Case report

Cerebral syphilitic gumma mimicking a brain tumor that enlarged temporarily after commencing antibiotic treatment

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Abstract

In this case report, we describe a 60-year-old man who presented with headaches for 1 year and mild confusion for 3 weeks and was initially diagnosed as having a cerebral tumor on the basis of finding a round lesion in the right lentiform nucleus with ring enhancement on gadolinium-enhanced T1-weighted brain magnetic resonance imaging. However, the discovery of positive serology for Treponema pallidum infection on routine tests on admission prompted analysis of cerebrospinal fluid, which was also positive on Treponema pallidum hemagglutination (TPHA), rapid plasma reagin (RPR), and treponemal antibody absorption (FTA-ABS) tests. Thus, he was diagnosed as having an intracranial syphilitic gumma. After commencing treatment with penicillin G, the lesion temporarily increased in size, but subsequently resolved completely with continuing antibiotic treatment. In the present era of increasing prevalence of syphilitic infection and because they are eminently treatable, syphilitic gummas should be included in the differential diagnosis of apparent brain tumors. Additionally, temporary enlargement of a probable gumma after instituting antibiotic treatment should not prompt cessation or change of the antibiotics.

1. Introduction

Cerebral syphilitic gummas, a rare disease of the central nervous system, can develop in patients with late-stage neurosyphilis. Because the rates of syphilis have recently increased in many parts of the world, cerebral syphilitic gummas mimicking tumors may occur more frequently in the future. The optimal duration of treatment for cerebral syphilitic gummas has not been clearly defined and few reports have described the clinical course in detail. Here we report an immunocompetent patient with a cerebral gumma located in the basal ganglia mimicking a brain tumor in whom detailed imaging showed temporary enlargement of the lesion after commencement of antibiotic treatment.

2. Case report

A 60-year-old man had been experiencing headaches for 1 year and mild confusion for 3 weeks. He suddenly developed left inferior quadranopia, which resolved spontaneously 10 min after onset. Upon visiting our emergency clinic, he had a normal body temperature of 36.7°C, and he was alert and fully conscious. A neurological examination revealed mild muscle weakness in the left lower extremity. All other neurological findings were normal. Brain magnetic resonance imaging (MRI) showed a round lesion in the right lentiform nucleus with slight hypointensity in T1-weighted images (T1WI) (Fig. 1a) and slight hyperintensity in diffusion-weighted images, T2-weighted images (T2WI), and fluid-attenuated inversion recovery (FLAIR). Additionally, white matter edema surrounded the lesion, as shown by T2WI and FLAIR.
images (Fig. 1b–d). Gadolinium-enhanced T1WI showed ring enhancement of the lesion (13 × 10 × 8 mm) (Fig. 1e, f). He was admitted to our hospital with a suspected brain tumor.

Tests ordered routinely on admission showed positivity for serum Treponema pallidum hemagglutination (TPHA) and rapid plasma reagin (RPR), whereas HIV antigen/antibodies were negative. Cerebrospinal fluid (CSF) analysis showed an initial pressure of 280 mm H2O, cell count of 120/μL (99% monocytes), protein concentration 149 mg/dL, glucose 52 mg/dL, positive TPHA titer at 1:1280, positive fluorescent treponemal antibody absorption (FTA-ABS) titer at 1:80, and positive RPR titer at 1:3.2. The patient was therefore diagnosed with a cerebral syphilitic gumma. He had a history of developing a possible chancre after intercourse with a commercial sex worker more than 10 years previously.

18F-fluorodeoxy-glucose (FDG) uptake in a positron-emission tomography (PET)/computed tomography (CT) scan showed increased uptake in the lesion in the right lenticular nucleus, with a maximum standardized uptake value (SUVmax) of 12.1 (Fig. 1g, h).

Prednisolone therapy (40 mg/day for 3 days) was initiated from Day 12 to prevent a Jarisch–Herxheimer reaction (JHR), followed by continuous intravenous penicillin G (24 million units/day) from Day 13. After this treatment, the patient’s headache and muscle weakness improved without any evidence of JHR. However, a brain MRI on Day 19 showed enlargement of the ring-enhancing lesion (14 × 11 × 13 mm) in gadolinium-enhanced T1WI and surrounding white matter edema in FLAIR images (Fig. 2).

