

## Atypical Radiological Presentation of Neurosyphilis Mimicking Multiple Metastatic Tumors: a Case Report

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### ABSTRACT

Multi-center intracranial syphilitic granuloma is an unusual presentation of neurosyphilis which may mimic metastatic tumors leading to misdiagnosis and unnecessary surgery. We report a case of a 52-year-old woman with multiple intracranial lesions with homogeneous contrast enhancement, which mimicked the appearance of multiple metastases. A biopsy was performed. Pathological diagnosis of the lesion was chronic granulomatous inflammation. Taking the laboratory findings in to account, intracranial syphilitic granuloma was diagnosed. Anti-syphilis treatment was followed. The patient recovered without neurological deficit or radiological abnormalities. Literatures were reviewed for the radiological differential diagnosis of neurosyphilis and other multiple lesions with contrast enhancement, as well as the treatment and assessment of neurosyphilis.

**Keywords:** Syphilis, Intracranial syphilitic granuloma, Differential diagnosis

### INTRODUCTION

As a sexually transmitted disease, syphilis had been effectively controlled in the last three decades, while its incidence has raised in recent years [1,2]. It is challenging to make a pathological diagnosis of syphilitic granuloma only based on symptoms and radiological findings, but understanding of radiological feature of this entity is important because appropriate radiological diagnosis of neurosyphilis may prevent unnecessary open surgery or biopsy.

### CASE DESCRIPTION

#### History and Physical Examination

A 52-year-old woman presented with a 3-month of recurrent headache and dizziness was admitted to our hospital. The headache was intermittent, can be alleviated by rest. The patient had no fever, chills, or weight loss. She had no history of trauma or cancer. She had a single sexual partner, denied any history of exposure to sexually transmitted diseases.

Physical examination revealed no obvious neurological deficits.

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#### Laboratory and Radiographic Evaluation

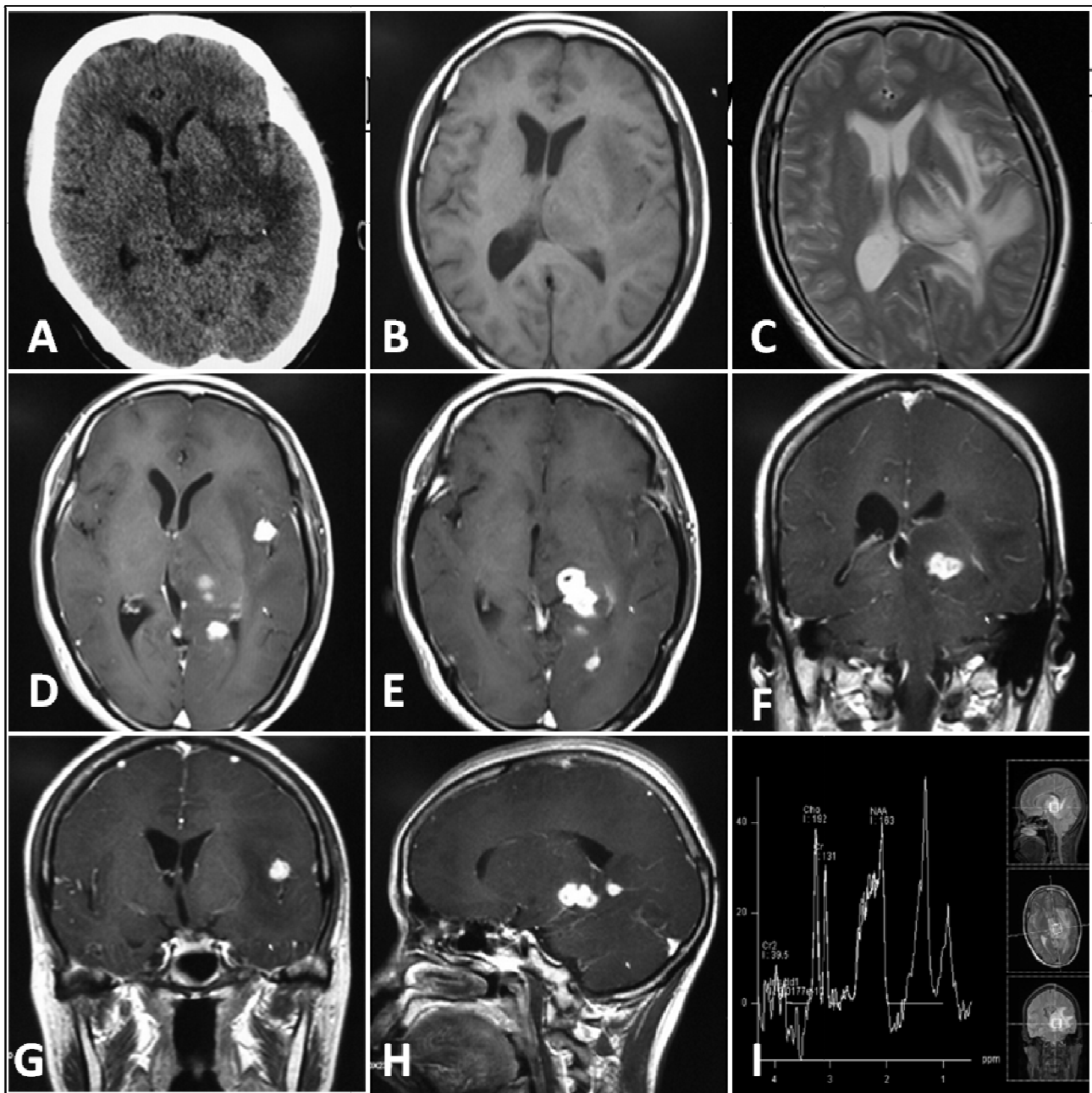
Syphilis serology test was positive, with a syphilis RPR (rapid plasma reagin) titer 1:8. Lumbar puncture was performed, the venereal diseases research laboratory of cerebral spinal fluid (VDRL-CSF) test was positive with syphilis RPR titer of 1:4.

