CASE REPORTS

Endogenous *Nocardia asteroides* endophthalmitis in a patient with systemic lupus erythematosus

Y Ishibashi, R Watanabe, S Hommura, A Koyama, T Ishikawa, Y Mikami

Institute of Clinical
Medicine, University of
Tsukuba, Tsukuba
Department of
Ophthalmology
Y Ishibashi
R Watanabe
S Hommura

Department of Internal
Medicine
A Koyama
T Ishikawa

Research Centre for
Pathogenic Fungi and
Microbial Toxins,
Chiba University, Chiba,
Japan
Y Mikami

Correspondence to:
Dr Y Ishibashi,
Department of
Ophthalmology, Institute
of Clinical Medicine,
University of Tsukuba,
Tsukuba-shi, Ibaraki, 305
Japan.

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Abstract

We report a case of endogenous *Nocardia* endophthalmitis in a patient with systemic lupus erythematosus (SLE). He developed a parafoveal lesion in the right fundus while on systemic corticosteroid and antibiotic treatment. Initially we suspected a fungal origin and treated him with antifungal drugs. The intraocular disease progressed without improvement and advanced to the vitreous cavity. *Nocardia asteroides* was found in a specimen obtained at pars plana vitrectomy and was also cultured from the same specimen. The intraocular infection was controlled by antibacterial drugs, though the visual acuity of the right eye was reduced to only light perception owing to heavy vitreous opacity and secondary cataract. This case is the first report of endogenous *Nocardia* endophthalmitis in Japan and also the first case of this disease reported from outside the United States of America.

Nocardia asteroides is a Gram-positive, weakly acid-fast, filamentous, aerobic organism which is

generally considered to be a bacterium despite certain morphological and staining properties in common with fungi.¹ The clinical features of nocardial infection closely resemble those of fungal infections, though *Nocardia* has no sensitivity to antifungal agents. It is evident from some studies that nocardiosis is a disease of much greater frequency than was formerly recognised.^{2,3} Lung, skin and subcutaneous tissue, brain, and pleura are common sites of the infection. Haematogenous dissemination, usually from a primary pulmonary focus, has been estimated to occur in approximately one-third of the cases. Intraocular infection, a rare site, has been reported in 14 patients,⁴⁻¹⁴ typically leading to enucleation or death. Endogenous ocular dissemination has been found in patients with renal transplants,^{7,8} lymphocytic lymphoma,⁹ hypogammaglobulinaemia,¹⁰ Hodgkin's disease,¹¹ lupus erythematosus,¹² diabetes mellitus,¹³ and systemic sclerosis.¹⁴ We observed endogenous *Nocardia* endophthalmitis in a patient with systemic lupus erythematosus (SLE).

Case report

The subject was a 27-year-old man who had a history of admission to hospital with systemic eruption, fever, nasal bleeding, and photosensitivity. He was diagnosed as having systemic lupus erythematosus by a biopsy of the kidney when he was 14 years old. He was also admitted to hospital at 16 years old, 19 years old, and 24 years old with various symptoms considered to be unrelated to the systemic lupus erythematosus. The histopathological diagnosis by biopsy of the kidney was diffuse mesangial proliferation with adhesions, at his last admission to hospital. He took oral corticosteroid (prednisolone 10 mg/day) as an outpatient but stopped suddenly without consulting his doctor.

The patient developed systemic oedema and ascites, symptoms of nephrotic syndrome, at the beginning of March 1987, and entered the University Hospital of Tsukuba on 15 May, 1987. His condition was controlled with 60 mg of oral prednisolone. He had a fever of 39°C on 1 August. Multiple nodular shadows in the lungs were found on x-ray (Fig 1), and cavity formation was disclosed by roentgeno-tomography. The fever was reduced to 37°C by administration of antibiotics, but the patient complained of blurred vision in his right eye on 19 August. He

Figure 1: Chest x-ray showed multiple nodular shadows in the lung (arrows) when the patient had a fever of 39°C.

Figure 2: Right ocular fundus of the patient at initial examination. Temporal to the macula is an exudative lesion with thin retinal detachment.

was referred to the Department of Ophthalmology on 27 August 1987.

The visual acuity of his right eye was 20/25, and a slit-lamp examination disclosed a mildly inflamed conjunctiva. There was a moderate inflammatory reaction in the anterior chamber and vitreous body. No changes were recognised in the cornea or the lens. Ophthalmoscopic examination of the right eye disclosed a paramacular exudative lesion located temporally of the macula. The lesion was round, whitish yellow, 1 mm in diameter, slightly elevated towards the vitreous cavity, with a thin retinal detachment (Fig 2). In the left eye there were mild inflammatory cells in the anterior chamber and vitreous body, but no changes were found in the cornea, lens, or fundus.

