Glioblastoma Multiforme Mimicking Mixed Primary Progressive Aphasia: A Case Report

Miks Primer Progresif Afazi Kliniğini Taklit Eden Glioblastome Multiforme: Olgu Sunumu

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ABSTRACT
Glioblastoma multiforme (GBM) is the most common malignant primary central nervous system tumor with rapid progression and poor prognosis. In addition to focal neurologic deficits, headache, seizures, and cognitive impairment might be seen in patients with GBM. Here, we present a 72-year-old-woman who had aphasia and forgetfulness, and normal brain MRI scanned three months earlier. A hypermetabolic lesion was shown in the left temporal lobe on her brain fluorodeoxyglucose Positron Emission Tomography (FDG-PET/CT) imaging which was performed for the differential diagnosis of primary progressive aphasia (PPA). A repeat MRI examination confirmed the presence of a mass lesion. The mass lesion was surgically resected and histopathological diagnosis was GBM. We emphasize that brain tumor should be considered in the differential diagnosis of rapidly progressive PPA.

Key words: Glioblastoma multiforme, FDG-positron emission tomography, dementia, primary progressive aphasia

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OZET

Anahit kelime: Glioblastoma multiforme, FDG pozitron emisyon tomografı, demans, primer progresif afazi

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Introduction
Glioblastoma multiforme (GBM) is the most common primary central nervous system tumor seen in USA and European countries, with about 3 in 100,000 people newly diagnosed each year (1). GBM constitutes approximately 20-30% of all primary brain tumors, may manifest at any age including neonatal period and childhood and it accounts for 10% of childhood tumors. Peak incidence is, however, in adults older than 40 years. Males are more frequently affected than females (1,2).

Currently, contrast-enhanced, multiplanar magnetic resonance imaging (MRI) is the standard technique for imaging gliomas. Since many authors have still debated the value of FDG-PET/CT imaging, new, targeted radiolabeled tracers for PET studies have been investigated in the visualization of more specific aspects of glioma biology, such as the degree of hypoxia and cellular proliferation (3). The most common presenting symptoms and signs of GBM are progressive focal neurologic deficits, headache, and seizures (1). Here, we present the case of a patient with forgetfulness and global aphasia whose MRI was normal three months before presentation and who turned to have GBM.
Case

A 72-year-old, right-handed housewife with a grade school education was referred to our memory clinic. She was living alone and the informants were her neighbors. They gave a history of forgetfulness, which had become noticeable largely within the last 5-6 months. A scrutiny of the history revealed that the main problem was indeed language deficits, such as word-finding difficulties and paraphasias but not memory problems per se. She was independent in all her daily living activities (ADL’s), including outdoor and domestic ADL’s, other than language-related functional activities, such as using a telephone. In her own words she described her main concern as “How I wish I’d say nothing”, “I think I know everything, but when I try to say something it disappears.” She had been diagnosed with Alzheimer’s disease in another hospital and put on the on cholinesterase inhibitor treatment.

Her medical history was unremarkable other than hypertension and hyperlipidemia. She had no family history of any neurological illness. Her neurologic examination was normal with no lateralizing signs. Her mental status examination revealed that, her spontaneous speech was non-fluent with initiation hesitancy, word finding pauses, stuttering, phonemic paraphasias and grammatical word omissions. Her confrontation naming, auditory and reading comprehension of sentences and writing to dictation were moderately, reading aloud and repetitions were mildly impaired, thus, fulfilling the criteria for global aphasia. Her single-word comprehension and object recognition were intact. The severity of her aphasia precluded the testing of other verbally-mediated cognitive domains, such as memory, attention, problem solving.

Non-verbal skills, including the visuospatial perception were normal. Her responses to questions were largely repetitive utterings of the similar phrases, such as “Always I know but cannot bring” or “also I know can’t bring water”. She was diagnosed as having PPA. MMSE score dramatically declined to 13/30 from 19/30 within the ensuing one month.

