Abstract

We report a case of a 25 year old man presenting with acute headache, vomiting and nuchal rigidity. Computed Tomography (CT) scan and MRI without contrast showed a right ventricular hemorrhage surrounding a mass lesion. The tumor and hematoma were completely removed by neurosurgical transcortical-transventricular approach. Anatomopathological analysis revealed a central neurocytoma. Central neurocytoma seldom present with hemorrhage. We review 16 cases of neurocytoma with hemorrhage. It is important to recognize central neurocytoma as a cause of intraventricular hemorrhage, especially in adolescents and young adults. Outcome is often favorable when the tumor is completely removed. In some patients the clinical course is less favorable and additional treatment such as radiotherapy, radiosurgery or chemotherapy is needed (Metellus et al., 2000 ; Rades et al., 2002).

Case report

A 25 year old man was transferred to our clinic, complaining of acute headache and vomiting for three days. Analgesics did not relieve the pain. Clinical examination showed nuchal rigidity, but there were no focal neurological signs. Blood pressure was 150/90 mm Hg. EEG, X-ray of the sinuses and fundoscopy were normal. Blood analysis showed a sedimentation rate of 23 mm/h and a thrombocytopenia of 100000/mm³, other blood coagulation tests were normal. There was also a chronic hepatitis B infection. CT scan of the brain showed an intraventricular hemorrhage surrounding a small round lesion (Fig. 1). On MRI, performed two days later, there was blood in the lateral ventricles, more prominent on the right side on T1weighted images (T1WI). In the right lateral ventricle a small nodular lesion in relation with the corpus callosum was seen. The mass was isointense to white matter on T1WI and slightly inhomogeneous and hyperintense on T2WI (Fig. 2). The nodule measured 17 mm. There was no enhancement after injection with Gadolinium. No relation with the circle of Willis and no vascular malformation were seen on MR angiographic sequences. MRI of the spine showed no additional masses on T2WI and T1WI.

The blue-grayish tumor mass was completely removed by neurosurgical transcortical-transventricular approach. On histological analysis the
lesion had oligodendroglial-like features and was composed of small, round cells exhibiting minimal atypical features (Fig. 3). No areas of necrosis, no vascular proliferation were evident. There were no mitotic figures and labeling with the nuclear marker Ki-67 disclosed few proliferating cells. The growth pattern was rather diffuse, focally exhibiting a nested pattern, surrounded by small capillaries. The cells were isomorphous and had a minimal, mostly clear cytoplasm with a small, round nucleus having speckled chromatin. The tumor cells were immunoreactive for synaptophysin (Fig. 4). There was no labeling for chromogranin. All these features were compatible with the diagnosis of central neurocytoma. After the operation a control CT scan showed a small subdural collection in the right frontal region. The thrombocytopenia remained. Patient was discharged in good health and no additional treatment was needed.

**Discussion**

**Clinical presentation and microscopic findings**

The classical site for a central neurocytoma is within the ventricular system (Hassoun et al.,...
Extraventricular neurocytomas are definitely rare (Goergen et al., 1992). In the reviewed literature of 17 central neurocytomas with hemorrhage, 15 tumors were situated in the ventricles and only 2 were found in the cerebral parenchyma (see table). We describe these 17 tumors, according to their localization and according to their bleeding pattern. The 2 main divisions in this description are: tumors, located in the ventricle and tumors, located in the parenchyma. Those 2 divisions are again subdivided according to the hemorrhage pattern: a purely intratumoral hemorrhage, an intratumoral hemorrhage with breakthrough to the ventricle, an intratumoral hemorrhage with breakthrough to the parenchyma, and both intraparenchymal and intraventricular hemorrhage caused by an aneurysm of a feeding artery of the tumor (see table).

Central neurocytomas are most often found in adolescents and young adults. The reviewed patients have a mean age of presentation of 22 years; 11 male patients and 4 females patients were found (in 2 cases no information about age and gender was found). In a large series of Hassoun et al. (Hassoun et al., 1993) the mean age of presentation was 29 years and the incidence of this tumor was similar in both males and females.

In the literature, most patients with a central neurocytoma, presented with signs of raised intracranial pressure. The 17 presented patients had an acute onset of symptoms, because of the hemorrhage in the tumor (see table, symptoms).

