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*Clinical Articles*

# Spontaneous Intracranial Haematomas Caused by Neoplasms

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## Summary

We report about 50 patients with spontaneous intracerebral haematomas (ICH) caused by intracranial neoplasms to assess the underlying histological condition, their presentation on admission, diagnostic work-up, treatment, histological diagnosis, and clinical outcome. These patients were identified in a prospective series of 2041 patients with intracranial neoplasms and 692 patients with spontaneous ICH, which were both consecutively collected over a nine-year-period.

The frequency of ICH in patients with intracranial neoplasms was 2.4%. The frequency of tumour related ICH in the ICH group was 7.2%. The leading cause of tumour related ICH were metastases of extracranial origin (n = 18; 36%), followed by glioblastoma multiforme (n = 15; 30%). Nine patients (18%) had benign primary intracranial neoplasms. On admission 18 patients were somnolent (36%) and 14 patients (28%) were comatose. In 29 cases (58%) ICH was the first clinical sign of neoplastic disease, while in 21 patients (42%) a malignant tumour was already known. We operated on 45 patients (90%), four patients (8%) were not operated on because of poor clinical condition and died, one patient refused surgical treatment. Six patients (12%) died despite surgery.

This series confirms the importance of a proper neuroradiological and clinical work-up of patients with suspected tumour related ICH followed by operative treatment and histological confirmation of the diagnosis. This is supported by the fact that 18% of patients had prognostically favourable intracranial tumours which would not otherwise have been adequately treated.

*Keywords:* Intracranial neoplasms; intracerebral haematoma; haemorrhagic stroke; computerised tomography; outcome.

## Introduction

In pathological and radiological studies the frequency of spontaneous intracerebral haemorrhage (ICH) in intracranial neoplasms ranges from 1.4 to 10% [14, 15, 21, 32] with an average of 2–3% [14, 15, 30]. The frequency of ICH as the initial clinical presentation of intracranial neoplasms has been reported between 9 and 42%. Jellinger *et al.* report a frequency of 3.7% in a synopsis of multiple post mortem examination series [15]. In comparison the frequency of intracranial neoplasms in spontaneous ICH ranges from 0.8 to 7.4%. In general, any type of intracranial neoplasm can cause ICH, however the frequency varies widely among different tumour types [1, 3, 4, 6, 8, 11, 16, 25, 29]. Naturally, fast growing and highly vascularised neoplasms with an irregular and fragile vascular architecture are most frequently associated with ICH [5, 23].

During daily clinical practice it is important to remember that, although rather rarely, sometimes neoplasms can be hidden behind an ICH. This study reports on a consecutive series of 50 patients with spontaneous ICH caused by intracranial neoplasms. Based on this experience we propose our recommendations on optimal diagnosis and treatment.

## Patients and Methods

Over a nine-year period we have prospectively collected a series of 2041 patients with intracranial neoplasms and 692 patients with spontaneous ICH. All patients were consecutively admitted to our department between 1th January 1991 and 31th December 1998. At the same time we collected data on: a. presentation on admission; b. diagnostic work-up; c. treatment; d. histological diagnosis; and e. and clinical outcome on discharge.

## Results

We identified 50 patients with spontaneous ICH caused by intracranial neoplasms in this series excluding those cases with primary or secondary pituitary haemorrhage. There were 26 male and 24 female patients with an age range between 5 months and 82 years (mean age 51.6 years). The overall peak incidence was found in the sixth decade. In female patients

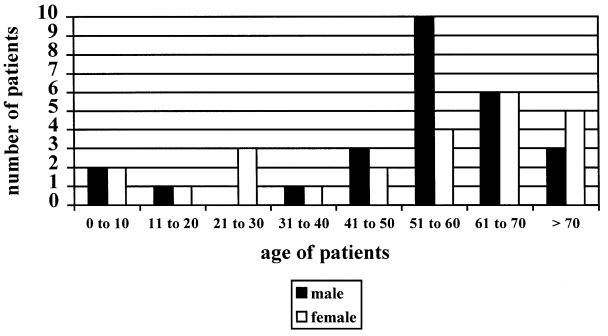



Fig. 1. The distribution of age and gender in 50 patients with tumour-related spontaneous intracerebral haemorrhage.