Penicillin G was continued because his condition had improved. A further brain MRI on Day 27 showed reduction of the ring-enhancing lesion and surrounding edema (Fig. 2). On Day 28, the patient was discharged on amoxicillin (3 g/day) plus probenecid (750 mg/day). Brain MRI on Day 43 showed further reduction of the enhancing lesion and surrounding edema. The amoxicillin and probenecid were stopped on Day 58. Brain MRI showed a slightly enhanced lesion on Day 86 and completely resolution of the lesion on Day 379 (Fig. 2). After the antibiotic treatment, serum and CSF RPR titers gradually decreased. CSF cell count and protein concentration also showed a decrease, but remained slightly high on Day 379 (Table 1). There was no recurrence of the cerebral gumma during about a year of follow-up.

3. Discussion

Our patient was found to have a syphilitic cerebral gumma in the basal ganglia with ring enhancement on brain MRI and increased FDG uptake in PET/CT, mimicking a brain tumor. However, the correct diagnosis was made and appropriate treatment instituted because neurosyphilis was suspected on the basis of routine tests on admission. Our patient’s lesion temporarily enlarged despite antibiotic treatment, but resolved completely with continued antibiotic treatment. Multiple brain MRIs showed details of the lesion’s enlargement and subsequent resolution (Fig. 2).

Cerebral syphilitic gumma is a rare disease of the central nervous system. There were only five gummas (0.2%) in a previous case series of 2326 intracranial tumors [1]. Most (66%) of 156 reported cases of cerebral syphilitic gummas were located on the convexities; only six patients (3.2%) in that series having basal ganglia lesions. Additionally, six of 29 patients (20.7%) showed ring-enhancing lesions on CT [5]. Thus, ring-enhancing lesions in the basal ganglia are very rarely cerebral gummas. Previous study suggested two important points regarding the neuroimaging findings of intracranial syphilitic gumma; first, syphilitic gumma predominantly appeared in the superficial part of the cerebral hemisphere, which mostly involved the grey matter, second, meningeal

![Fig. 1. Brain MRI showing a round lesion in the right lenticular nucleus with (a) slight hypointensity in T1WI and (b) slight hyperintensity in DWI. (c) T2WI and (d) FLAIR images showing edema in the white matter surrounding the slight hyperintensity. (e) Axial and (f) coronal gadolinium-enhanced T1WI showing ring enhancement of the lesion. (g) Axial and (h) coronal 18F-FDG PET/CT showing increased uptake in the lesion of the right lenticular nucleus, with a SUVmax of 12.1 (arrows). 18F-FDG PET/CT, 18F-fluorodeoxyglucose positron-emission tomography/computed tomography; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; Rt, right; SUV max, maximum standardized uptake value; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.](image-url)
thickening and enhancement adjacent to syphilitic gumma could be of great significance [6]. However, these two points did not apply to syphilitic gumma located in the basal ganglia, as in the present case, and misdiagnosis may occur more frequently in clinical practice. Therefore, if screening tests for syphilis are positive, a syphilitic gumma should be suspected. Early diagnosis of neurosyphilis and appropriate antibiotic treatment leads to notable clinical improvement, making brain biopsy or surgical therapy unnecessary, as in the present case. In our patient, PET/CT showed increased FDG uptake in the cerebral lesion, which was suspected to be a high-grade glioma, malignant lymphoma, or metastatic tumor. Previous studies have reported that FDG uptake can be higher or lower than the normal surrounding area on PET/CT scans of syphilitic cerebral lesions [6-8]. Because the pathological features of syphilitic gummas are classic examples of granulomatous inflammation [5,6], PET/CT findings of syphilitic gummas may relate to the degree of inflammatory activity similar to other inflammatory diseases [9]. Interestingly, our patient's lesion enlarged temporarily despite antibiotic treatment (Fig. 2). To the best of our knowledge, no previous reports have described temporary enlargement of a syphilitic gumma after instituting treatment. We were therefore concerned about the efficacy of the antibiotic treatment and accuracy of the diagnosis. We continued treatment with PCG because his condition had improved and this decision proved to be correct, as evidenced by subsequent shrinkage of the lesion. One possible cause of the temporary enlargement of our patient's gumma is that this was its natural course. However, the immunopathologic features of syphilitic gummas are granulomatous reactions to long-term smoldering infection with Treponema pallidum and/or its residual antigens [10], which did not support the hypothesis that acute enlargement of our patient's lesion is caused by natural course. Another possible explanation is development of JHR, which involves an increase in inflammatory cytokines within 24 h after antibiotic therapy for spirochetal infections [11]. JHR is caused by the rapid uptake of antibiotic-altered spirochetes by polymorphonuclears. Because the central area of syphilitic gumma can contain viable organisms that are separated from the surrounding tissue, JHR can cause acute focal inflammation in syphilitic gumma and results in temporary enlargement of our patient's lesion after antibiotic therapy.