She had a cranial MRI that was performed 3 months earlier, which was normal (Figure 1). A brain FDG-PET/CT examination was performed for the differential diagnosis of PPA subtypes. FDG-PET/CT showed a hypermetabolic lesion in the left temporal lobe and hypometabolism around the hypermetabolic mass lesion encroaching on thalamus, and lentiform nucleus, probably due to the oedematous changes (Figure 2). A repeat cranial MRI examination confirmed the presence of a mass lesion in the left temporal lobe corresponding to the hypermetabolic lesion on PET scans (Figure 3). The mass lesion was surgically resected and histopathological diagnosis was GBM.

Discussion

Among gliomas, glioblastoma is the most malignant astrocytic primary brain tumor that represents 20-30% of all primary intracranial tumors (2). The peak incidence is between 45 and 75 years (4). GBM is located preferentially in the cerebral hemispheres, more often in the frontal lobes. Clinical presentation that similar to that of any other central nervous system tumor includes motor weakness depending on the location and size of tumor, partial or generalized seizures, visual field defects and symptoms of increased intracranial pressure, such as headache, nausea and vomiting. History is generally short, less than a few months. Although symptoms mostly occur when the tumor reaches a sizable mass, they may also arise even if the tumor is too small. If the survival is prolonged, then the cognitive impairment and neurological deficits resulting from communicating hydrocephalus, radiation necrosis, cranial neuropathies and polyradiculopathies from leptomeningeal spread may be observed. In addition to subtle personality changes, such as anxiety and mood changes, specific cognitive deficits, such as dysgraphia, apraxia or aphasia may accompany the clinical picture in such patients with GBM (2,3,4). Yet, to our knowledge no patient with GBM mimicking a PPA syndrome was previously reported in the literature.

Figure 1. November 2009 MRI: Axial diffusion (A) T 1-weighted (B), and T 2-weighted (C) MRI showing no abnormality

Figure 2. February 2010 axial FDG-PET imaging showing a hypermetabolic lesion in the left temporal lobe which is surrounded with hypometabolism due to the oedematous changes

Figure 3. March 2010 MRI: Axial unenhanced T 1-weighted images showing hypointense (A) and axial contrast enhanced T 1-weighted images showing mass lesion with contrast enhancement (B) in the left temporal lobe corresponds to hypermetabolic lesion in FDG-PET imaging. Oedematous changes are also seen around the mass lesion
Our patient showed none of the common features, such as headache, seizures, lateralizing signs that could be ascribed to a cerebral mass lesion. She presented with progressive language difficulties which had started apparently less than a year earlier and which was the isolated cognitive problem without affecting non-language-related ADLs. This picture fits the very recent definition of PPA proposed by the international consortium (5), which necessitates the presence of PPA before determining the specific PPA subtype. The specific criteria for the diagnosis of 3 major subtypes, namely non-fluent agrammatic (NFAV-PPA), semantic (SV-PPA) and logopenic variants (LV-PPA), are also provided in the same paper. When she first presented, the aphasic profile of our patient did not fit any of these definitions, since she displayed both non-fluency and sentence-comprehension deficits, as well as impaired repetition. This profile resembles to a combination of NFAV-PPA (i.e., non-fluency, agrammatism, effortful speech) and LV-PPA (i.e., anomia and impaired repetition, but intact single-word comprehension). The term mixed PPA was proposed for those patients who do not fit one of the major subtypes and who mainly display both non-fluency and sentence comprehension deficits as we have documented in our patient (6,7). The demonstration of a non-degenerative CNS disorder, psychiatric or medical condition that could explain the clinical picture is an exclusion criterion for the PPA diagnosis. As her initial MRI scan did not show any secondary causes, we considered the patient as fulfilling the criteria for mixed PPA. Subsequent diagnostic work-up heralded by the demonstration of the left temporal mass lesion resulted in the correct diagnosis. In the present case, we chose FDG-PET/CT before repeating the MRI scanning, since it has been shown that FDG-PET/CT is helpful in the differential diagnosis of the variants of PPA (8,9).

It is known that Creutzfeldt-Jacob disease can mimic a rapidly progressive version of PPA (10). Our case demonstrates that GBM should also be considered in the differential diagnosis of rapidly progressive PPAs.

References

1. Adamson C, Kanu OO, Mehta Al, Di C, Lin N, Mattox AK, Bigner DD. Glioblastoma multiforme: a review of where we have been and where we are going. Expert Opin Investig Drugs 2009; 18:1061-1082.