Central neurocytomas comprise 0.25%-0.50% of brain tumors (Schmidt et al., 2004). Since Hassoun’s original description in 1982, more than 500 cases have been reported (Rades et al., 2002). Their true incidence may be higher, because many central neurocytomas were previously described as oligodendrogliomas (Agranovich et al., 1993; Yamshidi et al., 2001). The light microscopic appearances of central neurocytomas and oligodendrogliomas are similar, but the tumor cells of central neurocytomas have ultrastructural features of neurons. Also immunohistochemical markers of neuronal differentiation, like synaptophysin or neuron specific enolase are used to differentiate them from oligodendrogliomas (von Deimling et al., 1990; Barbarossa et al., 1990; von Deimling et al., 1991).

Central neurocytomas are not known as tumors prone to hemorrhage, in contrast with oligodendroglomas, which have a high tendency to bleed (Russell and Rubinstein, 1977; Okamura et al., 1995). Thus, it is possible that the incidence of central neurocytomas with hemorrhage has been underestimated because some were previously diagnosed as oligodendroglomas. Our own case was immediately diagnosed as central neurocytoma. In the reviewed literature, 2 cases were first misdiagnosed as oligodendrogloma (see table, case 1, case 14). Case 16 showed features of a central neurocytoma combined with neoplastic ganglion and glial cells and was called ‘ganglioglioneurocytoma’, because of the presence of these ganglion and glial cells (Taylor et al., 1998; Tortori-Donati et al., 1999). One could ask if this tumor is not merely another type and that we should separate this tumor from the other 16 cases we have found.

Central neurocytomas usually exhibit rare or no mitotic activity, no apoptosis, no necrosis, nor vascular endothelial proliferation. Atypical forms have been reported (Mc Cutchen et al., 1999; Söylemezoglu et al., 1997; Elek et al., 1999). Although anaplasia has been demonstrated in central neurocytoma, the influence of this feature on prognosis remains uncertain. Elevated MIB-1 monoclonal antibody index might be more useful in predicting relapse (von Deimling et al., 1990; von Deimling et al., 1991). The presented case report showed no anaplasia and no elevated proliferative potential was seen. In the reviewed cases, only case 17 showed anaplastic features. The tumor had numerous mitoses and frequent apoptosis, giving it a more aggressive appearance than the classical central neurocytoma (Mc Cutchen et al., 1999).

Medical Imaging

Central neurocytomas have heterogeneous appearances on CT or MRI (Chang et al., 1993) because of the variable components, like cysts, calcifications and vascular structures and also the radiological findings of hemorrhages may change in time. So, it is not always easy to differentiate a tumor hemorrhage from other etiologies. Careful attention to small lesions in the hemorrhage zone is needed. If a CT scan on admission only reveals a large amount of blood in the ventricles, further investigations, like MRI imaging, MR angiography and angiography are certainly needed and imaging should be repeated in order to detect the cause of the hemorrhage. In our own case the diagnosis of a tumor as cause of the hemorrhage was quite easily made, because a small round lesion was noticed on the CT scan on admission. In case 12 and 15 the etiology of the hemorrhage was not immediately found, but detailed review of the previously performed CT scans on admission also showed tumor masses within the hemorrhages.

Angiographic findings in central neurocytoma have been reported and lesions may be vascular or avascular (Yasargil et al., 1992; Smoker et al., 1991; Namiki et al., 1998; Peak et al., 2003). Angiographic findings can be very useful in excluding aneurysms or vascular malformations as the cause of the hemorrhages or they can help locating a tumor. In our case no aneurysm nor vascular malformation was seen. In case 10 and
case 13 angiographic findings showed an avascular mass effect, bowing vessels laterally and this suggested the presence of a tumor. In case 15, a cerebral angiogram revealed a small fusiform aneurysm on a lenticulostriate artery, which was the cause of the hemorrhage.