Because the rates of syphilis have recently increased in many parts of the world, including Japan, cerebral syphilitic gummas mimicking tumors may present more frequently in the future [2-4]. Our case indicates that cerebral gummas should be included in the differential diagnosis of any intracranial mass lesion, even if the lesion is located in the basal ganglia and/or shows ring enhancement on brain MRI and/or increased FDG uptake in PET/CT. We believe this is the first report of temporary enlargement of a cerebral gumma despite antibiotic treatment; with resolution of the lesion with continuing antibiotic treatment. Our case indicates that temporary enlargement of a probable gumma after instituting antibiotic treatment should not prompt cessation or change of the antibiotics.

![Fig. 2. Medical treatment of the patient after admission to our hospital and axial brain MRIs (upper column, gadolinium-enhanced T1WI; lower column, FLAIR) on Days 1, 19, 27, 43, 86, and 379 after admission. On Day 1, gadolinium-enhanced T1WI showed a lesion with ring enhancement in the right lenticular nucleus, and FLAIR showed white matter edema surrounding the enhanced lesion. On Day 19, the ring-enhancing lesion as visualized on gadolinium-enhanced T1WI and white matter edema on as visualized on FLAIR images had enlarged despite antibiotic treatment. On Days 27 and 43, the ring-enhancing lesion on gadolinium-enhanced T1WI and white matter edema on FLAIR had decreased in size after continuous antibiotic treatment. On Day 86, the enhancing lesion on gadolinium-enhanced T1WI was still faintly present, but the white matter edema on FLAIR had completely resolved. On Day 379, the lesion on gadolinium-enhanced T1WI had also completely resolved. AMPC, amoxicillin; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; PCG, penicillin G; PSL, prednisolone; T1WI, T1-weighted imaging.](image-url)

Table 1
The course of serum and CSF findings.

| Admission day | 5   | 12  | 43  | 106 | 148 | 197 | 379 |
|---------------|-----|-----|-----|-----|-----|-----|-----|
| PRP titer (Serum) | 5.7 | 4.6 | 4.2 | 3.3 | 3.2 | 2.8 |     |
| Cell count (/μL) (CSF) | 120 | 10  | 9   | 12  |     |     |     |
| Protein (mg/dL) (CSF) | 149 | 84  | 58  | 64  |     |     |     |
| PRP titer (CSF) | 3.2 | 2.3 | 1.8 | 1.0 |     |     |     |
Declaration of Competing Interest

The authors declare no conflicts of interest.

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CRediT authorship contribution statement

Yoshiaki Takahashi: Conceptualization, Writing – original draft, Supervision. Nobutoshi Morimoto: Conceptualization, Writing – review & editing. Mizuki Morimoto: Visualization. Shunsuke Mori: Visualization. Yu Takahashi: Visualization. Tomotsugu Ichikawa: Visualization. Kyoko Yokota: Writing – review & editing, Visualization. Toru Yamashita: Writing – review & editing, Visualization.

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