Magnetic resonance imaging (MRI) indicated multiple lesions with homogeneous enhancement, in the left temporal and insular lobe, thalamus and basal ganglia, which mimicked the appearance of multiple metastases (**Figure 1**).

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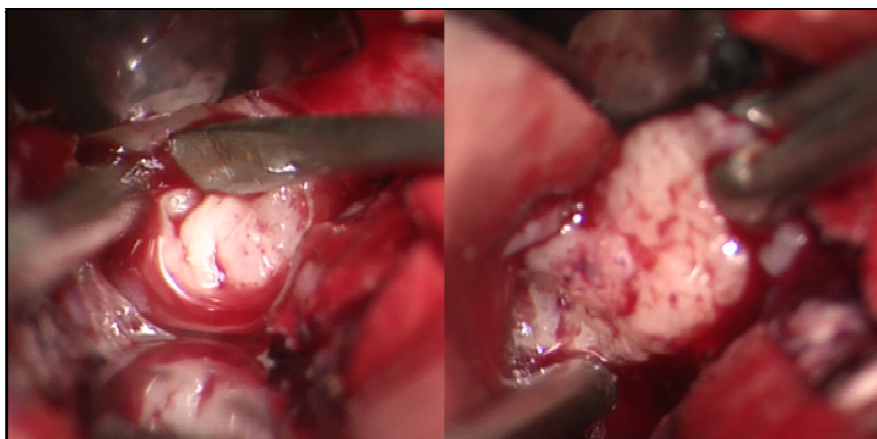


**Figure 1.** The CT and MR images of this patient. A: cranial CT scan showed mass effect on the left side of the brain with finger-like edema. B-H: Gadolinium enhancement MR showed homogeneous enhanced lesions in the left temporal and insular lobe, thalamus and basal ganglia. I: MRS showed a relative normal ratio of Cho/NAA ( $<1$ ), lactic peak was visible indicating anaerobic metabolism inside the lesion.

