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Perioperative management of patients with lung carcinoma and cerebral metastases

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ABSTRACT

Objective: *The present study proposes to present the importance of perioperative therapeutic management in survival prolongation and the quality of life for patients that have undergone surgery for cerebral metastases secondary to pulmonary tumors.*

Method: *During 2001-2009, 40 patients with ages between 43-74 years have been diagnosed in our clinic with pulmonary tumor and cerebral metastases. The patients presented single cerebral lesion (excepting one patient with 2 cerebral metastases) and pulmonary tumor. Intracranial pressure (ICP) was high in all cases. All patients have undergone operation with general anesthesia.*

Results: *For all patients the reduction of ICP and keeping an optimal CPP (cerebral perfusion pressure) was pursued. In 38 cases, general anesthesia was performed with Sevoflurane and opioids (fentanyl, remifentanyl, sufentanyl) and in 2 cases the TIVA (total intravenous anesthesia) technique was used with propofol and remifentanyl. 14 of the patients required intraoperative depletive treatment through administering mannitol 20%. 37 patients (92%) have been discharged with improved neurological condition without showing signs of intracranial hypertension, convulsive seizures and with partially or totally remitted hemiparesis and one patient had worse postoperative neurological status.*

Conclusion: *Pulmonary tumor with cerebral metastases represent an important cause for death rate. To solve secondary cerebral lesions, the perioperative management must include assesment and choosing an anesthesia technique with a proper intraoperative management.*

Key words: cerebral metastases, lung cancer, cerebral edema, surgery

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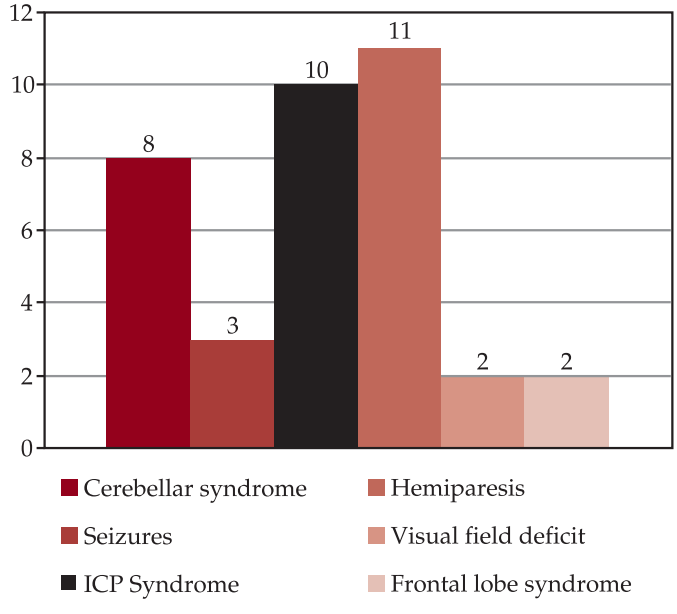
Cerebral metastases represent an important source of both morbidity and death rate for patients with systemic cancer. Cerebral metastases represent the most frequent cerebral tumors for an adult (1). Pulmonary cancer with big cells represents the most frequent type. 87% of the pulmonary cancer is related to smoking. Approximately 20-40% of the cancer patients develop cerebral metastases, the most frequent having a pulmonary starting point. Pulmonary cerebral metastases show high multiplicity incidence (2).

Comparing to other methods of treatment, surgery is capable of rapidly diminishing symptomatology and eliminating the lesions and lowering intracranial pressure (normal values = 10 mmHg).