HEMORRHAGES TRULY ORIGINATING WITHIN THE TUMORS

Intraventricular hemorrhages can be caused by small parenchymatous hypertensive bleeds originating in the tissues close to the ventricular system. Some of these hemorrhages go undetected by CT. Some very small hemorrhages arise in the plexus choroideus (Graeb et al., 1982; Caplan et al., 1994; Marti-Fabregas et al., 1999). Intraventricular hemorrhages can also be caused by vascular malformations adjacent to the ependymal lining or by very small malformations that self-destruct as a result of the hemorrhage or which do not opacify in the angiography. Those malformations are often found at autopsy (Graeb et al., 1982; Caplan et al., 1994). In our case and almost all the other presented cases, anatomopathological evidence for tumor hemorrhage was found. Microscopically, hemosiderin deposits have been found in the tumors and macroscopically, hemorrhagic zones were also found in some tumor biopsies (see table: anatomopathological evidence). Radiological findings also suggested that the hemorrhages arose in the tumors, because large hemorrhagic zones or hemosiderin deposits were seen in the tumors on MRI or CT images. Thus, we believe that the bleedings arose within the tumors. Case 15 is the only exception, this case shows an aneurysm on a feeding artery of the tumor.

CAUSATIVE FACTORS FOR TUMOR HEMORRHAGE

Peak et al. (Peak et al., 2003) found that the degree of tumor staining on angiography seemed to be related to the size of the tumor. One could conclude that larger central neurocytomas are more prone to cause hemorrhage. In these vascularized tumors, abnormally developed and friable blood vessels can cause the hemorrhage. In the reviewed literature, 4 tumors (cases 1, 3, 6 and 9) were very large and they also had a marked vascularity on anatomopathological examination. However, not all large central neurocytomas are well vascularized and even avascular large tumor masses have been described (Bolen et al., 1989). In our own case, the tumor was small, but the patient showed a thrombocytopenia that could have contributed to the bleeding.

Rupture of arteries, invaded by neoplasms, has also been reported as cause of tumor hemorrhage (Cowen et al., 1970; Hart et al., 1974). This mechanism of hemorrhage, was not found in the 12 described patients, where angiography was performed. Also rapid tumor growth is often a cause of spontaneous bleeding in malignant tumors, but central neurocytomas are considered benign. All the reviewed cases, with exception of case 17, did not show malignant features, so this could not have caused the hemorrhages. In Case 17, tumor growth could have caused the vessels to rupture, although no sequential CT images, that would have confirmed rapid tumor growth and no MIB-proliferation index were performed. In case 3, the authors (Balko et al., 1999) suggested that the remarkable cardiomegaly, attributed to hypertensive heart disease, predisposed the tumor to the possibility of acute hemorrhage and in case 14, the authors (Namiki et al., 1998) suggested that abnormal tissue vascularisation after radiotherapy could have caused the bleeding.

Conclusion

When a young patient presents with an intraventricular bleeding, repeated imaging and MR imaging is of great importance to elucidate the underlying cause, such as a tumor. The importance of accurate diagnosis of a central neurocytoma lies in the relatively good prognosis of this tumor after maximal surgical removal.

Acknowledgments

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REFERENCES

Cowen R. L., Siqueira E. B., George E. Angiographic demonstration of a glioma involving the wall of