Table 1. *Neurological Condition on Admission*

| | |
|---|---|
| Normal | 18 |
| Coma | 14 |
| Somnolence | 18 |
| Anisocoria | 12 |
| Cranial nerve dysfunction | 3 |
| Hemiparesis | 31 |

the mean age was slightly higher than in male patients. Figure 1 shows the age distribution in detail.

The frequency of ICH in patients with intracranial neoplasms was 2.5%. The frequency of tumour-related ICH in the ICH group was 7.2%. Among 692 patients with spontaneous ICH 413 (59%) were operated on and haemorrhage was identified as tumour-related in 45 (10.9%) cases. The number of tumour-related ICH in the conservatively treated group of patients remains uncertain. The leading cause were metastases of extracranial origin (n = 18; 36%), followed by glioblastoma multiforme (n = 15; 30%). Nine patients (18%) had benign primary intracranial neoplasms.

During neurological examination on admission we found a decreased level of consciousness in 32 patients (64%), of whom 18 patients (36%) were somnolent and 14 patients (28%) were comatose. Thirty-one patients (62%) were hemiparetic, twelve patients (24%) had a unilateral dilated pupil. Three patients had a sixth cranial nerve palsy (see Table 1).

All patients with a spontaneous ICH received a cranial CT scan on admission. However, we do not routinely perform magnetic resonance imaging (MRI) at that time because of the unstable clinical condition of most patients. There was a suspicion of an underlying intracranial tumour in 25 patients after CT. Cranial MRI was eventually performed in 12 (24%) and digital subtraction angiography (DSA) in 11 (22%) patients in whom a tumour-related ICH was suspected. Among them were 21 patients with known extracranial neoplastic disease. In the remaining 25 cases there was no clear preoperative suspicion of a tumour-related ICH (see Table 2).

Table 2. *Time of Tumour Diagnosis*

| | |
|---|---|
| Known extracranial tumour disease | 21 |
| Suspicion of tumour after CT/DSA | 25 |
| No preoperative suspicion of tumour | 25 |

Thirty-eight (76%) of 50 tumour-related ICH patients had a supratentorial ICH. Twelve patients (24%) had an infratentorial ICH, nine of which were cerebellar, and 3 of which were located in the brainstem. In 13 patients we found multiple haemorrhages, in 11 patients the ICH had penetrated into the ventricular system.

The indication for operative evacuation of haematoma and tumour removal was taken as long as no symptoms of irreversible brainstem damage were present. Open microsurgical haematoma evacuation was performed in 45 patients. In 43 cases the haematoma was removed successfully together with the tumour. An additional external ventricular drain was inserted in 11 patients with intraventricular extravasation of blood. Two patients received external ventricular drainage only. The remaining 5 patients were not operated on; among them was a patient with multiple supra- and infratentorial metastases from histologically confirmed thyroid cancer who refused operative therapy. Four patients presented initially with signs of extensive brainstem damage and there was no indication for operative therapy.

In 18 patients haemorrhage was due to metastases from extracranial primary tumours, including 9 cases with multiple haemorrhage. One patient suffered from systemic leucosis with cerebral manifestation, in another patient we diagnosed a tuberculoma-related ICH. In 30 patients ICH was caused by primary intracranial tumours of different types. Figures 2a-h show several examples of tumour-related ICH. The distinct tumour entities are provided in Table 3.

The further course of treatment was complicated by recurrent haemorrhage in 3 patients. Two of them had disseminated cerebral metastatic disease (malignant melanoma, choriocarcinoma) and developed additional ICH in different sites. One patient with an oligodendroglioma was re-operated on after recurrent bleeding at the site of the original ICH. The functional outcome, assessed by the Karnofsky Index, in relation to the initial state of consciousness is demonstrated

in Fig. 3. The overall in-hospital mortality was 22% (n = 11). 12 patients (24%) were discharged with a Karnofsky score of less than 60. 14 patients (28%) reached a Karnofsky score between 60 and 80, while 13 patients (26%) reached a Karnofsky score of 90 or 100.

