Lemierre Syndrome with Blepharoptosis

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Abstract

A 51-year-old woman was hospitalized with a high fever, occipital pain, blepharoptosis, and trismus. Enhanced CT showed thrombophlebitis of her left cavernous sinus, maxillary vein, and multiple pulmonary nodular lesions. $^{18}$F-FDG PET/CT showed significant uptakes in the same lesions. *Streptococcus constellatus* was detected in her blood. Therefore, she was diagnosed as a Lemierre syndrome variant. After administration of antibiotics, all symptoms, inflammatory reactions, and thrombi disappeared. Since Lemierre syndrome has life-threatening potential, early diagnosis and initiation of appropriate therapy are important. In this case, $^{18}$F-FDG PET/CT was useful to detect the focus and extent of infection.

Key words: Lemierre syndrome, septic pulmonary embolism, blepharoptosis, FDG-PET


Introduction

Lemierre syndrome is defined as an acute otolaryngologic infection, followed by thrombosis of the internal jugular vein, septicemia, and septic emboli (1). Although this syndrome is now called “forgotten syndrome”, it has a life-threatening potential if appropriate therapy is not performed (2). Here, we present a rare case of Lemierre syndrome variant, which exhibited multiple symptoms including blepharoptosis. We also propose the usefulness of $^{18}$F-FDG PET/CT ($^{18}$F-fluorodeoxyglucose-positron emission tomography/computed tomography) as a supportive tool to detect the focus and extent of infection in such cases.

Case Report

A 51-year-old Japanese woman presented at a primary care doctor with a high fever (40°C) and sore throat in late June 2008. Although she was treated with oral cefdinir (CFDN), her fever worsened. Five days later she had left blepharoptosis. On the following day she also had an occipital pain and thus she visited the emergency department of our hospital to be admitted. There was nothing noteworthy in her past history except for appendicitis at the age of 21 years old.

Physical findings on admission were as follows: height 166 cm, weight 60 kg, BMI 21.8 kg/m$^2$, pulse rate 73/min, regular rhythm, and blood pressure 108/63 mmHg. Her consciousness was clear and body temperature was 37.7°C, and SpO$_2$ was 98% with no oxygen. She had left blepharoptosis, slight redness of the pharynx, and spontaneous pain and tenderness of her left posterior cervical region. Her bulbar conjunctiva was not icteric, palpebral conjunctiva was not anemic, and light reflex was prompt and complete. She had no stiffness in her neck. The auscultatory findings of her chest and heart were basically normal. On neurological examination, other than the left blepharoptosis, she did not have any cranial nerve problems. She also had no motor, sensation, nor coordination abnormalities. In the examination by an ophthalmologist, she had left exophthalmos (Right 16 mm, Left 18 mm), measured by Hertel’s exophthalmometer. She had no visual loss, eyeball movement disorder, pupillary anomaly, nor venous stasis in her retina. Laboratory data on

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admission (Table 1) revealed a high inflammatory reaction and her serum biochemistry revealed hepatic dysfunction. All viral antibody tests and tumor marker levels, which were tested, were normal. After admission, we first suspected of an acute infection of the left neck and treated her with intravenous administration of cefotaxime sodium (CTX, 1 g ×2/day). In order to rule out the infection in her central nervous system (ex. meningitis), we performed lumbar puncture. But her cerebrospinal fluid examination was basically normal (Table 1). Her chest X-ray, head and abdominal computed tomography (plain), head magnetic resonance imaging, echocardiography, and abdominal ultrasonography revealed no obvious abnormality. Three days after admission, her fever remained high and the serum chemistry showed that her hepatic dysfunction had worsened. Thus, taking drug-induced hepatitis into consideration, we stopped CTX. On the following day, she had trismus due to swelling and tenderness in her left cheek. Therefore, emergency contrast-media-enhanced CT (from eye pit to chest) was performed. It showed the filling defects in her left cavernous sinus and maxillary vein (Fig. 1a and 1b white arrow), inhomogeneous high CT value of the fat tissue density around the sinus, and swelling of the left maseter muscle (Fig. 1a and 1b). These findings suggested thrombophlebitis of the left sinus and maxillary vein. It also showed multiple pulmonary nodules with ground glass attenuation around them (Fig. 1c). A dens serotinus continuous with left maxilla and the thickening of the mucosa of the left maxillary sinus suggested sinusitis (Fig. 1d).