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<td>Tumor located in the ventricle</td>
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<tr>
<td>Purely intratumoral hemorrhage (6)</td>
<td>1</td>
<td>Kim, 1992</td>
<td>25y/M</td>
<td>Signs of raised intracranial pressure hemorrhage, CE</td>
<td>Isodense mass + intratumoral</td>
<td>Not performed</td>
<td>Vascular staining Mi: high vascularity</td>
<td>Ma: hemorrhage in tumor</td>
<td>1. OG 2. CN</td>
<td>STR/RT</td>
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<td></td>
<td>2</td>
<td>Metellus, 2001</td>
<td>38y/M</td>
<td>Sudden headache, vomiting, left hemiparesis</td>
<td>Intraventricular hemorrhage, no blood at bottom of trigonum</td>
<td>T1W1: isointense mass CE</td>
<td>T2W2: hyperintense mass</td>
<td>No AVM, no aneurysms</td>
<td>/</td>
<td>CN</td>
<td>GTR</td>
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<td></td>
<td>3</td>
<td>Balko, 1999</td>
<td>51y/M</td>
<td>Found dead at home</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>Ma: mass, friable, areas of hemorrhage, hemosiderin deposits Mi: acute hemorrhage, numerous capillaries</td>
<td>Autopsy:</td>
<td>CN</td>
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<td></td>
<td>4</td>
<td>Chang, 1993</td>
<td>?</td>
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<td>High intensity areas on all pulse sequences = intratumoral hemorrhage</td>
<td>?</td>
<td>Not performed</td>
<td>CN</td>
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<td>Chang, 1993</td>
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<td>High intensity areas on all pulse sequences = intratumoral hemorrhage</td>
<td>?</td>
<td>Not performed</td>
<td>CN</td>
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<td></td>
<td>6</td>
<td>Kubota, 1991</td>
<td>25y/M</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>Autopsy: Ma: giant hemorrhagic mass Mi: multiple blood vessels</td>
<td>CN</td>
<td>Dead after STR</td>
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<td>Intratumoral hemorrhage with breakthrough to the ventricles (7)</td>
<td>7</td>
<td>Smets, 2005</td>
<td>25y/M</td>
<td>Sudden headache, nuchal rigidity, vomiting</td>
<td>Intraventricular hemorrhage, round lesion</td>
<td>T1W1: isointense mass T2W2: heterogeneous mass No CE</td>
<td>No AVM, no aneurysms</td>
<td>Small capillaries</td>
<td>CN</td>
<td>GTR</td>
<td></td>
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<td>No.</td>
<td>Author</td>
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<td>First clinical presentation</td>
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<td>MRI</td>
<td>Angiographic findings</td>
<td>AP evidence of hemorrhage/ vascularisation</td>
<td>Treatment</td>
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<td>8</td>
<td>Hanel, 35y/F</td>
<td>2001</td>
<td>Sudden headache, nuchal rigidity, vomiting</td>
<td>Intraventricular hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: heterogeneous lesion, bottom of trigonum = hemorrhage, T2W1: hypointense</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
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<td>9</td>
<td>Yamshidi, 22y/F</td>
<td>1998</td>
<td>Acute headache, huge mass with heterogeneous density</td>
<td>Intraventricular and subarachnoidal hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: isointense mass, slight blush</td>
<td>Some blood clots within the tumor</td>
<td>Not performed</td>
<td>GTR, ventricular shunt</td>
<td></td>
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<td>10</td>
<td>Smoker, 26y/M</td>
<td>1991</td>
<td>Tonic clonic seizure</td>
<td>Intraventricular hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T2W1: heterogeneous mass, 5d later: intraventricular Avascular mass effect displacing brain structures</td>
<td>Not performed</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
<td></td>
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<td>11</td>
<td>Goergen, 18y/F</td>
<td>1992</td>
<td>Sudden headache</td>
<td>Intraventricular hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: heterogeneous mass, 3m later: hemorrhage</td>
<td>Not performed</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
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<td>12</td>
<td>Okamura, 23y/M</td>
<td>1995</td>
<td>1) unconsciousness, 1) intraventricular hemorrhage</td>
<td>Intraventricular hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: isointense mass, 2) 2y later: sudden headache</td>
<td>Not performed</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
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<tr>
<td>13</td>
<td>Agranovich, 28y/M</td>
<td>1993</td>
<td>Sudden headache, vomiting</td>
<td>Intraventricular hemorrhage</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: isointense mass, 3) severe headache</td>
<td>Not performed</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
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<td>14</td>
<td>Namiki, 50y/M</td>
<td>1998</td>
<td>1) headache, gait disturbances, 2) 1) intraventricular hemorrhage</td>
<td>Intratumoral hemorrhage with breakthrough to the parenchyma</td>
<td>Lesion with intraventricular hemorrhage</td>
<td>T1W1: heterogeneous mass, 2y later: right hemiparesis, speech disturbances</td>
<td>Not performed</td>
<td>No information on hemorrhosis or vascularisation</td>
<td>No AVM</td>
<td>GTR, ventricular shunt</td>
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</tbody>
</table>

**CT findings:**
- T1W1: heterogeneous lesion
- T2W1: hypointense
- 3m later: hemorrhage
- Slight blush in posterior chorioid
- Mass, hemorrhage within the tumor
- Mass, hemorrhage at the bottom of the trigone
- Intraventricular hemorrhage
- Lesion with intraventricular hemorrhage
- T1W1: isointense mass
- T2W1: heterogeneous mass
- 3m later: hemorrhage
- Mass, hemorrhage within the tumor
- Intraventricular hemorrhage
- T1W1: isointense mass
- 2y later: sudden headache
- T1W1: isointense mass
- 3) severe headache
- Intraventricular hemorrhage
- Intratumoral hemorrhage