We suspected initially fungal infection from his history and clinical features; moreover a *Candida* sp. was found in a culture of sputum. Itraconazole, 150 mg/day by mouth, a new triazole antifungal agent, was started for the ocular infection. Despite this treatment the retinal lesion developed gradually (Fig 3). Intravenous miconazole 1200 mg/day, was added to the therapy on 6 September, but the infection progressed without improvement. Pars plana vitrectomy with miconazole infusion (100 mg/l) was performed on 18 September, 1987. Gram-positive, filamentous organisms (Fig 4) were found in the specimen obtained at vitrectomy,

Figure 3: One week later the ocular lesion had gradually progressed in spite of taking oral itraconazole.

Figure 4: Gram-positive, filamentous organisms were found in the specimen obtained from a pars plana vitrectomy. (Gram stain, original magnification, $\times 100$).

and many orange colonies grew on heart infusion agar. This organism was determined as *Nocardia asteroides* by morphological features on Sabouraud agar and brain heart infusion agar (Fig 5), by microscopic features on a slide culture, and by biochemical and physiological studies such as analysis of cell wall compositions, ability to hydrolyse adenine, caseine, hypoxanthine, tyrosine, urea, or xanthine, and utilisation of acid production from various carbon sources.

Immediately after the diagnosis of nocardiosis on 22 September, 1987 the treatment was changed to oral trimethoprim (1600 mg) and sulfamethoxazole (320 mg) per day, but the ocular infection did not improve. On 30 September, in line with the results of a sensitivity test (Table I), intravenous cefotaxime (2 g/day), oral minocycline (200 mg/day), and intramuscular amikacin (100 mg/day) were started instead of trimethoprim and sulphamethoxazole. The ocular infection reacted gradually to this therapy. On 13 October, the doses of these drugs were reduced to 1 g of cefotaxime, 100 mg of minocycline, and 50 mg of amikacin. During this time intraocular and pulmonary infections were well controlled by the therapy.

After one month of treatment the infection had subsided, though the right ocular fundus was not observable, and visual acuity was reduced to only light perception because of secondary cataract and heavy vitreous opacity. There were no signs of chronic inflammation in his right eye, and B-scan ultrasonography

Figure 5: A macrocolony of *Nocardia asteroides* on brain-heart infusion agar (Difco) for three weeks at 27°C. The size of colony was 20 to 35 mm in diameter.

TABLE I *In vitro* susceptibility of this strain of *Nocardia asteroides* to various antimicrobial agents

Agent	MIC value (mg/l)*
Ampicillin	100.00
Amikacin	0.78
Cefotaxime	3.12
Gentamicin	50.0
Doxycycline	1.5
Minocycline	0.39
TMP-SMX†	25.0
SMX	100.0

* Minimum inhibitory concentration (MIC) was defined as the lowest concentration suppressing all growth during seven days of incubation at 27°C. Sensitivity disc agar (Nissui, Japan) was used.
 † TMP=Trimethoprim. SMX=sulfamethoxazole, combination in fixed-weight ratio (1:5).

showed no retinal detachment at the end of therapy. Moreover, the left eye had no inflammation in the anterior chamber or the vitreous, and the visual acuity remained at 20/20. The pulmonary infection also reacted to the systemic treatment, and the patient was discharged on 18 November, 1987.

Discussion

Endogenous *Nocardia* endophthalmitis is disseminated from the primary site of infection, mainly from pulmonary lesions, and has been reported in only 14 patients (Table II). All were from the United States. In 1961 Murray and associates³ stated that no documented cases had been found in the oriental literature. Although nocardiosis has been recognised throughout the rest of the world, most reports on it have originated from the United States and Europe. This case is the first report of endogenous *Nocardia* endophthalmitis in Japan and also the first case from outside of the United States. All reported cases of endogenous endophthalmitis were caused by *Nocardia asteroides* except for one case which was not determined in detail.⁷ Our case was also caused by *N. asteroides*. Beaman and associates² reported that *N. asteroides* accounted for 86% of infections clinically limited to the lung, 92% of central nervous system infections, and 73% of systemic infections.

