Nocardial cerebral abscess associated with mycetoma, pneumonia and membranoproliferative glomerulonephritis

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ABSTRACT

Nocardial brain abscesses remain a clinical challenge. We successfully treated a patient with nocardial brain abscess, mycetoma, pneumonia, and glomerulonephritis. Nocardial soft tissue involvement, mycetoma, is well known. However, the fact that Actinomycetoma can metastasize may not be as well appreciated. Association between nocardiosis and glomerulonephritis should be better clarified.

Key Words: Cerebral abscess, glomerulonephritis, mycetoma, nocardiosis.

CASE REPORT

A 49-year-old male, who was a businessman, was admitted to our hospital with complaints of severe edema of the lower extremities. Clinically, the diagnosis was nephrotic syndrome. A renal biopsy showed fibrosis with mesangial hypercellularity and tubular atrophy on light-microscopy. Immunofluorescent staining revealed deposition of IgG and C3 at the glomeruli, basal membranes and mesangia. The diagnosis of a membranoproliferative glomerulonephritis was established and the patient received oral treatment with prednisolone at 60 mg/kg per day. Because of persistent proteinuria, he underwent monthly intravenous pulse cyclophosphamide therapy. When the patient was hospitalized for his third course of cyclophosphamide therapy nine months later, he was febrile and physical examination revealed a tender mass in the anterolateral region of the left thigh. Laboratory findings revealed: white blood cell count = 13360/mm3 (normal range 4-10 x 10^9/L), hemoglobin =10.4g/dL (normal range 11-16g/dL), hematocrit =32.1% (normal range 37-50%), erythrocyte sedimentation rate = 63 mm/hr (normal range <25mm/hr), CRP =16.2 mg/dL (normal range <0.8mg/dL), urea=35mg/dL (normal range 10-50mg/dL), creatinine =0.8mg/dL(normal range 0.7-1.2mg/dL), AST=68U/mL (normal range 14-36 U/l), and ALT=116/mL (normal range 9-52 U/l). There was 5gr/day proteinuria. A magnetic resonance imaging (MRI) of the left lower extremity showed a mass lesion within the vastus
lateralis muscle (Figure 1). The mass had cystic characteristics and was multiloculated. The microbiological diagnosis was made from the aspirated pus of the mass lesion in the left lower extremity. The specimens, cultured on sheep blood agar, brain-heart infusion agar and Sabouraud dextrose agar plates were incubated at 37 °C in the presence of 10% CO₂ plus air. Gram stained direct microscopic examination of aspirated pus showed gram-positive cocci, gram-positive filamentous branching bacilli, and polymorphonuclear neutrophils. The smear was stained modified acid-fast. After incubation for 24 hrs, typical smooth, yellow pigmented, hemolized colonies were tested with catalase test, oxidase test, coagulase test and ID 32 Staph test (Bio Merieux, Nutingen, Germany), oxacillin on the Mueller-Hinton agar. Methicillin sensitive Staphylococcus aureus was identified. After 3 days of incubation, typical dry chalky dull, tough colonies appeared on the media. All species were gram-positive branching bacilli. Theses bacilli were identified as Nocardioides species. The identification was made using biochemical and physiologic tests which utilize casein, tyrosine, xanthine, hypoxanthine, urease, gelatine, lactose, xylose and arabinose. The isolates did not utilize casein, tyrosine, xanthine, hypoxanthine and were urease positive. Gelatin hydrolysis was negative, as was acid production from lactose, xylose and arabinose. These features identified the causative agent as Nocardia asteroides complex. An antibiotic sensitivity test performed on Mueller-Hinton agar using the disc diffusion method showed that there was sensitivity to cotrimexazole, cefotaxime and tobramycine after 72 hrs. Although the NCCLS advises agar dilution tests for Nocardiae, agar dilution test could not be performed in our laboratory at that time (13). Instead, the disk susceptibility was done using susceptibility break points for gram-positive bacilli. The specific species, however, could not be identified with routine laboratory examination.

The patient was diagnosed as having a mycetoma and antibiotics therapy was started with orally administered trimethoprim /sulphamethoxazole (TMP/SMX) and intravenously...
administered cephazoline. The following day, the patient had a seizure and developed amnesia. Cranial MRI studies were consistent with abscess formation in the left temporo-occipital region (Figure 2). Because of suspicion of multisystem nocardiosis, the patient underwent a thorax CT scanning. It revealed areas of consolidation and atelectasia in the basal segments of the left lung, and centrally necrotizing lymphadenopathy in the left paraaortic region. Since there was no adequate response to medical therapy with TMP/SMX for two months, the patient underwent a left temporo-occipital craniotomy and the abscess was excised with its capsule (Figure 3). Using the same isolation methods mentioned above (including the smears), Nocardia Asteroides complex was again identified in the cultures of the drainage specimen obtained from the cerebral abscess excised on July 26, 2004. After the surgery, the patient recovered progressively. At the fourth month after the surgery, medical therapy with TMP/SMX continued with a dose of 10 mg/kg trimethoprim per day and the patient had no complaints. The laboratory findings remained normal. Post-operative cranial MR images showed no abscess in the brain.