ICP is determined by the volume of the intracranial components: the cerebral tissue (80%), cerebrospinal fluid (7-10%) and blood component (5-8%) (3). Because the cranium has a precise volume, the increased growth of any intracranial component must be compensated by a decrease of the others (4). The growth in the cerebral tissue's volume might be due to a tumor or to vasogenic edema. The lung tumor represents a high potential for metastasis and it is different in function of the various cellular types. Approximately 60-70% of the patients with lung cancer show metastases (5). The carcinoma with small cells produce the fastest metastasis, being one of the most aggressive and with the highest malignity rate of the histological subtypes. The squamous carcinoma has a slow growth and starts to metastasis later on, and adenocarcinoma starts to metastasis sooner and has an intermediate growth rate. The cerebral metastases appear most frequently in the non small cell carcinoma and in adenocarcinoma (5). ❑



GRAPH 1. Symptoms of patients with brain metastases

DATA AND METHOD

Between 2001-2009, a number of 40 patients (32 men and 8 women) were admitted in the Emergency Clinical Hospital "Bagdasar-Arseni" into the IVth Neurosurgical Department diagnosed with pulmonary tumor and cerebral metastases. All patients have been neurologically, imagistic and clinically evaluated. The respiratory assessment has been performed through the means of a clinical exam, radiological, SPO_2, PaO_2, $PaCO_2$, pH of the blood and ventilation tests. All of the tumors had over 3 cm diameter and showed a mass effect on MRI, therefore surgery was the treatment of choice. ❑

RESULTS

The age of the patients included in the study was between 43 and 74 years of age with an average of 56 years. Among the all 41 tumors 33 (80.48%) were located predominantly supratentorial, and 8 (19.52%), infratentorial (Table 1). From the supratentorial localized lesions, 72.72% were located in the right cerebral hemisphere and only 27.28% in the left hemisphere.

LOCATION	No. patients	Ratio
SUPRATENTORIAL	***33***	***80.48%***
Frontal lobe	11	33.33%
Parietal lobe	13	39.39%
Occipital lobe	3	9.09%
Temporal lobe	6	18.19%
INFRATENTORIAL	***8***	***19.52%***

TABLE 1. Location of brain lesions

A patient presented 2 cerebral tumors (frontal and right temporal), tumors which have been surgically removed in the same operating session. 27.5% of the patients showed hemiparesis, at admission and 25% presented with in

tracranial hypertension signs (Graph 1). 2 patients showed clinical and imagistic signs of obstructive internal hydrocephaly, for which reason a ventriculo-peritoneal shunt was performed. We performed in all patients imaging by chest X-ray, brain CT (N+K) and chest CT.

The pulmonary tumor was diagnosed in 5 patients (12.5%) before the admission in the neurosurgical department and 35 of the patients (87.5%) after the admission.

The final pathological results showed in 24 cases (60%) adenocarcinoma, 6 cases (15%) non defined non-small cell, 4 cases (10%) squamous carcinoma, 3 cases (7.5%) carcinoma