Delays in the early diagnosis and treatment of nocardiosis are often due to confusion with pulmonary tuberculosis, systemic mycoses, and the closely related actinomycosis.² We initially confused the infection with one of fungal origin because of similarity of clinical features, the patient's past history, and cultivation of a

Candida sp. from the sputum. *Candida* sp. are sometimes cultured from the throat, intestinal duct, or sputum as clinically saprophytes. The correct diagnosis is imperative, because nocardiosis is refractory to antifungal agents. After pars plana vitrectomy *N. asteroides* was found to be the causative agent of the intraocular and pulmonary infections.

The distribution of nocardiosis by sex shows that men outnumber women by about 3:1,² though for endogenous intraocular infections men outnumbered women by about 7:1. Most patients have been between the ages of 21 and 50, though the age range for *Nocardia* infections in the United States is broader.² The 15 patients with endogenous *Nocardia* endophthalmitis were between the ages of 15 and 77 (average 46.2) years.

Presant and associates¹⁵ suggested that patients who had received corticosteroids or immunosuppressive therapy had a significantly higher mortality rate from localised nocardiosis than previously healthy persons or patients with serious underlying conditions but who were not receiving corticosteroids or immunosuppressive drugs. Ophthalmologists should consider endogenous *Nocardia* endophthalmitis as well as intraocular mycosis or tuberculosis when patients have metastatic infectious lesions in their ocular fundi while on corticosteroids or are on immunosuppressive therapy.

In this case the diagnosis was confirmed by examination of a specimen obtained from a pars plana vitrectomy. The diagnostic value of the vitrectomy was excellent, though the therapeutic effect was not clear. Sher *et al.*¹⁰ reported a case of bilateral intraocular *Nocardia* infection, in which the condition in the left eye partially resolved after pars plana vitrectomy whereas the right eye, which had not undergone vitrectomy, had active ocular infection at the patient's death. In their case the diagnosis was established before the vitrectomy, and the patient was treated with several drugs for nocardiosis. They found filamentous beaded organisms resembling *Nocardia* in a specimen removed at surgery, though cultures of this material, inoculated on to several media, showed no growth after four weeks of incubation. We considered that *Nocardia* was not alive in their case at the time of the vitrectomy. On the other hand *Nocardia* was confirmed by both direct examination and cultures of the vitreous specimen in our case, and

TABLE II Summary of reported cases

Study	Patient	Organism	Steroid	Immunosuppressive drug	Previous disease
Davidson and Foerster ⁴	46, M	<i>N. asteroides</i>	Yes	No	Gall bladder disease
Meyer <i>et al.</i> ⁵	67, M	<i>N. asteroides</i>	No	No	Gunshot wound
Meyer <i>et al.</i> ⁵	56, M	<i>N. asteroides</i>	?	?	?
Burpee and Starke ⁶	20, M	<i>N. asteroides</i>	No	No	Leg wound
Panijayanond <i>et al.</i> ⁷	50, M	<i>N. asteroides</i>	Yes	Yes	Renal transplant
Jampol <i>et al.</i> ⁸	40, M	<i>N. asteroides</i>	Yes	Yes	Wegener's granuloma, renal transplant
Rogers and Johnson ⁹	77, F	<i>Nocardia</i> sp.	Yes	Yes	Malignant lymphoma
Sher <i>et al.</i> ¹⁰	38, M	<i>N. asteroides</i>	Yes	No	Hypogammaglobulinaemia
Lissner <i>et al.</i> ¹¹	60, M	<i>N. asteroides</i>	Yes	No	Hodgkin's disease
Smith <i>et al.</i> ¹²	23, M	<i>N. asteroides</i>	Yes	Yes	Lupus erythematosus, renal transplant
Bullock ¹³	15, M	<i>N. asteroides</i>	Yes	Yes	Paroxysmal nocturnal haemoglobinuria
Bullock ¹³	59, M	<i>N. asteroides</i>	No	No	Diabetes mellitus
Ferry <i>et al.</i> ¹⁴	66, M	<i>N. asteroides</i>	No	No	?
Ferry <i>et al.</i> ¹⁴	49, F	<i>N. asteroides</i>	Yes	No	Scleroderma
Ishibashi <i>et al.</i>	27, M	<i>N. asteroides</i>	Yes	No	Systemic lupus erythematosus

M=male. F=female.

adequate treatment was not performed at surgery, because the diagnosis was not definite. To determine the value of vitrectomy in the treatment of intraocular *Nocardia* infection we need more clinical experience and experimental study.

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