CASE REPORT
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Primary glioblastoma multiforme of cerebellum: a case report and review of literature

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Abstract

The most common primary malignant brain tumour in adults is glioblastoma multiforme (GBM), classified as grade IV glioma. GBM is the most aggressive of astrocytic gliomas, considered to be an incurable disease, with median survival of only 15 months when treated with surgery in combination with concomitant chemoradiotherapy. Most of GBM lesions are localised supratentorially, and all available guidelines about treatment of GBM refer to those tumours. Tumours in the infratentorial area are rarely suspected to be GBM; however, about 0.4-3.4% of GBM occur in the cerebellum. The rarity of cerebellar GBM means that pathogenesis, treatment, and prognosis in such cases are still not well defined. We report a case of a 46-year-old patient with primary cerebellar GBM treated in our centre.

Key words: cerebellar glioblastoma, cerebellum, radiotherapy.

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INTRODUCTION

The most common primary malignant brain tumour in adults is glioblastoma multiforme (GBM), classified as grade IV glioma [1]. GBM is the most aggressive of astrocytic gliomas with an incidence of 3.19 per 100,000 persons [1, 2]. GBM is considered as an incurable disease, with median survival of 15 months with complex treatment [3]. The 2016 World Health Organisation (WHO) classification of central nervous system tumours divides GBM into two subtypes: isocitrate dehydrogenase (IDH) wildtype and IDH mutant [1, 4]. Most GBM lesions are localised in the cerebral hemispheres and only 0.4-3.4% occur in the cerebellum (GBMc) [5, 6]. It is postulated, that GBMc patients are younger than GBM patients. The mean age at GBMc diagnosis is the fourth to the fifth decade of life; however, it can occur at any age [6]. GBMc affects males more frequently than females [6]. The rarity of the GBMc means that pathogenesis, treatment, and prognosis in such cases are still not well defined.

We report a case of a 46-year-old patient with primary GBMc treated in our centre.

CASE REPORT

The 46-year-old patient, performance status (PS) 1 in Zubrod scale, presented with dizziness for five months. Magnetic resonance imaging (MRI) scans of the head showed a tumour of the right lobe of the cerebellum, 34 × 32 × 30 mm in size, without surrounding oedema. The tumour was inoperable. After surgical biopsy, GBMc was diagnosed histologically. The O6-methylguanine-DNA methyltransferase (MGMT) and isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) mutation statuses were unknown. The patient was referred to our outpatient oncological clinic. He was qualified to chemoradiotherapy with temozolomide.

The MRI scans for planning external beam radiotherapy (EBRT) revealed progression of the neoplasm. The tumour was 48 × 38 × 45 mm in diameter, being localised in the right lobe of the cerebellum (Figs. 1-3). The GBMc presented necrosis that was not described in the previous examination and oedema involving the hippocampus, hypothalamus, and cortex of the right frontal lobe. Two planning target volumes (PTV) were defined: PTV1 – 3 mm