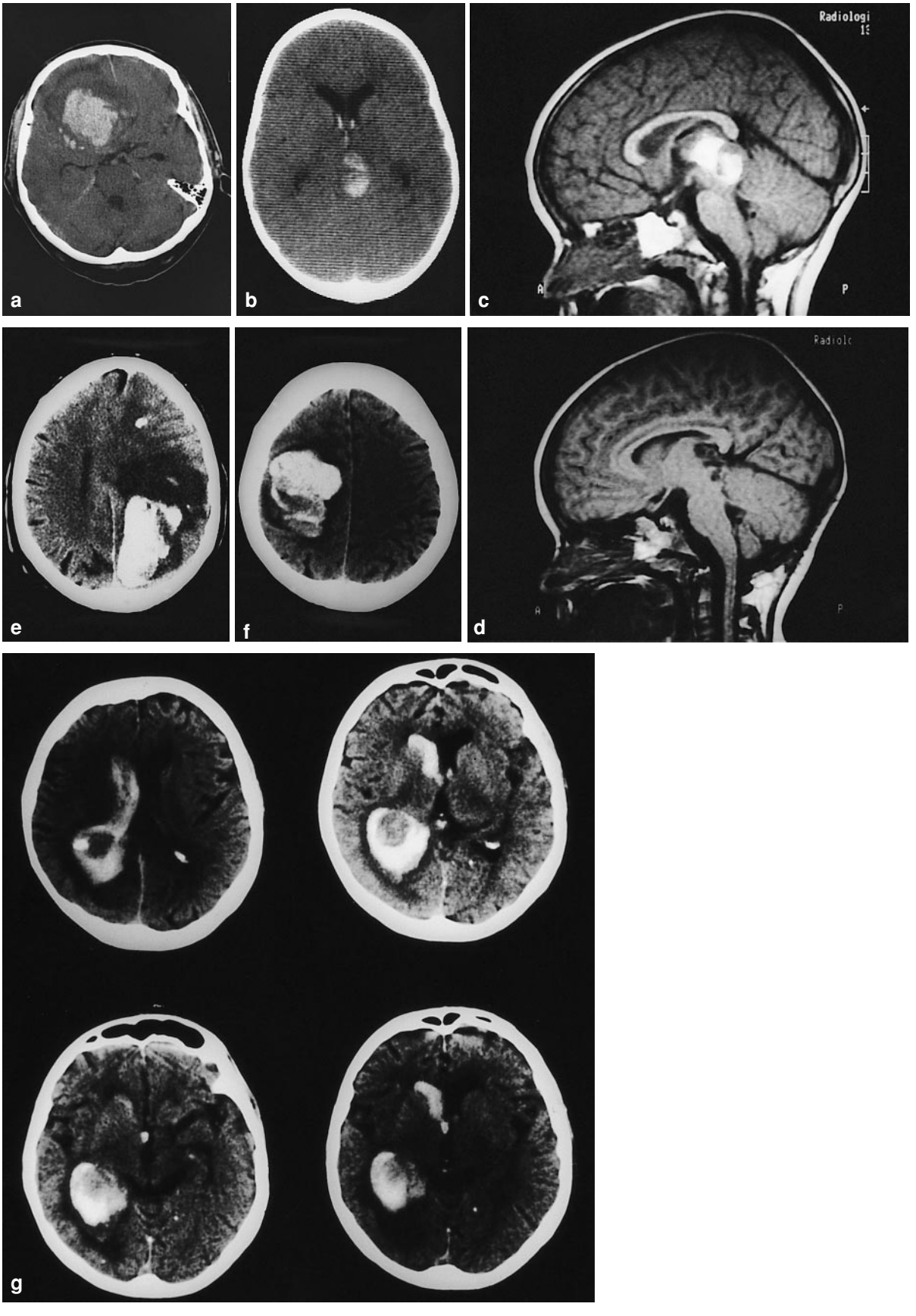
## Discussion

Causes of spontaneous ICH include a number of important differential diagnoses [28], among which intracranial neoplasms are rare with a mean frequency between 2 and 4%, which is somewhat lower than our frequency but stays in the reported range with 7.2% [2, 4, 15, 21, 30, 32]. However, if we took 413 operatively treated and histologically confirmed patients with spontaneous ICH into consideration, a number of 45 surgically treated tumour-related ICH leads to a much higher frequency (10.9%) which clearly exceeds the reported range in the literature. The correct number of tumour-related ICH among conservatively treated patients might be higher than those 5 patients who were not operated upon and remains uncertain. Acute ICH as the initial clinical presentation in cerebral neoplasms ranges between 9 and 42% [30]. In such cases, the clinical presentation may be identical to that of a hypertensive ICH and may possibly lead to an incorrect diagnosis and inadequate treatment. CT is not always able to clearly identify a tumour-related ICH. If such patients are treated conservatively, the correct diagnosis will be delayed or missed, except if a MRI is obtained because of persisting signs and symptoms [9]. In patients who are operated on histological examination will confirm suspicious findings and provide information for treatment planning. Adjacent tissue should also be histologically evaluated on a routine basis because the tumour tissue may be very small. At the same time tumour/ICH removal will lower intracranial pressure possibly leading to a faster and better recovery. Naturally the suspicion of tumour-related ICH is greater in patients with known neoplastic disease. This, however, was the case in only 42% of our patients. In the remaining 58% of patients (n = 29) ICH was the initial lesion of neoplastic disease, among whom there were 9 cases with benign and prognostically favourable primary intracranial tumours.

