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Glioblastoma Single Lesion with Extra Cranial Metastasis *versus* Multiple Lesions: Serial Rare Case

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ABSTRACT

Glioblastoma is the most aggressive primary malignant brain tumor in adults. Head MRI is the high accurately imaging modality detect of Glioblastoma. Glioblastoma often seen as single parenchymal lesion; multiple lesion glioblastoma is rare. Metastasis outside CNS was very rare. There are several factors for extra cranial metastases e.g. the first factor, age during diagnosis; second factor, lifespan; third factor, surgical treatment; last factor is chemo radiotherapy. We present two rare cases, first case a female patient with glioblastoma single lesion with extra cranial metastasis on her left neck with complete surgical, radiotherapy, and chemotherapy and survive more than 2 years and second case, a female patient with Head MRI revealed with glioblastoma multiple lesion.

Keywords: Glioblastoma; Single lesion; Multiple lesions; Extra cranial; Metastasis

INTRODUCTION

Glioblastoma is the most aggressive primary malignancy brain tumor in adults. This kind of tumor prevalence is 33%-45% from all of primary malignancy brain tumor which male is prone than woman. Universal incidence of glioblastoma is rare, comprising 3, 2 per 100.000 population. Head MRI is the high accurately imaging modality detect of glioblastoma. Glioblastoma often seen as solitary parenchymal lesion and multiple lesion are rare. Particularly in patients with known multiple brain lesions, often lead to the diagnosis of brain metastasis. Distinguishing of brain metastases from glioblastoma, which is exhibit overlapping imaging finding on conventional MRI, but more advanced MRI, such as perfusion-weighted imaging can aid in the differentiation [1].

Metastasis outside CNS was uncommon in GBM but it could occur with frequency 0.2% and can spread in head and neck sites. The pathophysiology of extra cranial metastases is not clear. The hypothesis about spreading glioblastoma extra cranial metastases was a direct lymphatic connection, by the venous system and the adjacent structure like dura and bone [2].

The outcome treatment is usually unsatisfactory. The recommendation therapeutic methods include a radical surgical procedure, combined with radio-chemo-therapy. Mortality with a median survival time only 3 months in untreated patients. In statistically, the combined therapy have significant prolonged the total survival time from 12, 1 to 14, 6 months and the rate of 2-year survival was 26.5% compared to 10.4% for radiotherapy alone [3]. In another research it revealed either racial influenced in further prognostic, or tumor site in brain. According to guideline, secondary glioblastoma is more frequent in older than 45 years and woman gender. The mechanism has been presumed to underlie glioblastoma extracranial metastasis by direct lymphatic connections, the venous system, dura, and bone [4].

Because of rarity case, we present 2 case glioblastoma patients with different lesion, first is Glioblastoma single lesion and second is glioblastoma multiple lesions.

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CASE PRESENTATION

First Case

A 37-year-old woman with chronic progressive right hemiparesis for 1 year before admission, accompanied by left asymmetrical face and dysarthria, she also has motoric aphasia, a protruding right eye, and blindness in both eyes, and a mass in the left neck. History of chronic progressive cephalgia about 2 years before admission and also had general tonic-clonic seizure 3 years before admission.

The head CT scan two years ago revealed diagnosed with a brain tumor and had 2 surgeries in the left frontparietal region. Head MRI was found a cystic encephalomalacia in the left frontotemporal lobe with a solid mass within, possibly a residual mass and moderate communicant hydrocephalus **(Figure 1)** [5].

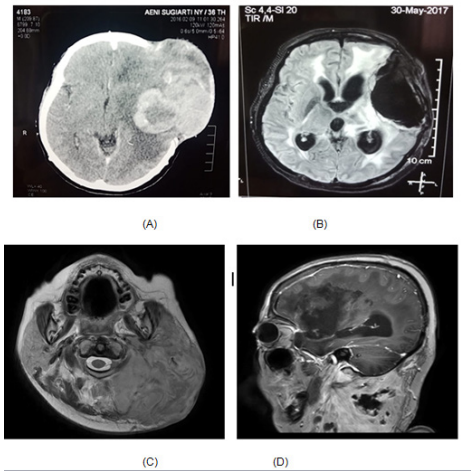

Figure 1: A) Head CT scan 1-year post first surgery, the tumor was residif; B) head MRI post second surgery, revealed cystic encephalomalacia; C,D) head and Neck MRI 2 months after second surgery show mass in left neck region.

While at admission, head and neck examination found a mass in the left neck region while at admission, head and neck examination found a mass in the left neck region (dimension 10 x 15 x 3 cm), solid, with clear edge and fixated the mass is suggestive of a malignancy [6].