On the basis of these findings, she was diagnosed as a Lemierre syndrome variant with pulmonary septic emboli due to thrombosis from the left cavernous sinus and maxillary vein. The left dens serotinus was considered to be the origin of infection. After diagnosis, she was started on intravenous meropenem hydrate (MEPM, 0.5×3 g/day) as a broad-spectrum antimicrobial agent. On the following day, Streptococcus constellatus (viridans) was detected by one of two sets of blood cultures, from blood drawn on admission day. Thus, the antibiotic was changed from MEPM to sulbactam sodium/ampicillin sodium (SBT/ABPC, 1.5 g ×4/ day), which was sensitive to Streptococcus constellatus (minimal inhibitory concentration; MIC ≤0.25 μg/mL).

Six days after admission, we performed 18F-FDG PET/CT in order to rule out any malignancy, which might be the cause of her fever. Interestingly, 18F-FDG was abnormally accumulated in the left cavernous sinus, the soft tissue around the left maxillary vein, and multiple lung nodular lesions (Fig. 2a-c), which were detected as abnormal findings by enhanced CT, suggesting that the inflammatory process existed in these lesions. And the coronal images showed no other abnormal uptakes except for the left maxillary region and the lung nodules (Fig. 2d).

After the administration of SBT/ABPC, all of her symptoms (left blepharoptosis, swelling of left cheek, trismus, and left posterior cervical pain) disappeared within a week. The data of laboratory analyses also improved (Fig. 3). On day 33, she underwent the extraction of the dens serotinus. On day 37, the antibiotic was changed to oral administration of ampicillin (250 mg ×3/day), and on day 39, she was discharged from our hospital. Her hepatic dysfunction improved after we stopped CTX. After her discharge from hospital, the lymphocyte blast transformation test for cefdinir...
Figure 1. Enhanced computed tomography (CT) images of the orbit, neck, and lung are shown (Day 4). The filling defects in the left cavernous sinus and maxillary vein (Fig. 1a and 1b white arrow), the inhomogeneous high CT value of the fat tissue density around the sinus, and the swelling of the left masseter muscle are shown (Fig. 1a and 1b). These findings suggested thrombophlebitis of the left sinus and maxillary vein. Multiple pulmonary nodular lesions were surrounded by ground glass attenuation (Fig. 1c). A dens serotinus continuous with left maxilla and the thickening of the mucosa of the left maxillary sinus suggested sinusitis (Fig. 1d).

(CFDN) turned out to be positive. Therefore, we thought that the elevation of hepatic enzymes was caused by cefdinir-induced hepatitis.

**Discussion**

Lemierre syndrome was comprehensively described in 1936 by Lemierre (3). This syndrome is usually heralded by an acute otolaryngologic infection, followed by thrombosis of the internal jugular vein with septicemia and can be complicated by septic emboli (1). The thrombosis most frequently affects the internal jugular veins but may also involve other veins, and the latter case is considered as a Lemierre syndrome variant (4). Septic emboli may spread from the internal jugular vein and most often affect lung tissue and also the spleen, liver, joints, bones, and soft tissues (5). Cranial nerve disorders could also appear when cranial nerves have inflammation involvement (6).