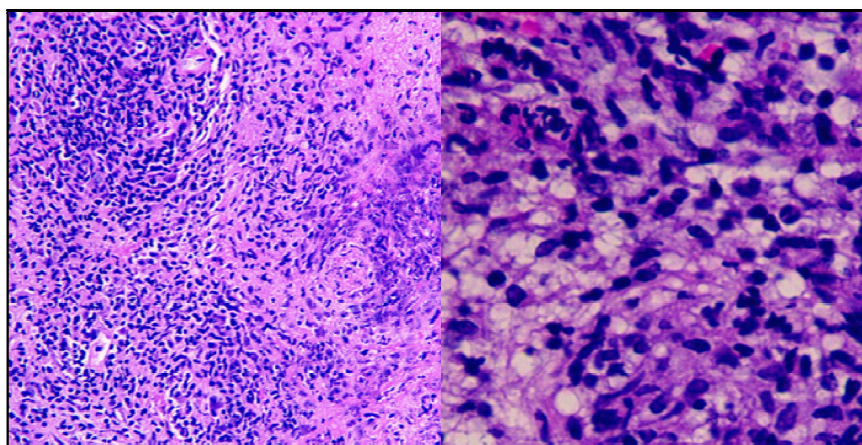
#### Surgical Findings and Pathological Results

An open biopsy surgery was performed. Under the microscope, the lesion was white colored, not well demarcated from the circumstantial brain tissue with normal blood supply, mimicking normal white matter but with a slightly harder texture (**Figure 2**). Intraoperative frozen

sections revealed an inflammatory granuloma. Pathology of paraffin embedded section demonstrated a granuloma with massive plasma cell infiltration and vasculitis (**Figure 3**).



**Figure 2.** Surgery screen shot showing the lesion was white colored, not well demarcated from the brain tissue with normal blood supply, the lesion mimicked normal white matter but with a slightly harder texture.



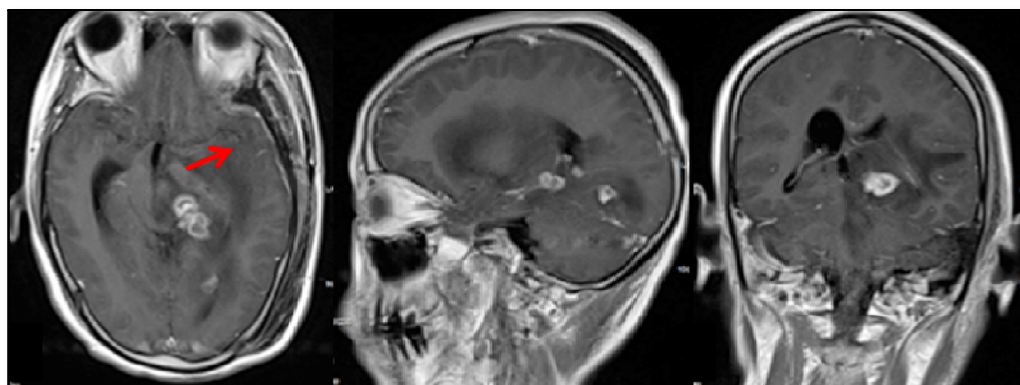
**Figure 3.** Paraffin embedded section of the lesion. Granuloma with massive plasma cell infiltration and vasculitis.

### Systemic Treatment and Follow-Up

Postoperative MRI performed within 72 hours after the operation confirmed the left temporosphenoidlobe lesion had been resected (**Figure 4**). Standard antibiotic treatment for syphilis was administered with intravenous penicillin G (24 million U/day) for 14 days. Methylprednisolone was

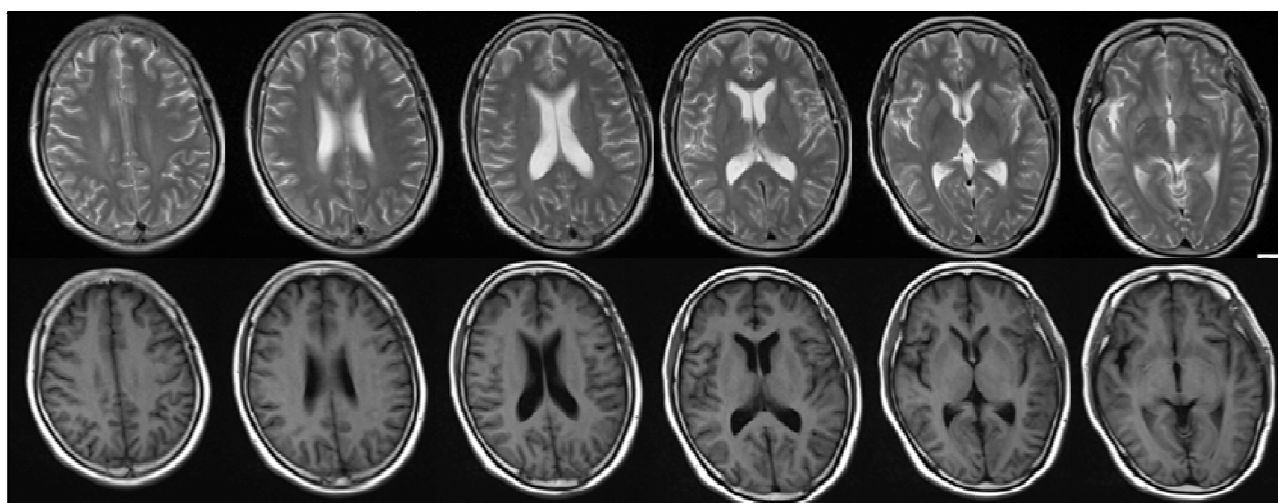
administered at early stages to avoid Jarisch-Herxheimer reaction.

