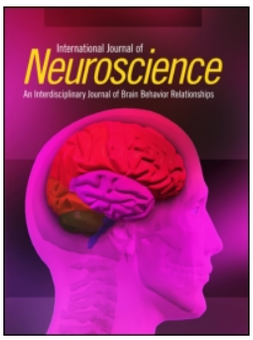

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Glioblastoma evolving within 10 days following unremarkable computer tomography of the brain: A case report

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Abstract

Glioblastoma multiforme might develop radiologically within a few days following unremarkable CT scan of the brain. Glioblastoma multiforme is the most frequent primary brain tumor. Initial presentations are diverse, including headache, seizures and transient or persistent neurological deficits. Cerebral imaging followed by histological examination of a tissue specimen is the mainstay of diagnosis. We report the case of a 79-year-old female patient whose computer tomography (CT) of the brain was unremarkable at first clinical presentation with a transient hemiparesis of the right side, but revealed a cerebral space-occupying lesion ultimately diagnosed as glioblastoma only 10 days later. According to our case presentation glioblastoma might develop radiologically within a few days following unremarkable CT scan of the brain. Since clinical manifestation with a transient ischemic attack (TIA)-like episode was preceding CT manifestation, this case indicates, that a magnetic resonance imaging (MRI) should be routinely performed in all patients presenting with TIA.

Key words: Glioblastoma multiforme, occult brain tumor, Cerebral Imaging

Glioblastoma multiforme (GBM) is the most frequent primary brain tumor, yet rare with an incidence rate of 3.2 / 100,000 / year. However, incidence rates are expected to rise due to increasing life expectancy [15,17]. The spectrum of clinical symptoms at presentation is diverse, including headache, seizures and transient or persistent neurological deficits [4]. Cerebral magnetic resonance imaging (MRI) followed by either surgical removal or stereotactic biopsy for histological and molecular analyses are the mainstay of diagnosis. Due to rapid tumor growth early diagnosis is mandatory in order to allow timely treatment initiation [16]. However, prognosis still is poor with a mean 1-year survival rate of 39.3% [12]. We here report the case of a 79-year-old female patient whose computer tomography of the brain was unremarkable at first clinical presentation with neurological symptoms, but revealed a cerebral space-occupying lesion ultimately diagnosed as GBM only 10 days later.

Case Report

In November 2018, a 79-year-old female patient presented to an external medical department with an acute onset transient hemiparesis of the right side lasting for 60 minutes. Due to atrial fibrillation she was on oral anticoagulation with apixaban 2.5 mg twice daily. Computer tomography (CT) of the brain (Figure 1a) and investigations for potential other sources of embolic stroke were normal. She was discharged with the diagnosis of a transient ischemic attack (TIA).

Ten days later, the patient presented to our department with persistent hemiparesis of the right side and quadrantanopia of the right lower quadrant. CT scan of the brain showed a hemorrhagic space-occupying lesion in the left thalamus without vascular abnormalities on CT angiography (Figure 1b,c). In order to neutralize apixaban efficacy 3000 IE prothrombin complex (PPSB) were given. MRI of the brain another six days later revealed a lesion with ring-shaped gadolinium enhancement with central necrotic and partly hemorrhagic areas (Figure 1d,e), but without diffusion restriction (not shown in figure 1), suggesting a high-grade glioma rather than an abscess. However, histological examination of a stereotactic biopsy showed predominantly reactive gliotic CNS tissue, fibrin, fresh hemorrhages, necrotic material and regionally also macrophages and numerous granulocytes. Due to the necrosis and granulocytic infiltrates as well as the lack of tumor detection, the diagnosis of an abscess was made (Figure 2a-f). However, microbiological pathogens could not be detected. Furthermore, screening for infectious foci (transthoracic and transesophageal echocardiography, dental examination including panoramic X-ray, X-ray of the thorax, CT of paranasal sinuses) or predisposing immunodeficiency (differential blood count, HIV serology and immunoglobulin levels) was unremarkable. Under the assumption of a cerebral abscess an empiric antibiotic therapy with metronidazole and ceftriaxone was initiated.

Since follow-up MRI six weeks later showed a progressive lesion with persistent contrast enhancement (Figure 1f,g), a second stereotactic biopsy was performed, revealing the final histological diagnosis of GBM (WHO grade IV) (Figure 2g,h). Since the patient rejected tumor specific therapy, she was discharged home for best supportive care.

Discussion

We here present the case of a patient with GBM that exhibited an extraordinary fast tumor growth since radiologically evolving within 10 days after an unremarkable CT scan of the brain.

The initial presentation with transient neurological symptoms and normal CT scan of the

brain was most likely the first clinical manifestation of the glioblastoma, since these tumors might present as “TIA” induced by the following mechanisms: (1) direct infiltration of cerebral blood vessels leading to either obstruction [10] or dissection [2], (2) leptomeningeal spreading mimicking cerebral vasculitis [7], (3) glioma induced vasospasms [14], and (4) procoagulant factors induced by the tumor [13].
The most relevant finding of this report is the extremely rapid tumor growth with evolution of a GBM within several days following a normal CT scan. As previously shown by various methods, velocity of growth is particularly high in the early phases of tumor manifestation. Hence, an early diagnosis of GBM is highly relevant regarding possible therapeutic options[15], [1].

