tasks, executive functions and frontal lobe functions was found in those with major depression [4].

Hutter and Gilsbach [16] found no relation between tests of frontal cognitive functions and depression, but demonstrated a relation between depression and the patients' subjective impact of the perceived deficits. Another study [30] also suggested that the patient's attitude toward a disease has more effect on mood than the severity of the physical disability. This finding may be relevant because none of PM SAH subjects had neurological deficits on the follow-up evaluation. The individual ability to react to a life-threatening event such as SAH could also influence the presence of depression. Brilstra et al. [5] reported no reduction in quality of life in 25 patients with PM SAH using the Sickness Impact Profile. They found more psychosocial complains than physical consequences and concluded that the longterm complaints of PM SAH patients might be related to either the haemorrhage or the experience of a sudden illness.

Depressive symptoms were the most frequent finding in this cohort of PM SAH patients. Memory deficits were associated with higher scores in the HDRS. The cognitive impairment present in these patients had no impact on their functional level. Patient reassurance, explaining the benign course of this type of SAH, early resumption of previous activities, recognition and treatment of depression and eventually neuropsychological rehabilitation in the early phase of recovery, are interventions likely to improve the long term outcome of PM SAH patients.

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