Tumour-related ICH show distinct features, which should be carefully considered when interpreting ICH on CT. It has been reported that an irregular shape and an atypical location can hint at a tumour-related ICH. A heterogeneous appearance with solid areas of blood, multiple haemorrhage, and a ring-shaped haemorrhage can also point towards that diagnosis [22, 24]. An enhanced peritumoural vascularisation, particularly at its margins may account for that feature as well as the fact that the tumour itself can cause vascular erosions in non-neoplastic tissue at its margins [5]. Zuccarello *et al.* pointed out that neoplasms show areas of both high and low density in the centre surrounded by punctuate haemorrhages in its periphery. They also emphasised the diagnostic relevance of peritumoural oedema [32]. According to Grumme *et al.* such peritumoural oedema is an important feature in the differential diagnosis because it is only rarely seen in the acute phase of spontaneous ICH while it is a very common feature in expanding, space occupying lesions such as tumours [10]. The need for contrast-enhanced scans for the differential diagnosis of tumour-related ICH was addressed by Kazner *et al.*, who have pointed out that administration of contrast agent sometimes shows a tumour which would otherwise be concealed by a blood clot [17]. There should also be a high suspicion for a tumour-related ICH if they are found in an atypical location e.g. subcortical or close to dural membranes such as the falx or the tentorium, if they are located close to major cerebral veins or sinuses, or if they are calcified.

In the pre-magnetic resonance imaging era, Picard *et al.* [26] have stressed that a CT-examination alone might be insufficient in some cases of tumour-related ICH and cerebral angiography should be performed if a tumour is suspected. This was the case in 11 patients in our series in whom the combination of young age, atypical location and lack of hypertension made a tumour-related ICH highly probable after the differential diagnosis of a vascular malformation had been ruled out. MRI is clearly superior to CT scanning for the work-up of patients with acute ICH [28]. However, it is only rarely readily available in patients with acute haemorrhagic stroke and even less so if they are somnolent or comatose.