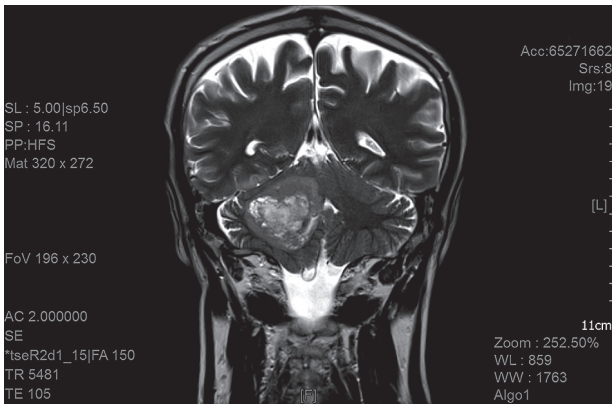

Fig. 1. MRI of head before treatment – coronal

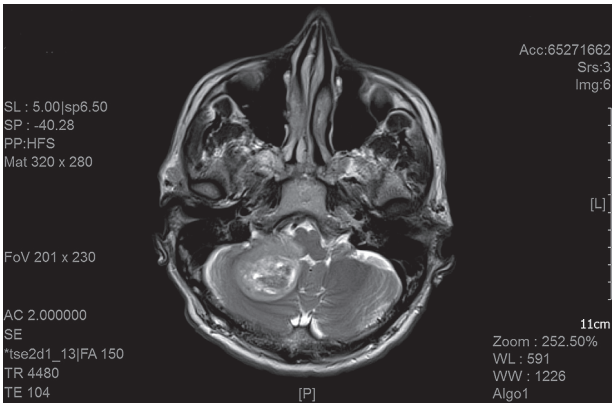

Fig. 2. MRI of head before treatment – transversal

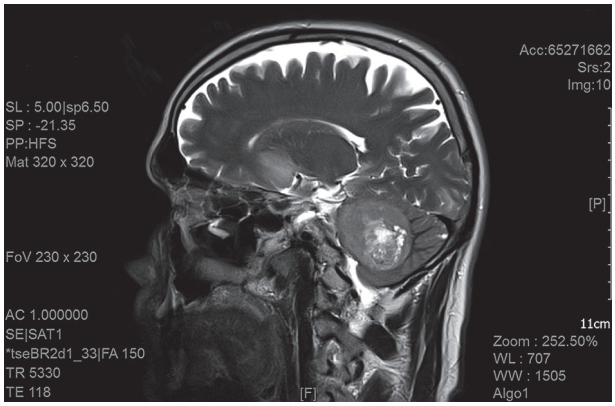

Fig. 3. MRI of head before treatment – sagittal

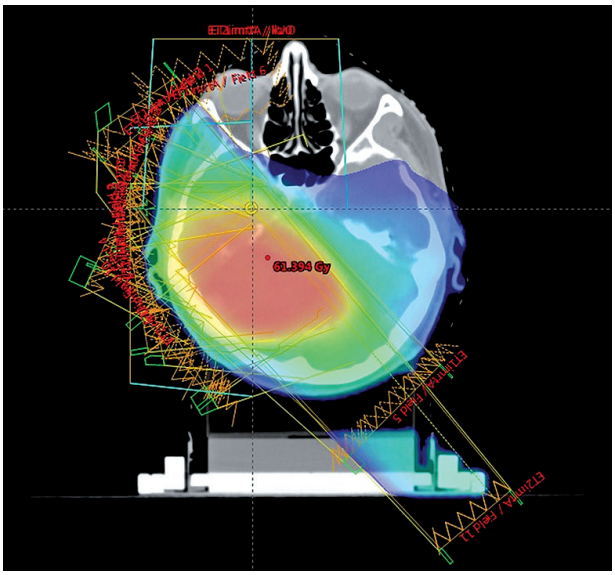

Fig. 4. Radiotherapy treatment plan – transversal

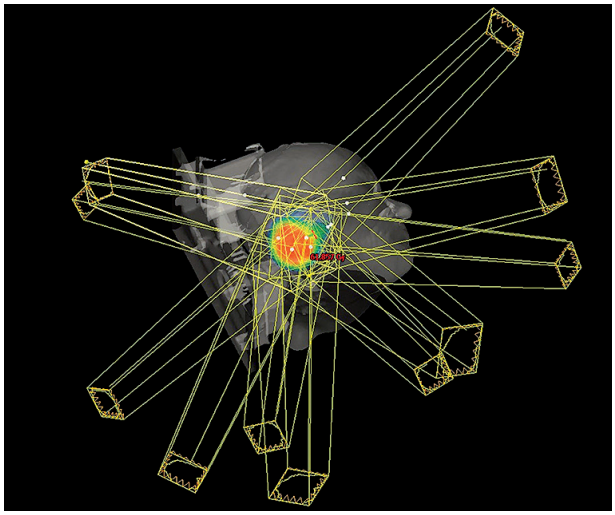

Fig. 5. Radiotherapy treatment plan – 3D all external beams

margin added to clinical target volume (CTV) 1 (tumour with 10 mm margin) and PTV2 – 3 mm margin to CTV 2 (CTV 1 with additional margin to encompass whole oedema). The tumour and oedema were defined using both T1- and T2-weighted MRI scans. Prescribed doses were 60 Greys (Gy) for PTV1 and 44 Gy for PTV2. The treatment scheme assumed EBRT with step and shoot intensity-modulated radiation therapy technique (IMRT) to PTVs up to a prescribed dose fractionated in 2 Gy daily five times weekly and temozolomide 150 mg daily (Figs. 4, 5).