Histopathology examination of brain tissue revealed tumor cell proliferation with variated size and shape, pleomorphic, hyper chromatic, which partial prominent core, mitosis 30/10 HPF, giant cell was found, endothelial proliferation and necrotic tissue; it is concluded as Glioblastoma (WHO grade IV). FNAB biopsy mass in the left neck region found small round cell tumor appearance which usually found in blastoma. Immuno histo chemical examination revealed Glial Fibrillary Acidic Protein (GFAP) positive and Neuron-Specific Enolase (NSE), so it has concluded as glioblastoma metastasis in mass from left colli region. The conclusion from upon all examination is extracranial metastasis from glioblastoma, patient planned to tumor excision in colli region and head MRI evaluation with Response Assessment in Neuro-Oncology (RANO) criteria **(Figure 2)** [7].

The patient got radiotherapy for 6 weeks and concomitant with Temozolomide chemotherapy for 6 months. In spite of the aggressive treatment for the tumor, the patient was deteriorating and passed away 3 months later **(Figure 3)**.

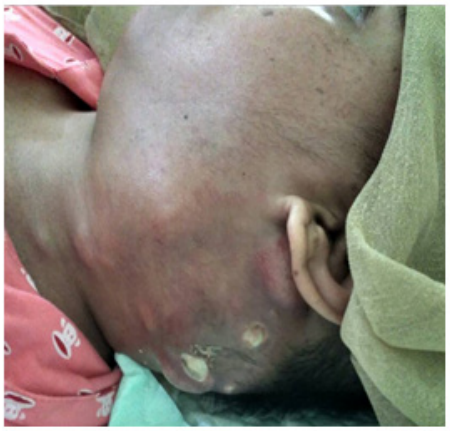

Figure 2: Mass in left neck region.

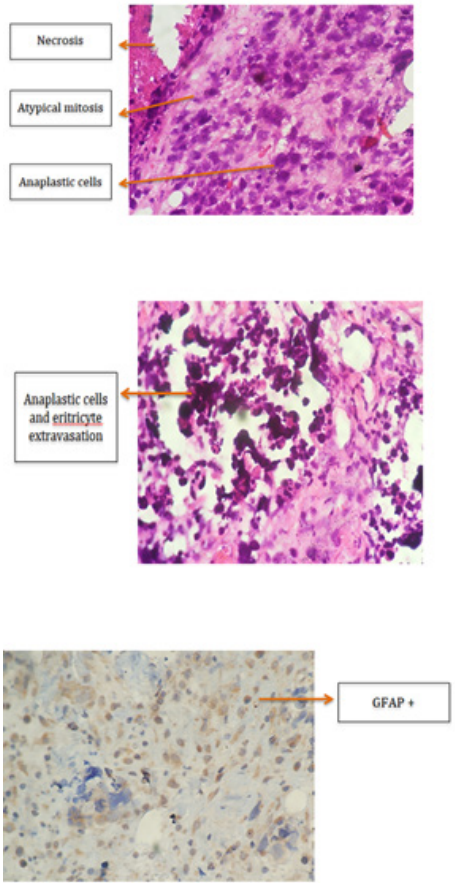

Figure 3: Mass in left neck region.

Second Case

A 52-year-old woman with gradual doc, myoclonic seizure, and projectile vomiting for 20 days before admission, accompanied by right hemiparesis, right asymmetrical face and dysarthria. History of behavioral changes became uncommunicative, fright for 1 year before admission.

the patient had a struma operation, 28 years ago with pathological result benign, the patient had thyroidectomy with the pathological result: Benign goiter neoplasms. Breast and abdomen ultrasound examination results are normal, the abdomen CT scan result is normal [8].

Head MRI, 3 months before admission was found a multiple lesion with nodular and ring enhancement on temporal, external capsule, frontal subcortex and temporal Sinistra, non-restrict-

ed, diffusion with increase ratio Cho/Cr suspicious malignancy (metastasis).

The symptoms getting worse and the patient got head CT scan for evaluation, 1 month before admission revealed with hyper dense and heterogonous mass with multiple nodular rings, contrast enhancement until left external capsule suspicious Glioblastoma.

The patient finally got the stereotactic biopsy, 1 month before admission with the result is astrocytoma grade II, and Head MRI evaluation revealed with multiple lesion on left centrum semiovale, left external capsule, left internal capsule limb anterior posterior, left lentiform nuclei and left periventricular cornu posterior support high-grade glioma with volume increase [9,10]. Edema cerebral with subfalcine herniation to the right 20mm, 3 mm and trans tentorial downward as level as mesencephalon [11,12]. The patients got Radiotherapy 15 x 3 gy, planned to surgery and also continue concomitant therapy between radiotherapy and chemotherapy **(Figure 4)**.