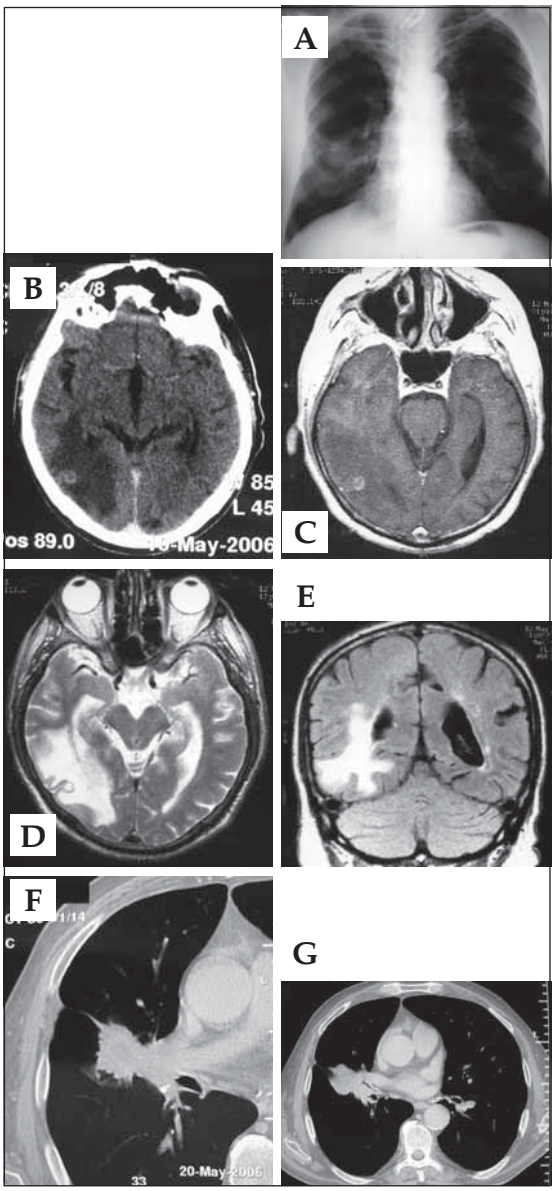
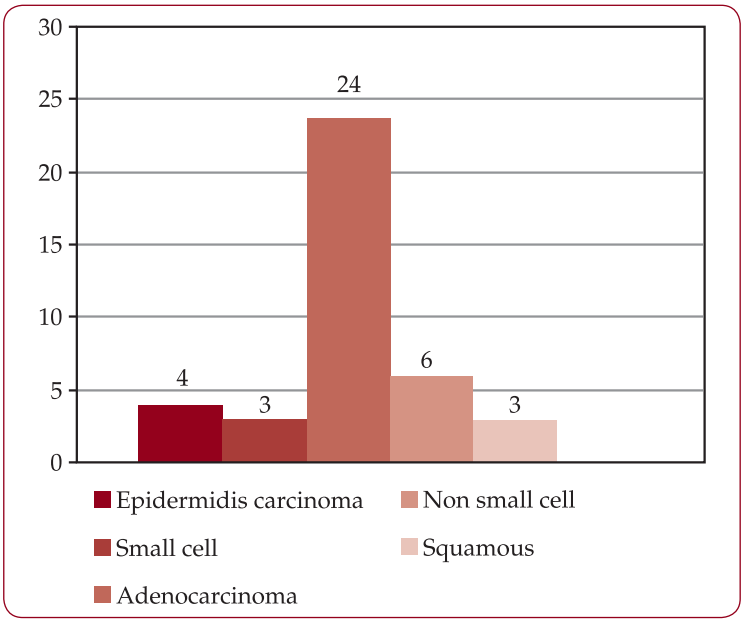


FIGURE 1. Right temporal brain metastasis operated. Lung cancer.
A. Chest X-ray; B. Brain CT; C, D, E. Brain IRM (T1, T2); F,G. chest CT



GRAPH 2. Frequency of histological types of brain metastases

with small cells and 3 cases (7.5%) squamous adenocarcinoma (Graph 2).

7 patients showed, at the moment of hospitalization, associated comorbidities: hypotension, cardiac ischemic disease, cachexia, diabetes, chronic bronchitis, asthma.

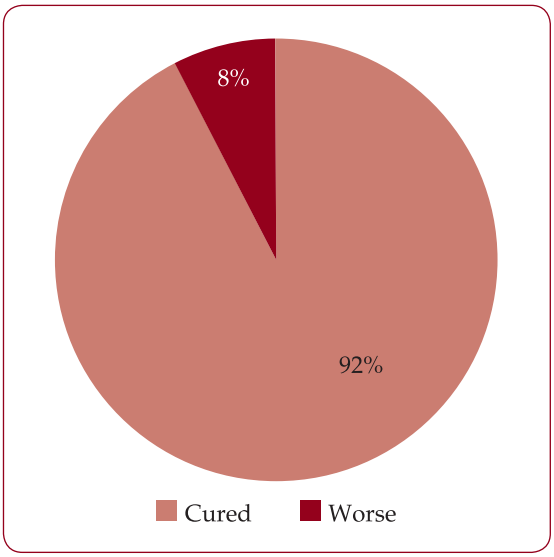
The therapeutic presurgical measures have, first of all, targeted the intracranial hypertension syndrome, steroidal anti-inflammatory drugs being administered (dexamethasone, 8 mg every 12h) with gastric protectors. Osmotic diuretics (mannitol 20%, 0.25-0.5 g/kg of body weight to 6-8 h) and diuretics (furosemide) have been successfully used as a depletive treatment. During the course of hospitalization in the ICU department, the hemodynamic parameters were permanently assessed. The average duration of the preoperative therapy was of 48-72 h. Exception made 2 cases that have presented acute internal hydrocephaly and 5 cases with cerebral edema with the shifting of the median linage; 33 operated patients (82.5%) were in improved neurological condition comparative to the condition preceding the moment of hospitalization.