At the last visit half a month after the systematic treatment for syphilis, the patient's symptom was relieved; the intracranial multiple lesions were disappeared on MRI scan (**Figure 5**). The patient was lost in the long-term follow up.



**Figure 4.** Post-operative MRI scan showed the left temporosphenoidlobe lesion had been resected.





**Figure 5.** The enhanced lesions and intracranial edema disappeared in the MRI follow-up 15 days after the systematic treatment.

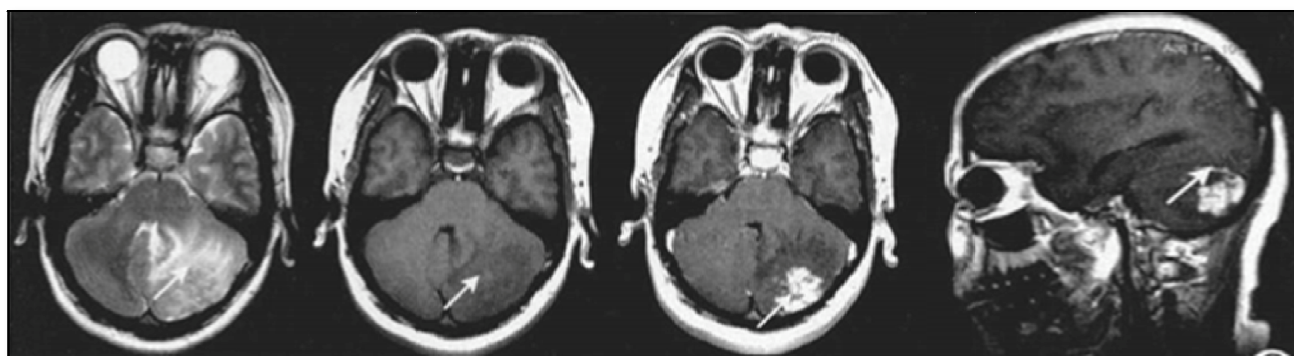
## DISCUSSION

In this case report, we presented an atypical case of intracranial neurosyphilis with multiple enhanced lesions. These findings are often confounding with metastatic tumors. Although the laboratory test suggested the diagnosis of neurosyphilis, the metastatic tumors cannot be excluded, so biopsy surgery was performed. In the discussion, we reviewed the literatures and summarize the key points for the differential diagnosis of neurosyphilis granuloma and metastatic tumors.

### 1. Radiological Characteristics of Syphilitic Granuloma

Neurosyphilis can be radiologically classified as syphilitic granuloma and syphilis encephalopathy. The MRI features

of syphilitic granuloma includes tubercular and uneven enhancement, surrounded by large heterogeneous enhancement edema (**Figure 6**) [3,4]. The common MRI findings of syphilis encephalopathy can be described as brain atrophy, cerebral infarction, encephalitis and meningitis. The MR angiography may help to detect the major artery stenosis or occlusion caused by syphilis [5,6]. The Magnetic Resonance Spectroscopy (MRS) often demonstrates a decreased NAA peak and increased Cho peak, Lactate peak is often visible because of anaerobic metabolism within the lesions. History of primary tumors is common in brain metastases. In some cases, tumor markers can be positive.



