Successful Treatment of Pituitary Abscess with Oral Administration of Sparfloxacin

Yujiro Uchida¹, Noriko Tsuchimochi¹, Miwako Oku¹, Naoko Fujihara¹, Nobuyuki Shimono¹, Kaoru Okada¹ and Mine Harada¹ ²

Abstract

Pituitary abscess is a rare infection and it is difficult to make the correct diagnosis. It is usually treated by a combination of surgical drainage and intravenous administration of antibiotics. We describe a 74-year-old woman with recurrent meningo-encephalitis due to pituitary abscess. The abscess increased in size in spite of the intravenous administration of panipenem/betamipron (PAPM/BP), clindamycin (CLDM) and chloramphenicol (CP). Finally she was successfully treated with oral administration of sparfloxacin (SPFX) without operation.

Key words: intrasellar cystic mass, meningo-encephalitis, magnetic resonance imaging, sparfloxacin


Introduction

Since the first case of pituitary abscess was reported in 1912, only 121 cases have been reported (1). Pituitary abscess is a rare but life-threatening disease. Pre-CT scan era, Donimue and Wilson reviewed 29 patients, with 28% mortality, and this rate increased to 45% when meningitis was involved (2). The recommended management of pituitary abscess is surgical drainage by the transsphenoidal approach followed by antibiotic treatment (3-5). Furthermore, the standard empiric treatment of brain abscess is based on parenteral administration of cephalosporins or carbapenems. We present a case of pituitary abscess that was successfully treated with oral administration of sparfloxacin (SPFX) after failure of standard therapy (1).

Case Report

A 74-year-old woman with ear fullness feeling was diagnosed as bilateral otitis media with effusion at an otolaryngology clinic 2 years before admission to our hospital. She had received regular outpatient treatment with periodic drainage of the middle ears. She had a headache and nausea after drainage in April 1999, and a drain tube was placed in the right middle ear the following day. Her symptoms improved in several days. In May, however, high fever and nausea appeared with loss of consciousness and she was admitted to a rural hospital. She was diagnosed as bacterial meningo-encephalitis with negative gram stain or cultures of the cerebro-spinal fluid (CSF). Clinical recovery was achieved after 2 weeks of treatment with cefotaxime (CTX) (2 g/day), dexamethasone (DEX) (4 mg/day), glycerol and high-dose immunoglobulin (5 g/day). Then she had recurrent meningitis twice and was treated with the same medication. To investigate the cause of these repeated meningitis symptoms, she was referred to us in August 1999.

On admission, she had no complaint including headache, nausea, fatigue, or visual disturbance. Her body temperature was 36.7°C. Physical examination revealed no abnormality with absence of neck stiffness or Kernig’s sign. Heart sounds were normal with no murmur and normal vesicular breath sounds were heard on the chest.

Laboratory examinations revealed a normal white blood cell count (WBC) with differentials of neutrophils 62% and lymphocytes 34%. An erythrocyte sedimentation rate (ESR) was 44 mm/hr, and C-reactive protein (CRP) 0.2 mg/dl. Serum level of total protein was 6.2 g/dl, lactate dehydroge-
Figure 1. Pituitary mass examined by T1-weighed images of magnetic resonance imaging (MRI).
These are sagittal image (A, C, E, G, I, K, M) and coronal image (B, D, F, H, J, L, N). A and B, on admission in August 1999; C and D, after treatments with panipenem/betamipron and clindamycin in mid-October; E and F, after treatments with chloramphenicol in mid-November; G and H, after 4 weeks treatments with sparfloxacin in mid-December 1999; I and J, in late January 2000; K and L, in February 2002; M and N, in January 2005.

nase 485 IU/l, total cholesterol 268 mg/dl, triglyceride 173 mg/dl, and glucose 89 mg/dl.

The patient’s cerebrospinal fluid (CSF) was slightly opalescent with a glucose concentration of 41 mg/dl, a protein level of 56 mg/dl, a white cell count of 78/μl with 3% polymorphonuclear leukocytes (PMNs) and 97% lymphocytes, and no malignant cells. No organisms were detected with gram staining or acid fast staining and by CSF culture. Detection of Mycobacterium sp. by PCR and Cryptococcus antigen by latex agglutination assay were negative. The chest and abdominal radiographs showed no abnormality.

Although symptoms of meningitis were not manifested on admission, bacterial infection and malignant tumor in para-meningeal area were considered as a tentative diagnosis, in which case antibiotic or steroid therapy was effective for repeating meningitis. T1-weighted image of MRI revealed an intrasellar cystic mass with ring enhancement (Fig. 1A and B). High intensity signal in the posterior lobe was seen at the posterior side of the intrasellar region. The cystic mass was considered as an abscess or adenoma.