Discussion. Nocardiae are gram-positive, aerobic actinomycetes found naturally in the soil, air and sewage (1,12). Members of the Nocardia Asteroides complex account for 80% of cases of noncutaneous invasive nocardiosis and most of systemic or central nervous system nocardiosis (6). Nocardial brain abscesses remain a clinical challenge associated with high mortality and morbidity rates (2, 6, 9, 12, 14).

The patient was a businessman and hence inoculation of the nocardia could not be directly related to his occupation. It is generally accepted that the primary infection by nocardiae is most commonly acquired via the respiratory tract (6). Primary pulmonary lesions may be subclinical or overt, chronic, or rarely, acute (3). Nocardia asteroides may cause mycetomas. Mycetoma is a chronic granulomatous process resulting from the implantation of one of various fungi or
actinomycetes into soft tissues, usually of the foot (7, 11). The disease is almost painless and there are few or no constitutional symptoms unless there is a secondary bacterial infection (7). The microbial colonies form grains and sinuses in soft tissues. A literature survey revealed that the flora causing mycetoma in Turkey consists of various pathogens such as Nocardia asteroides, Nocardia brasiliensis, Scedosporium apiospermum, Aspergillus niger, and Streptomyces madurae (4).

Nocardiosis is an opportunistic infection that has been noted in patients with malignancies, systemic lupus erythematosus, long term steroid users, HIV infection and transplant recipients (2, 5, 8). However, recent data demonstrate that central nervous system (CNS) nocardiosis is as common or more prevalent in patients with normal immune systems (12). Therefore, nocardiae may have a predilection for some, but not all of the immunocompromised patients. For example, most of the transplant patients reported to have nocardiosis are renal transplant recipients. In 1998, Matthew et al reported an association between mesangiocapillary glomerulonephritis and nocardiosis (10). There are similarities between our patient and their patient. There were no primary immune deficiency disorders in either cases. Both patients had glomerulonephritis and received corticosteroids, although the patient in the case report of Matthew et al received prednisolone up to 100mg daily for 6 years because of cluster headaches not for glomerulonephritis. In our case, it is unclear whether there was a predisposition to Nocardia infection directly linked to the glomerulonephritis or if it was a secondary consequence of prolonged immunosupression due to treatment with prednisolone 60 mg daily and cyclophosphamide for 9 months. This therapy could have aggravated a silent chronic infection in the soft tissue of the leg, a mycetoma by Nocardia asteroides. In the literature, average duration of the symptoms in mycetomas has been calculated as 8 years (7). However, lesions in the lungs and in the brain were revealed in the relatively short time period after the symptoms of mycetoma
appeared in our case. Also, Matthew et al made the diagnoses of glomerulonephritis and nocardia in their case nearly simultaneously. Therefore, there may be a link between glomerulonephritis and Nocardiosis since the diagnoses of these clinical entities could be made sequentially in a relatively short time in the both cases.

In our case, the surgical excision of the nocardial brain abscess was successful. In 2002, Lee et al recommended that nocardial cerebral abscesses be initially treated via aspiration, with aggressive surgical management being reserved for the small proportion of patients who do not respond to minimally invasive surgery (6). However, only one patient in their series was discharged in good condition after a single aspiration procedure. In their other patients, more than one aspiration or excision of the abscess were necessary to achieve a positive outcome. These findings supported Mamelak et al who reviewed the medical literature in 1994 and stated that the mortality rate among patients undergoing craniotomy and excision (24%), was less than half that among patients undergoing aspiration and drainage alone (50%) (9).

Mycetomas may be confused with granulomas, abscesses, or benign soft tissue tumors and this may result in delayed diagnosis of a possible nocardial infection. It is well understood that nocardial mycetoma may lead to new lesions in the vital organs such as the lungs and brain. However, the fact that Actinomycetoma can metastasize may not be as well appreciated. Additionally, the relationship between nocardiosis and glomerulonephritis should not be regarded solely as an effect of immunosuppression but should also be clarified in terms of specific pathophysiological mechanisms. Surgical excision of nocardial cerebral abscesses instead of performing an aspiration procedure may be more beneficial in some patients.

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REFERENCES


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FIGURE LEGENDS

Figure 1. The lower extremity MR imaging showing a multiloculated cystic mass, measuring about 10x3 cm.

Figure 2. The cranial sagittal T1-weighted MR image showing an abscess formation in the left temporo-occipital region.

Figure 3. The cerebral abscess mass after complete removal.