All the surgical procedures were done with general anesthesia and with monitoring the vital functions. The target was the lowering of the intracranial pressure (ICP), as well as keeping an optimal CPP through maintaining the ventilating parameters to values as PaO_2=80-100 mmHg and $PaCO_2$=30-35mmHg and an inspiratory pressure as low as possible. The cerebral

protection was achieved through the choice of an appropriate anesthesia technique using anesthesia drugs that lower the cerebral metabolism and do not affect the cerebral self-regulation and the reactivity of the cerebral vessels at $PaCO_2$.

In 38 cases, general anesthesia was balanced with sevofluran and opioids (fentanyl, remifentanyl, sufentanyl) using a slight hyperventilation in order to obtain $PaCO_2$ of 30-35 mmHg, and in 2 cases the TIVA technique was used with propofol and remifentanyl. Monitoring the patients was a complex process and included respiratory monitoring (SpO_2, CO_2, repeated EAB, TV, MV, inspiratory pressures), hemodynamic monitoring (EKG, arterial pressure, ventricular rate) temperature, and diuresis. 14 patients required intraoperative depletive treatment through administering mannitol 20%, with doses that varied from 0.25-0.5 g/kgc at 6-8h. Concerning intraoperative fluid management, we administered solutions of NaCl 0.9% and plasma expanders, following to maintain normovolemy and normoosmolarity, in order to avoid cerebral edema. In need, an eritrocitary mass was used. All patients received antibiotics of type cephalosporin (II and III generation) with prophylactic purpose. In order to prevent vomiting and postoperatively shivering, Perfalgan and Zofran were administered. The prophylaxis of profound vessel thrombosis was performed for all the 40 patients with low molecular weight heparin (LMWH). 35 of the patients (87.5%) were postoperatively admitted in the intensive therapy department for monitoring the vital functions, hemodynamic and neurological condition. Following surgical and medical treatment, the 37 patients (92%) were released with a neurological improved condition showing no signs of intracranial hypertension, seizure crises and with partially or totally remitted hemiparesis. Out of the 37 patients surgically cured, 5 were sent to the oncology department and 32 were sent to the thoracic surgical department in order to solve pulmonary neoplasm.

One patient showed neurological postoperatively worsening and 2 patients were discharged at their family's request with agravated condition (Graph 3). ❑



GRAPH 3. Status of patients with brain metastasis

DISCUSSION

In the presented case study, the starting point of the disease in 87.5% of cases was with neurological symptomatology, only 12.5% being initially diagnosed with pulmonary cancer.

Due to the fact that the neurosurgical complication represents a significant vital risk, finding a solution for it, as fast as possible and in optimal conditions, offers the possibility of treating primary pulmonary lesions for prolonging the survival of these patients and improving quality of life.

As it is seen from the results, all the patients presented intracranial hypertension symptomatology and required preoperative therapy in view of undergoing the surgical intervention with reduced risks and good results.

The vasogenic peritumoral edema is usually associated to the cerebral tumor lesions and increases intracranial pressure. Therefore, of great significance in the perioperative management is the treatment of the peritumoral edema that is firstly accomplished with corticosteroids, which represents the basic therapy (6).

The most utilized in this category is dexamethasone, due to its minimal mineralo corticoid effect and a longer division time. The utilized dose in our case study was of 8-16mg/day, depending on the case.