The mortality rate of Lemierre syndrome was reported to be between 5 and 10% without appropriate antibiotics (2). Thus, the antibiotic therapy is critical and should be started as soon as possible. *Fusobacterium necrophorum*, an anaerobic, gram-negative bacillus, is the most common organism isolated in this syndrome (7). Traditionally, the agent of choice for *Fusobacterium necrophorum* has been penicillin, but penicillin-resistant (beta-lactamase positive) strains have been isolated. Therefore, when this syndrome is suspected, antibiotic coverage should include adequate anaerobic coverage with agents such as clindamycin, metronidazole, or beta-lactam combined with beta-lactamase inhibitor (5). And when it does not respond to antibiotics, heparin use for thrombosis or surgical intervention may also be required (8).

In this case, *Streptococcus constellatus* (viridans) was detected by one of two blood cultures. However, it is reported that several other organisms, such as *Fusobacterium necrophorum*, *Staphylococcus*, *Enterococcus*, *Bacteroides* and *Lactobacilli*, are often found together in Lemierre syndrome and these anaerobes are often found to be negative in the blood culture (2). Here, SBT/ABPC was sensitive to *Streptococcus constellatus* and also had adequate anaerobic coverage for above organisms. Therefore, SBT/ABPC was used as de-escalation from MEPM.

In the present case, the diagnosis of Lemierre syndrome variant was based on the following findings: 1) trismus and tenderness in left cheek due to inflammation of the left masseter muscle, 2) thrombosis of left maxillary vein and left cavernous sinus, 3) septicemia, and 4) pulmonary septic emboli. The left dens serotinus was considered as the origin of infection. Her blepharoptosis and exophthalmos may be caused by oculomotor nerve disorder in the cavernous sinus.
Figure 2. $^{18}$FDG PET-CT demonstrated increased uptake in the left cavernous sinus (Fig. 2a, white arrow), the soft tissue around the left maxillary vein (Fig. 2b), and multiple lung nodules (Fig. 2c). Coronal image showed no abnormal uptake other than the left maxillary region and the lung nodular lesions (Fig. 2d).

There are no reports describing blepharoptosis in Lemierre syndrome, although some cases of this syndrome that were affected with cavernous sinus thrombosis have been reported (9, 10). On this point, this was a rare case of Lemierre syndrome with blepharoptosis. When considering the mechanism of this syndrome and the fact that blepharoptosis appears in the diseases that show inflammation of cavernous sinus, such as cavernous sinus syndrome, Tolosa-Hunt syndrome, and meningitis, it is not strange that blepharoptosis appears in Lemierre syndrome.

There are increasing data demonstrating the role of $^{18}$FDG PET/CT in investigations for fever of unknown origin (FUO). This is because $^{18}$F-FDG is an indicator of increased intracellular glucose metabolism and therefore taken up not only by malignant cells but also by inflammatory cells (11-13). Increased glucose utilization has been reported to occur in activated granulocyte, lymphocytes, and macrophages in vitro and seems to be coupled with the over expression of high-affinity glucose transporter isotypes in these cells (14). In the present case, $^{18}$F-FDG PET/CT was helpful to find focuses and the extent of infection; left cavernous sinus, left maxillary vein, left masseter muscle, and nodules in bilateral lungs. It also helped to make sure that there was no other metastatic lesion. On the other hand, we also undertook evaluation via $^{67}$Ga scintigraphy nine days after admission, but it could not identify any focus of infection. Therefore, $^{18}$F-FDG PET/CT may be superior to $^{67}$Ga scintigraphy by providing precise information to reach an accurate diagnosis in FUO patients. From now on, $^{18}$F-FDG PET/CT may perform a more important role as an initial noninvasive diagnostic modality for FUO.

Thanks to the development of antibiotics, now Lemierre syndrome has become a clinically rare syndrome. However, since this syndrome still carries a life-threatening potential if the appropriate antibiotic therapy is not done, early diagnosis and initiation of appropriate therapy are very important. And this syndrome is known to show various symptoms due to the various involved lesions. Therefore, we emphasize...
that it is very essential for every physician to take this syndrome into consideration, when examining patients with acute otolaryngologic infection and FUO.

References


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