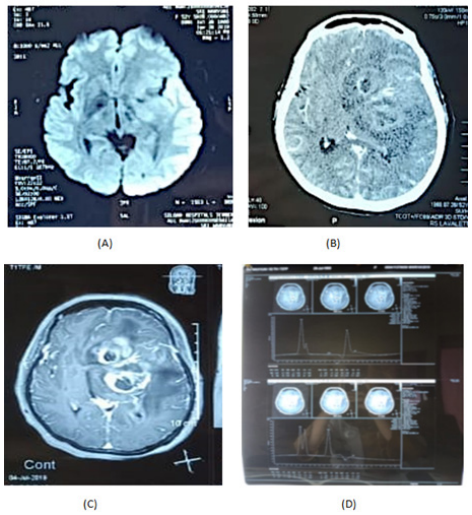

Figure 4: A) Head MRI, 3 months before admission, revealed multiple lesions with nodular and ring enhancement; B) head CT Scan, 1 month before admission, revealed with hyper dense and heterogenic mass with multiple nodular ring, enhancement, sup. GBM; C) head MRI while admission, revealed with multiple lesion support high grade glioma; D) head MRI Spectroscopy, Cho/Cr ratio increase, NAA ratio decrease on intratumoral.

DISCUSSION

We present two rare cases of glioblastoma single lesion extra cranial metastasis and glioblastoma multiple lesions. Epidemiology from two cases shows both cases are female and age below 62 years old meanwhile from epidemiology suggest are secondary glioblastoma. The commonest primary glioblastomas are the majority of cases (>90%) and affect mostly the elderly with mean age in 62 years, yet it even still lower percentage could appear in case [13,14]. Secondary glioblastomas are manifest in younger patients with mean age 45 years whereas female more frequent in women, and progression from low-grade diffuse astrocytoma (WHO grade II) or anaplastic astrocytoma (WHO grade III) [15]. Criteria diagnosis of secondary glioblastoma needed clinical (neuroimaging) or histopathological (bioptic) evidence of a progressively astrocytoma malignant.

Glioblastoma often seen as solitary parenchymal lesion and multiple glioblastomas are rare; it can be either multifocal or multicentric and appear subsequently (metachronous) or simultaneously (synchronous). The incidence of multiple glioblastomas between 2% until 20% [16,17]. Pathogenetic mechanism of multiple gioblastomas still not well understood. However, in some recent studies reveal existing genesis knowledge of these lesions. Willis in his hypothesis suggested that there are 2 stages in tumorigenesis which enhance to multiple glioblastoma. First stage was condition which made brain susceptible to malignancies changes. In the second stage, various kinds of stimulants like viral, mechanical or even biochemical will raise excessive cellular proliferation and subsequently occurred glioblastoma at multiple place. Whole process known as “promotion”.

In 1928 Davis was first present a case with metastasis GBM. Recently from published article found approximately 200 incidences of metastases in GBM patients. From epidemiology, it was found in younger and healthier patients more prone susceptible to develop extracranial metastasis than elderly GBM [18-20]. It is well known and broadly accepted that physical barrier around cerebral (Dura mater, thickened basement membrane and BBB/ blood brain barrier) is a solid barrier that will prevent tumor cells to spreading beyond the brain. Moreover, there is no connection in perivascular spaces from intra or extra-cranial made metastasis is difficult. However, 20% of GBM patients shown CTC (Circulating Tumor Cells) in peripheral blood even without metastases. It seems that CTC hindered to find an access to adjacent organs, maybe explained by intrinsic properties of glial filament, lack of ECM (Extracellular Matrix proteins) or peripheral immune response [21-23]. There are several factors for extracranial metastases e.g. first age during diagnosis which in younger age is more prevalent for metastases. Second factor is lifespan which better treatment will have a good prognosis, but meta-analysis has supported hypotheses that increasing survival rate will increase probability of glioblastoma cells to spreading out through hematogenous or lymphatic system [24]. Third factor is surgical treatment, almost 96% patient with GBMs metastasis have a recent surgical treatment [25,26]. Last factor is chemoradiotherapy which cause excessive apoptosis and DNA injury to the brain tissue even in tumor cells cause inhibition of glioma angiogenesis [27-31].

CONCLUSION

The patient in this first case with glioblastoma extra cranial metastasis presents the possibility main risk factor was the recurrent surgeries, a long lifespan, and chemo radiotherapy. The Second case, patient with Head MRI revealed with multiple brain lesions, can lead to the diagnosis of glioblastoma. MR Spectroscopy and DWI can aid the distinguishing between glioblastoma and brain metastasis.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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