**MRI findings:**
- T1W1: isointense mass
- T2W1: heterogeneous mass
- Mass, hemorrhage within the tumor
- Mass, hemorrhage at the bottom of the trigone
- Intraventricular hemorrhage
- Lesion with intraventricular hemorrhage
- T1W1: isointense mass
- T2W1: heterogeneous mass
- Mass, hemorrhage within the tumor
- Intraventricular hemorrhage
- Intraventricular hemorrhage
- Intraventricular hemorrhage

**Angiographic findings:**
- No AVM
- Mass, hemorrhage within the tumor
- Mass, hemorrhage at the bottom of the trigone
- Intraventricular hemorrhage
- Lesion with intraventricular hemorrhage
- T1W1: isointense mass
- T2W1: heterogeneous mass
- Mass, hemorrhage within the tumor
- Intraventricular hemorrhage
- Intraventricular hemorrhage
- Intraventricular hemorrhage

**AP evidence of hemorrhage/ vascularisation:**
- No blood clots within the tumor
- Mass, hemorrhage within the tumor
- Mass, hemorrhage at the bottom of the trigone
- Intraventricular hemorrhage
- Lesion with intraventricular hemorrhage
- T1W1: isointense mass
- T2W1: heterogeneous mass
- Mass, hemorrhage within the tumor
- Intraventricular hemorrhage
- Intraventricular hemorrhage
- Intraventricular hemorrhage

**Treatment:**
- GTR, ventricular shunt
- GTR, ventricular shunt
- GTR, ventricular shunt
- Not performed
- GTR, ventricular shunt
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<th>AP evidence of hemorrhage/</th>
<th>First AP diagnosis</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td>Intraparenchymal and intraventricular hemorrhage caused by an aneurysm of a feeding artery (1)</td>
<td>15</td>
<td>Bates, 2001</td>
<td>35y/M</td>
<td>1) left hemiparesis after sexual intercourse 2) left sided weakness</td>
<td>1) intraventricular hemorrhage with casting of the right ventricle (review mass lesion)</td>
<td>2) T1WI: heterogeneous mass, CE and large intraparenchymal clot in putamen, extending into ventricle</td>
<td>Fusiform aneurysm on lenticulostriate artery, abnormal tumor blush</td>
<td>Ma: not particularly vascular tumor</td>
<td>CN</td>
<td>1) ventricular drainage 2) GTR + hematoma removal + dissection of aneurysm</td>
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<td>Tumor located in the parenchyma</td>
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<td>Purely intratumoral hemorrhage (1)</td>
<td>16</td>
<td>Taylor, 1998</td>
<td>17y/M</td>
<td>Acute headache, vomiting, motor disturbances in right hand</td>
<td>Heterogeneous left parietal mass + central hematoma</td>
<td>Left hemispheric mass CE superior and anterior to the hematoma</td>
<td>No tumor blush, no AVM, no aneurysms</td>
<td>Ma: hypervascular tumor Mi: highly vascular stroma</td>
<td>Ganglioglio-neurocytoma</td>
<td>Left parietal craniotomy + GTR</td>
</tr>
<tr>
<td>Intumoral hemorrhage with breakthrough to the parenchyma (1)</td>
<td>17</td>
<td>Mc Cutchen, 1999</td>
<td>48y/F</td>
<td>1) past medical history: right hemiparesis 2) right hemiplegia, dysarthria, acute headache</td>
<td>2) hematoma, filled with fluid levels left frontoparietal mass, CE</td>
<td>1) T1WI: heterogeneous mass with high signal intensity = methemoglobin T2WI: mixed signal in mass, CE in superficial non hemorrhage portion of mass</td>
<td>Not performed</td>
<td>Ma: very hemorrhagic tumor Mi: liquefied clot, many mitoses and apoptosis</td>
<td>CN</td>
<td>1) Anti-epileptic 2) STR, clot resection, RT</td>
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