In other references, doses of minimum 4-8 mg/day are indicated. It seems that the corticotherapy leads to the remission of symptomatology and the increase of survival from 4 to 6 weeks, even without surgical intervention (8).

We have observed an improvement of the symptomatology to just a few hours after administering dexamethasone, with maximal effect 24 to 72 hours (7).

Studies show the fact that the increase of the dose strengthens the secondary effects of corticotherapy (glucose intolerance, corticoid myopathy, neuropsychic side effects, peptic ulcer, pulmonary infection, and so forth) without reaching evident additional neurological improvement (8).

Therefore, this dose was administered in an average time of two weeks, with the gradual decrease of 25% at every 3 to 5 days.

A treatment with inhibitors of protonic pump was associated, although some studies consider that the risk of peptic ulcer is very low (9,10).

Twelve percent of the patients showed convulsive seizures at first and have received an anticonvulsant therapy with phenhydan, carbamazepin or phenobarbital. No prophylactic anticonvulsivant therapy was prescribed. The prophylactic therapy for convulsive seizures is not advised due to its drugs interaction with corticoids. The anticonvulsants that are metabolized at hepatic level through the cytochrome P450 enzyme system speeds up the corticosteroid metabolism. This association can lead to the insufficient control of seizures or to the inadequate control of the peritumoral vasogenic edema (11). The same situation also exists with some chemotherapeutic agents.

The anticoagulant therapy for acute venous thromboembolism (VTE) prophylaxis was used in all of the cases starting from day one with a low molecular weight heparin, knowing the fact that VTE is a significant cause for morbidity and death rate for patients with malignant tumors and for those with cerebral tumors, especially in the postoperative period (12,13).

General anesthesia includes: hypnosis, analgesia and muscular relaxation and the abolition of the reactive vegetative symptoms (14). The most anesthetics lower the cerebral metabolism and the blood flow providing of cerebral protection and lowering intracranial pressure. Moderate hyperventilation reduces the cerebral blood flow and the brain volume (3). It is proven that barbiturates offer a certain degree of cerebral protection against ischemia, but there are evidences that a slight hypothermia has also a good cerebral protective effect (15).

When a patient is evaluated with pulmonary neoplasm and cerebral metastasis a special attention must be given to the moment of the installation of cerebral metastasis: synchronous (at the same time with the pulmonary tumor) or anachronous (at a different time in chronological order). Some authors show their pessimism concerning the synchronous cerebral metastases. One retrospective analysis of the 74 patients treated at the University of Pennsylvania showed that the 5 years survival rate was better at patients with anachronous metastases (respectively 18 months and 28.9%) than for patients with synchronous metastases (respectively 9.9 months and 0%) (16).

The development of a cerebral metastasis to a patient with pulmonary cancer determines an unfavorable prognosis. Without any treatment (medical or surgical) the survival rate is no higher than a month (17-19). Corticotherapy raises the survival rate to 2 months (19,20). Applying "whole brain" radiotherapy and steroids improves the survival rate to 3 and 6 months (17-19,21,22). The surgical cure of the single brain metastasis raises the survival rate to a value ranging from 9-14 months (16,23-25). Two random prospective studies, showed the benefit of surgery for single metastases. The patients with single brain metastases were randomly treated by surgery or by "whole brain" radiotherapy. The operated patients had a longer survival rate and a higher quality of life by comparison with those treated by "whole brain" radiotherapy. The benefit of surgery was greater for patients at whom the cancer was not discovered, cerebral metastases was single and the age of the patients was bellow 60 years. ❑

CONCLUSION

The presence of cerebral metastasis in the cases of patients with pulmonary primary tumor represents an important cause of mortality. In order to solve secondary cerebral lesions under conditions of maximum safety, the evaluation and appropriate preoperative training, the right intraoperative and postoperative management, offers these patients the chance of continuing surgical and oncological treatment of the primary lesions under good conditions. All these ensure the prolongation of survival and life improvement. ❑

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