According to Maiuri *et al.* [24], metastases are the most frequent cause of tumour-related ICH followed by glioblastoma multiforme. Among the metastases malignant melanomas are found most often. Metastases of choriocarcinoma represent a special feature because they directly erode cerebral vessels causing haemorrhage [7, 18]. Because recurrent ICH occurs in all types of tumours, several authors have stressed the importance of complete tumour resection [4, 13, 31].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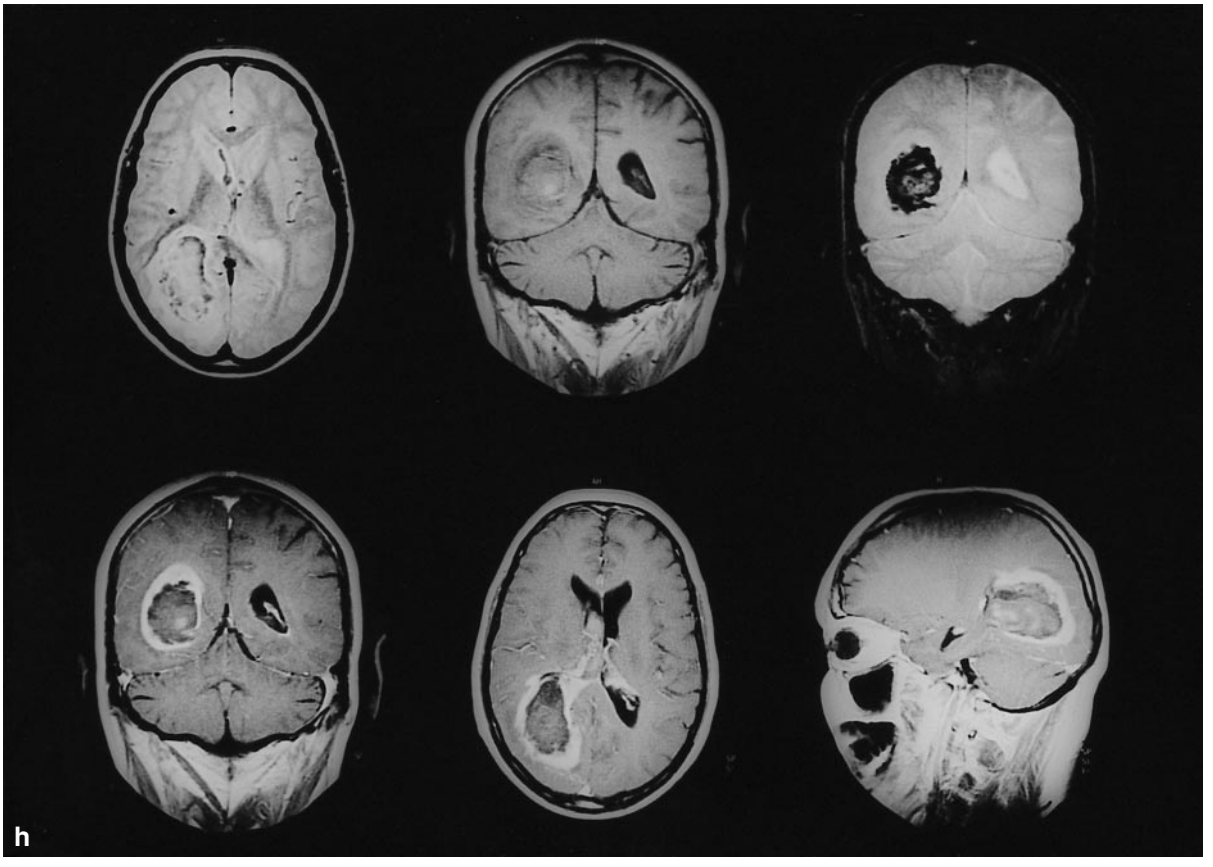


Fig. 2. (a) This is a 54-year-old male patient with a spontaneous intracerebral haemorrhage in the right frontal area. Note the marginal calcifications and perifocal oedema. Histology: Oligodendroglioma WHO II. After removal of this space occupying lesion the patient recovered from a critical condition on admission. He remained disabled requiring special care and assistance. (b) After mild cranial trauma this 3-year-old girl drowned and developed gaze paresis, anisocoria and hemiparesis. The CT-examination of the head showed an atypically located ICH in the area of the left quadrigeminal plate. On digital subtraction angiography we found no vascular abnormalities and managed her conservatively. (c) The same girl was further worked-up with MRI because of focal seizures six months later. In this examination there was evidence for a tumour which was eventually operated on. Histology: Astrocytoma WHO II. (d) The postoperative MRI confirmed complete removal of a low grade astrocytoma. In the further course of the disease ventriculo-peritoneal shunting was necessary and the gaze paresis persisted but no other neurological deficits occured. During a 7 year follow-up period we found no signs of tumour-recurrence. (e) This is a 69-year-old male patient with a solid ICH in the left occipito-temporal area and a smaller frontal lesion, both with extensive perifocal oedema. The histological examination of the operated space occupying occipito-temporal lesion showed a metastasis of a malignant melanoma. The patient remained disabled. (f) In this 67-year-old female patient the large, heterogeneous ICH in the right parietal lobe with perifocal oedema was caused by a leiomyosarcoma metastasis of pulmonary origin. After removal of the lesion she improved from a severely disabled condition and was discharged with a Karnofsky-score of 70. (g) A WHO I meningioma caused heterogeneous ICH projecting to the occipital horn of the right lateral ventricle, extending to the frontal horn and with tamponade of the ventricles. Some blood has passed through the Foramen Monroe invading the frontal horn of the left ventricle. There is perifocal oedema which is slightly accentuated in the occipital region. After surgical removal of tumour and ICH the 82-year-old female patient recovered and was discharged with a Karnofsky-score of 80. (h) This is a 61-year-old male patient with an ICH in the right occipital lobe and penetration into the ventricular system. A tumour-related haemorrhage was considered unlikely. Histology: Glioblastoma multiforme. After an initially stable condition the patient deteriorated rapidly in the course of the disease and died in the hospital

As we had expected, the outcome is worst in patients who are comatose on admission. This applies to both mortality and quality of life. Accordingly, the indication for surgery should be based on a combination of the neurological condition on admission, estimated overall prognosis, and accompanying diseases rather than on age.