The patient underwent chemoradiotherapy for seven weeks. During treatment two two-day interruptions occurred due to the patient refusing to take the temozolomide in the second and fourth week of treatment. Supportive treatment with dexamethasone up to 12 mg/day was delivered during radiochemotherapy with relief of the headaches that were present before onset of treatment. Also, ondansetron 8 mg/day was administered to prevent emetic episodes of concomitant chemotherapy. The patient was planned for continued treatment with adjuvant temozolomide after finishing the radiochemotherapy course. One month later, at the first visit after radiotherapy, the patient reported worsening headaches and dizziness. The first cycle of adjuvant temozolomide was postponed and MRI of the head was done. The MRI revealed progression of the GBMc, with tumour size of 47 × 50 × 45 mm. The patient was lost from follow-up and treatment after the second visit.

DISCUSSION

The GBMc is rarely taken into account during differential diagnosis of cerebellar tumours. Supratentorial GBM is commonly diagnosed with the first symptoms of worsening headaches, nausea, seizures, and neurological deficits, depending on the location of the tumour [5]. Patients with GBMc usually presents with gait disturbance, ataxia, and dizziness, as in our case. Less specific symptoms like headaches, nausea, and vomiting can be observed, as well [7, 8]. Our patient was initially free from headaches, but the symptoms occurred with progression of the disease.

The GBMcs are typically diagnosed as large tumours. In MRI they are often visualised as having thick, irregular-enhancing margins and a central necrotic core, which may also have a haemorrhagic component. The tumours are usually surrounded by vasogenic-type oedema, which usually contains infiltration by neoplastic cells. Intense, irregular, heterogeneous enhancement of the margins is almost always present [5, 9]. In our case, initially oedema was not visualised, but a second MRI showed progression of the tumour with the presence of oedema and necrosis.

The data from literature indicate that treatment for GBMc patients should be similar as for GBM located elsewhere [7, 8]. Nowadays, treatment for GBMc consist of maximally possible macroscopic resection with radiotherapy and temozolomide. In cases when surgery cannot be performed, as in our patient, chemoradiotherapy is considered to be the best option. The recommended dose prescribed to CTV contoured as tumour and oedema with margin or tumour bed with margin, is 60 Gy concomitantly with temozolomide, in a daily dose of 75 mg/m^2. In cases of large target volume, a dose of 60 Gy can be given to the tumour with margin only. Although there is also lack of evidence of chemotherapy efficacy in GBMc, it is widely used as a standard of care in high-grade gliomas [7, 8, 10, 11]. Nowadays radiotherapy is delivered with highly conformal techniques as step and shoot IMRT or volumetric modulated arc therapy (VMAT); both, in comparison to older 3D conformal radiotherapy (3D-CRT) allow for improved target conformity and better critical tissue sparing, which is highly useful in tumours located near brain stem, optic chiasm, and other critical organs [12].

Mutations in metabolic genes IDH1 and IDH2 are critical for prognosis in adult glioblastoma [4, 13]. IDH wildtype is more aggressive, having a worse prognosis than IDH mutant for GBM patients. However, IDH mutations are rare in infratentorial gliomas, with only eight cases reported in the literature [14-17]. Their prognostic significance in GBMc has not yet been proven. Another favourable prognostic factor is MGMT promoter methylation. Patients with supratentorial GBM and methylated MGMT promoter have proven higher benefit from temozolomide [18]. The prognosis for patients with GBMc is generally poor. Median overall survival (OS) depending on MGMT promoter methylation varies from 10 to 33 months with median progression-free survival (PFS) from five to 22 months [19]. Some authors described worse outcome of GBMc patients compared to supratentorial GBM [8]. In the presented case early progression despite treatment can confirm these findings, but lack of data about survival has to be taken into consideration.

CONCLUSIONS

Because of the rarity of GBMc, there is a need to report GBMc cases to improve our knowledge about these tumours, elaborate standards of treatment and consequently to improve prognosis.

The authors declare no conflict of interest.

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