On the twentieth day after admission, she had a high fever with loss of consciousness and neck stiffness. Laboratory examinations revealed that a WBC count of 10,900/μl with differentials of neutrophils 81% and lymphocytes 16%, CRP 7.7 mg/dl, and glucose 173 mg/dl. CSF was opalescent with a glucose concentration of 32 mg/dl, a protein level of 273 mg/dl, a WBC count of 825/μl with 52% PMNs and 48% lymphocytes. Microbiological examination of CSF showed negative results for gram staining and CSF culture.

She was treated with ampicillin/sulbactam (ABPC/SBT) (6 g/day), CLDM (1,200 mg/day) and DEX (8 mg/day) for bacterial meningo-encephalitis. The antibiotic therapy was changed from ABPC/SBT to PAPM/BP because there was a possibility that the causative organisms might be antibiotic resistant. As shown in Fig. 2, her symptoms of meningitis were improved abruptly after PAPM/BP therapy. Levels of WBC and CRP returned to normal and a white cell count in CSF decreased. The intrasellar cystic mass was considered to be the abscess due to bacterial infection and the intravenous antibiotics were administrated for 8 weeks. After the
therapy, head MRI showed the intracellar mass increased in size (Fig. 1C and D). Therefore, she was retreated with chloramphenicol (CP), which had good brain tissue distribution and was a different kind of antibiotic than β-lactams. After the 4 weeks of the treatment she was followed by the examination of MRI, which revealed that the mass was still developing and approaching the optic chiasma, especially on the sagittal image (Fig. 1E and F). The antibiotic therapy was changed to SPFX, which was also excellent for tissue distribution among fluoroquinolones, because meningitis would be recurrent without controlling the mass size in consideration of the clinical history. After four weeks of the therapy with 300 mg of SPFX, MRI showed mass regression in size (Fig. 1G and H). She was discharged in December 1999. The size of the pituitary abscess did not increase and she had no symptom of meningo-encephalitis one month after her discharge (Fig. 1I and J). Since the intrasellar mass existed, the treatment was continued as an outpatient for one more year.

Over subsequent years, MRI was performed (Fig. 1K-N). The intracellar mass decreased in size even after finishing the therapy and the recurrence of meningitis has never been noted until January 2008.

**Discussion**

Causes of pituitary abscess have been suggested as follows: bloodstream infection, direct extension from a focus around the intracellar region such as paranasal sinusesitis, a disease following an intrasellar tumor, and post-operation. However, in half of the cases with pituitary abscess, the primary lesions were unknown (6). In the present case the patient had bilateral otitis media with effusion and received treatment with chronic draining of the ears, although a specimen from the drainage fluid was not tested for causal organisms. Computed tomography (CT) performed after the first antibiotic treatment in the end of May showed a small quantity of fluid in the right mastoid. This finding indicated that the direct invasion from the infected middle ear might have caused the formation of abscess, though the sphenoid sinusesis was not clear.

Previous reports have stated that the incidence of a pituitary abscess in the sellar mass was 0.48% (1) or 0.6% (7). Clinical symptoms of pituitary abscess reported include hypopituitarism (70.2%), visual disturbance (51.1%), meningitis (42.1%), and diabetes insipidus (42.1%) (6, 8). The cases without inflammatory and/or meningeal symptoms and signs are reported to be 30-42% (6, 9). Accordingly, it is difficult to reach a proper diagnosis of pituitary mass without operation, because one-third of pituitary abscess are reported to originate from infectious pituitary tumor, craniopharingioma and Rathke’s left cyst (3-5, 8, 10-12). In the present case, the meningitis repeatedly occurred, though she had no symptoms such as hypopituitarism and diabetes insipidus. During the clinical course, there were no findings of chronic hypertrophic pachymeningitis, in which the main clinical features are chronic headache and cranial nerve palsies and MRI findings are diffuse or localized thickening of the dura.

In the present case, we could not isolate any organisms from several blood and CSF cultures, and a biopsy was not performed. The organism causing bilateral otitis media was not found because biological tests were not performed at the otolaryngology clinic prior to admission. The major pathogens of chronic otitis media are considered to be aerobic organisms such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Proteus* spp. (13). Several studies reported...
that anaerobic organisms are detected in 8 to 59% of cases with chronic otitis media such as *Peptostreptococcus intermedium*, *Bacteroides* spp., and *Fusobacterium* spp. (13). We analyzed for bacteria-specific 16S ribosomal DNA by PCR (22, 23) and pneumococcal antigen (Binax NOW *S. pneumoniae* urinary antigen test; Binax, Portland, Maine), using the stocked CSF when the patient had the last recurrence of meningitis. But all of the tests were negative. Therefore, the pathogen in this case was not identified, however, it is suggested that gram-positive cocci such as *Staphylococcus aureus* or *Streptococcus* spp. may be a causative microorganism based on antibiotics susceptibility, underlying disease and MRI findings without gas production (14-17).