## Conclusions

Neoplasms may be hidden behind each case of spontaneous ICH. Primary or secondary tumour-related ICH can be found in any age and among a wide variety of tumours. If there is a suspicion for a tumour-related ICH, additional neuro-imaging such as MRI

Table 3. *Histological Classification of Tumours (n = 50)*

| | |
|---|---|
| *Metastases of primary extracranial tumours* | 18 |
| Malignant melanoma | 8 |
| Metastases of carcinoma | 9 |
| Unknown primary | 3 |
| Bronchial carcinoma | 2 |
| Choriocarcinoma | 1 |
| Thyroid carcinoma | 1 |
| Hypernephroma | 2 |
| Embryonic leiomyosarcoma | 1 |
| *Primary intracranial tumours* | 30 |
| Glioblastoma WHO IV | 15 |
| Astrocytoma WHO III | 4 |
| Meningioma WHO I | 2 |
| Vestibular schwannoma WHO I | 1 |
| Astrocytoma WHO II | 1 |
| Oligodendroglioma WHO II | 2 |
| Ependymoma WHO III | 1 |
| Ependymoma WHO II | 1 |
| Hemangiopericytoma WHO II | 1 |
| Subependymal large cell astrocytoma WHO I | 1 |
| Dysembryoplastic neuroepithelial tumour WHO I | 1 |
| *Systemic disease* | 2 |
| Leucosis | 1 |
| Tuberculoma | 1 |

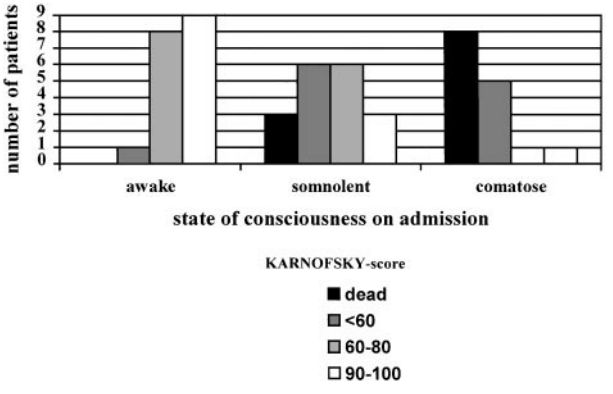


Fig. 3. The functional outcome on discharge assessed by the KARNOFSKY-score in relation to the state of consciousness on admission

or DSA should be performed if available following a thorough neurological examination with complete medical and surgical history-taking. CT features which can cause such suspicion are: atypically located haematoma, multiple haemorrhages, young age, contrast enhancement within the haematoma or in its periphery, and disproportionally large oedema after acute stroke.

We emphasise the importance of haematoma evacuation and complete tumour removal followed by a histological confirmation of diagnosis. This becomes particularly important because 18% of our acute cases of tumour-related ICH were associated with benign and prognostically favourable neoplasms. In addition there is a considerable risk of missing a potentially curable tumour if it is concealed under an ICH in a sensitive area such as the left basal ganglia or the motor cortex or if the patients have surgical risk factors. Furthermore, non-surgical management carries the risk of recurrent haemorrhage and further tumour growth.

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## Comment

The authors undertook a thorough prospective study concerning all the patients referred to the hospital with a spontaneous intracerebral hematoma, caused by an intracranial tumor, in the years 1991 to 1998. As far as I know this is one of the largest clinical studies concerning tumor-based intracranial hematomas. In addition an excellent survey of the literature in this field is presented.

The group of patients with hematomas in tumors is correlated with all the patients which are treated during those years for intracranial tumors and also correlated with the patients who have had a spontaneous intracerebral hematoma without a tumor. Interesting incidence rates are calculated in this way.

An important conclusion is that extensive neuroradiological examinations have to be performed in patients who are suspected of having a hematoma on the basis of a tumor, because in 18% of these cases there is a benign and prognostically favourable process, which deserves radical treatment. The authors did not include MR-findings since logistically it was not possible in their hospital to get an MRI in the acute state. Nevertheless I think MRI is probably the best way to differentiate between hematomas caused by a tumor and hematomas caused by other causes. Therefore the logistics of many departments of neurosurgery have probably to be adapted in such a way that MR-examination is as easily possible in the acute state as is CT-examination.

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