Thus far, tumor appearance within a few days has only been described in two children [9]. These were seven and 12-years-old. The 7-year-old had a normal CT scan of the brain and the 12-year-old even an unremarkable MRI when they initially presented with seizures, headache, vomiting and photophobia. Remarkably, they developed radiologically manifest GBM eight and five days later, respectively. However, these patients presented with seizures that according to current guidelines would have initiated a MRI scan during routine work-up anyhow [3], whereas our patient presented with a TIA. With regards to adult patients, a case series and review of the literature described a time span of a few weeks to years from first clinical presentation, primarily with seizures, to malignant brain tumor detection by CT scan[8]. However, in these cases CT scans were done in the 80ies when the technique was of significantly lower sensitivity compared to current technology. A more recent review summarized 60 case reports of patients with radiologically occult brain tumors of various grades [5], particularly 31 cases with GBM. Of the latter 14 had a negative MRI and 17 a negative CT scan at first clinical presentation, which was with seizures in the vast majority of cases. The median time to diagnosis by either CT or MRI of the brain was 3.2 months, ranging from 18 days to several months.

According to the present case report, a GBM might develop radiologically within a few days following unremarkable CT scan of the brain. Since clinical manifestation with a TIA was preceding CT detection, this case indicates, that a MRI should be routinely performed in these patients not only to differentiate TIA and minor stroke [6,11], but also to potentially detect a neoplasm.

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Figure 1: Serial computer tomography (CT) and magnetic resonance imaging (MRI), respectively, of the brain of a 79-year-old female patient with glioblastoma (clinical details are given in the main document). (**a)** Unremarkable CT of the brain at first clinical manifestation. (**b-c)** CT of the brain ten days later: Native CT scan (**b)** reveals an intracerebral hemorrhage in the left thalamus without pathological vessels after administration of a contrast agent (black arrow in **c**). **(d-e)** MRI of the brain another six days later showing a ring enhancing lesion in the left thalamus in the axial T1-weighted images post-gadolinium application (**d)**. T2-weighted images displayed substantial perifocal edema affecting the left optic tract (**e)**. **(f-g)** MRI of the brain another 6 weeks later revealing a persistent ring enhancing lesion in the left thalamus (**f)** with significant progression primarily into the midbrain in T1-weighted coronal sequences after gadolinium application (**g**).

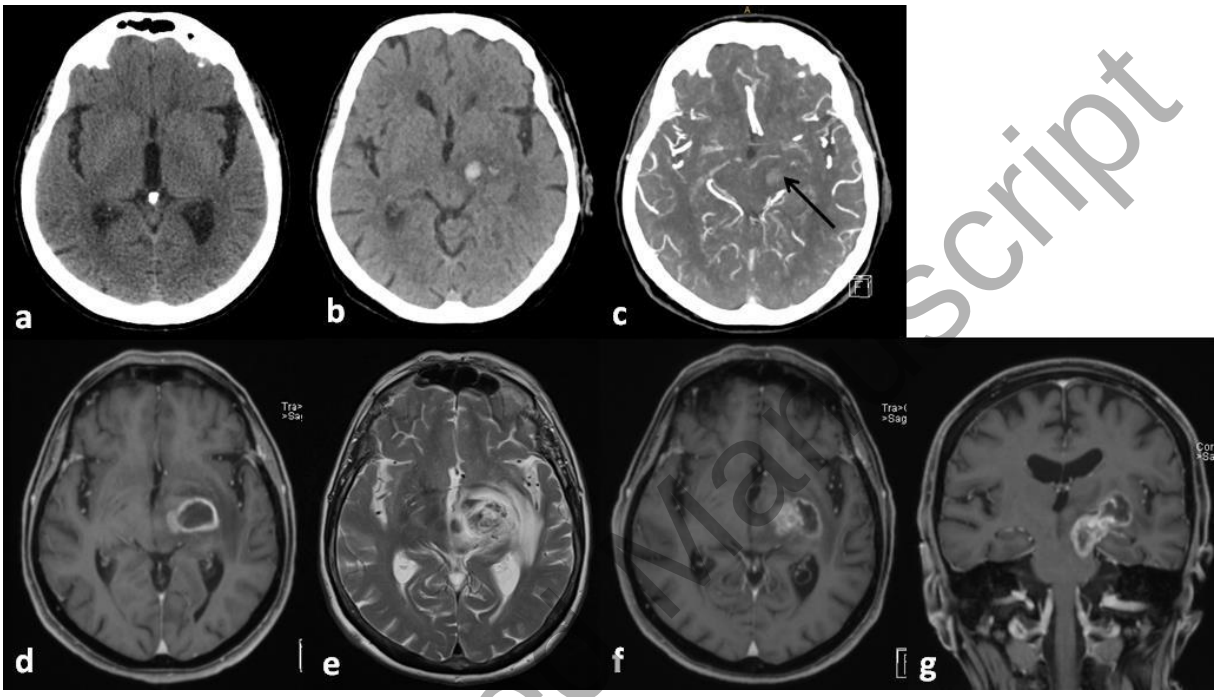

Figure 2: Histological examination of serial tissue samples of the lesion presented in figure 1 at primary manifestation **(a-f)** and six weeks later **(g-h),** respectively. **(a)** Hematoxylin and eosin (H&E) staining shows necrotic material, fibrin precipitates, granulocytes and mono-nuclear inflammatory infiltrates. **(b)** Within the same sample, no immunoreactivity for glial fibrillary acidic protein (GFAP) is detectable. **(c)** Diffuse distribution of several macrophages in the context of phagocytosis and clearance process in CD68 immunohistochemistry. **(d)** H&E: gliotic brain tissue from the neighborhood of necrosis with single neurons, small blood vessels and capillaries. No increased cell density, cell and nuclear pleomorphism, mitosis or pathological endothelial proliferates. **(e)** Several activated astrocytes are diffusely distributed in the GFAP immunohistochemistry. **(f)** No increased proliferation rate in MIB1 (Ki67) immunohistochemistry. **(g)** H&E staining displays a cell-rich glial tumor with pathological vascular proliferates. h) Many of the tumor cells show immunoreactivity for glial fibrillary acidic protein (GFAP).