The management recommended for pituitary abscess is surgical drainage by the transsphenoidal approach followed by antibiotic treatment (3-5). Other approaches may involve a risk of intracranial dissemination of infection. Regardless of the surgical approach used, the surgeon should be aware of a risk of postoperative meningitis, infectious vascular lesion and CSF fistula (18). In the pre-CT scan era, Donigune and Wilson reviewed 29 patients and reported 28% mortality, and this mortality increased up to 45% when meningitis was also present (2). Boggan reported that surgical treatment should be limited to the cases based on the severity and chronicity of preoperative damage (19). In contrast, the improvement of pituitary abscess only with medication consisting of administration of CTX and metronidazol for 1 month and netilmicin for 15 days was also reported (20). In the present case, pituitary surgery was not performed because of the patient’s age and condition without visual disturbance. Although CTX and PAPM/BP + CLDM are effective to relieve the symptoms of meningitis, those antibiotics including CP were not effective against the pituitary abscess in our case, according to the abscess size defined by MRI.

SPFX has a good anti-gram-positive activity (21). Furthermore, SPFX is a hydrophobic fluoroquinolone as well as moxifloxacin (22) and has an excellent distribution to brain tissue (23). Some reports showed good activity of oral fluoroquinolones for brain abscess patients and most of them suffered difficult experiences with an empirical therapy with other drugs such as β-lactams (24-32). There were no reports of brain abscess infected with common organisms causing otitis media treated with oral fluoroquinolone therapies, but fluoroquinolone therapy was considered effective for brain abscess patients in some cases (Table 1).

In the present case, SPFX (100 mg ×3/day) was administered for 4 weeks. The concentrations of SPFX were 2.11 μg/ml and 2.79 μg/ml in blood 2 hours before and after administration, respectively, and 1.49 μg/ml in CSF 2 hours after administration. To increase the peak concentration in blood and CSF, the dose of SPFX should be increased to 300 mg once daily. Although we did not have a chance to examine the concentration in blood and CSF after we changed the dose of SPFX, the size of the intrasellar mass was decreased on MRI. These results indicate that oral administration of SPFX is an alternative and effective therapy for pituitary abscess.

### Conclusion

We described a case with recurrent meningitis due to the pituitary abscess. Although the pathogen could not be detected, oral administration of SPFX was a successful treatment for the pituitary abscess. The management recommended for pituitary abscess is surgical drainage. However, some recent novel antibiotics show good distribution capacity to the tissues. Therefore, medical treatment without operation should be considered as an effective and alternative

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### Table 1. Summary of Patients with Brain Abscess Treated with Oral Fluoroquinolones (FQs)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age / Gender</th>
<th>Underlying Condition</th>
<th>Causal organisms</th>
<th>Drugs before FQs treatment</th>
<th>FQs</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filhan V</td>
<td>49 / M</td>
<td>Transplantation 6)</td>
<td><em>Nocardia farcinia</em></td>
<td>CTRX, OR, IPM, ST</td>
<td>MFLX</td>
<td>Success</td>
</tr>
<tr>
<td>Fellows GA</td>
<td>57 / M</td>
<td>no</td>
<td><em>Nocardia farcinia</em></td>
<td>ST, IPM</td>
<td>MFLX</td>
<td>Success</td>
</tr>
<tr>
<td>Justiniano M</td>
<td>37 / M</td>
<td>SLE</td>
<td><em>Nocardia asteroides</em></td>
<td>TOB, CFFM, MNZ</td>
<td>CFX</td>
<td>Relapse</td>
</tr>
<tr>
<td>Nakamura S</td>
<td>76 / F</td>
<td>Pneumococcosis</td>
<td><em>Nocardia asteroides</em></td>
<td>MEMP, ST</td>
<td>CFX</td>
<td>Success</td>
</tr>
<tr>
<td>Schroder J</td>
<td>46 / F</td>
<td>Brain tumor 3)</td>
<td><em>Salmonella enteritidis</em></td>
<td>-</td>
<td>CFX</td>
<td>Success</td>
</tr>
<tr>
<td>Bonvin P</td>
<td>43 / F</td>
<td>no</td>
<td><em>Salmonella enteritidis</em></td>
<td>CTX</td>
<td>CFX</td>
<td>Success</td>
</tr>
<tr>
<td>Visudhiphan P</td>
<td>5 M / M</td>
<td>no</td>
<td><em>Salmonella newport</em></td>
<td>CTX</td>
<td>CFX</td>
<td>Success</td>
</tr>
<tr>
<td>Hart AJ</td>
<td>42 / M</td>
<td>no</td>
<td><em>Haemophilus paraphrophilus</em></td>
<td>CTX</td>
<td>CFX</td>
<td>Success</td>
</tr>
<tr>
<td>Fiepp M</td>
<td>- / M</td>
<td>HIV 5)</td>
<td><em>Rhodococcus equi</em></td>
<td>-</td>
<td>CFX*</td>
<td>Success</td>
</tr>
</tbody>
</table>

* a) Renal transplantation for end-stage renal failure.
* b) Adamantinomatous craniopharyngeoma (post-operative state).
* c) HIV: human immunodeficiency virus infection.
* * CTX and CFX were used on an outpatient basis.
treatment option against pituitary abscess.

References