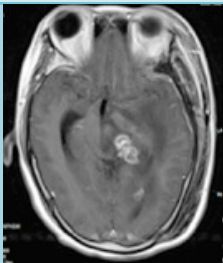
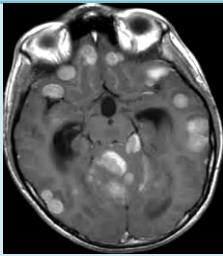
**Figure 6.** The MRI features of syphilitic granuloma: tubercular and uneven enhancement in the left cerebellum, surrounded by large heterogeneous enhancement edema.(from literature [3])

In addition, the syphilitic granuloma should be differentiated from other causes of granuloma, such as cryptococcus, tuberculosis, brain toxoplasma gondii, parasites etc. The clinical history, imaging, and appropriate laboratory tests

can be helpful for the differentiation. **Table 1.** summarized the image manifestation of syphilitic granuloma and intracranial metastases.



**Table 1.** The radiological differentiation of neurosyphilis and intracranial metastasis

| Diseases                    | Typical image                                                                      | Characteristic                                                                                           | Common features                                                               | Difference                                         |
|-----------------------------|------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------|
| <b>Syphilitic Granuloma</b> |   | Tubercular and uneven enhancement, surrounded by large heterogeneous enhancement edema belt.             | Wide spread edema; MRS: decreased NAA peak, increased Cho peak, lactate peak. | Tend to locate in midbrain, near the basal ganglia |
| <b>Metastatic Tumors</b>    |  | Enhancement in 95% cases, circular nodules, thicker and irregular ring wall; Small tumor and large edema |                                                                               | Tend to locate between gray and white matter       |

## 2. Diagnosis and Treatment of Syphilitic Granuloma

In addition to the radiological examinations, laboratory tests are important for the diagnosis of neurosyphilis [7]. The Centers for Disease Control and Prevention (CDC) of the United States has established criteria for the diagnosis of neurosyphilis: serological test: the helicoid antigen serum test is positive. Cerebrospinal fluid examination including cerebrospinal fluid cell count ( $WBC > 5/mm^3$ ) or abnormal protein determination or the venereal diseases research laboratory of cerebral spinal fluid (VDRL-CSF) is reactive, and associated with neurological symptoms and signs. The CSF VDRL is highly specific for the diagnosis of neurosyphilis, but the sensitivity is not satisfactory. Other experiments are neither sensitive nor specific. However, if the cerebrospinal fluid fluorescent treponemal antibody absorption test (FTA-ABS) is negative, the diagnosis of syphilis can be eliminated.

About 4%-10% of syphilis will develop into neurosyphilis, and the latency is about 4 to 7 years, if the patients fail to get timely, regular and adequate treatment, the early stage syphilis would develop to substantial neurosyphilis [8]. Penicillin remains the most effective and recommended therapy [1, 2]. The recommend treatment guidelines of neurosyphilis are: penicillin, 18-24 million U/d for 10-14 d, followed by benzathine penicillin 2.4 million U, intramuscular injection once a week, for 3 times. Alternative treatment: procaine penicillin, 2.4 million U, intramuscular, once a day, Probenecid 500 mg, orally, 4 times a day for 10-

14 d. Followed by benzathine penicillin 2.4 million U, intramuscular injection, once a week, for 3 times. If the patient is allergic to penicillin: 2g of ceftriaxone, intramuscular or intravenous drip, once a day, for 10 -14 d is recommended [9].

## 3. Will Syphilitic Granuloma Disappear After Treatment?

Clinical studies suggested that with standard treatment, only a few cases of the abnormalities of early stage neurosyphilis is reversible, while for some patients with severe neurological symptoms and signs, it is hard to fully recover even after treatment [10]. In our case, both the symptom and signs and the radiological abnormalities were well controlled and eliminated by standard penicillin treatment, which was fortunate but not common.

The main components of syphilisgranuloma is the proliferation of endothelial cells and fibrous tissue cells, accompanied by a large number of plasma cells, lymphocytes infiltration, Low dose radial therapy (20-30 Gy) may help to alleviate the symptom and shrink the lesion, without causing damage to normal brain tissue [11]. However, radiation does not kill the syphilis helicoid. Therefore, if neurologic symptoms were not alleviated by antisiphilic treatment, radiotherapy may be considered to improve the quality of life.

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