Arch. Immunol. Ther. Exp. (2012) 60:221–223
DOI 10.1007/s00005-012-0173-2

ORIGINAL ARTICLE

Myasthenia, Spondylitis and *Enterococcus faecalis* Endocarditis

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Received: 15 July 2011 / Accepted: 13 December 2011 / Published online: 10 April 2012

Abstract Parasympathomimetics, immunosuppression and plasmapheresis have considerably improved management and prognosis of myasthenia gravis. Side effects of these measures, however, may complicate the course of the disease. In a 66-year-old male with myasthenia gravis and lower back pain, blood cultures, echocardiography and magnetic resonance imaging led to the diagnosis of endocarditis and spondylodiscitis. *Enterococcus faecalis* grew in the blood cultures as well as on the aortic and tricuspid valve vegetations which were resected during cardiac surgery. Possible sources of the infection might be *E. faecalis* infections of catheter tips during a 46-day stay in the intensive care unit 11 months earlier where he had undergone plasmapheresis, hemodiafiltration and mechanical ventilation, or recurrent diarrheas since 18 months. Infection was favored by immunosuppression with glucocorticoids and azathioprine which received the patient because of myasthenia gravis and hypothyroidism. Patients with myasthenia gravis require close follow up, including infection parameters, especially when they receive immunosuppressive therapy and when microorganisms known to cause endocarditis, are identified.

Keywords Endocarditis · *Enterococcus faecalis* · Myasthenia gravis

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Introduction

Myasthenia gravis is an autoimmune disorder caused by autoantibodies against the nicotinic acetylcholine receptor on the postsynaptic membrane at the neuromuscular junction and characterized by weakness and fatigability of the voluntary muscles (Thanvi and Lo 2004). Parasympathomimetics, immunosuppression and plasmapheresis have improved management and prognosis of myasthenia gravis, however, they are not without complications.

Materials and Methods

Complications of immunosuppressive therapies and plasmapheresis are illustrated in a patient who developed spondylodiscitis and bivalvular endocarditis due to *Enterococcus faecalis*.

Results

A 66-year-old HIV-negative male suffered from severe low back pain in May 2007. In 1998, strumectomy had been performed because of struma nodosa. In August 2005, myasthenia gravis was diagnosed manifesting as easy fatigability, double vision and ptosis. The diagnosis was supported by a positive response to edrophonium, elevated serum antibodies against acetylcholine receptors, abnormal repetitive nerve stimulation, a positive response to pyridostigmine and corticosteroids, and the detection of a thymoma B1, which was resected in September 2005. In November 2005 he started to suffer from recurrent diarrhea. Gastroenterological examinations and stool cultures were negative. In March 2006 he complained about recurring fatigability,

muscle cramps and myalgias, and corticosteroids were discontinued because of the possibility of steroid-induced myopathy. In May 2006 azathioprine and oxazepam were added because of worsening myasthenic symptoms and anxious depression. In June 2006 corticosteroids were restarted and oxazepam discontinued because of a myasthenic crisis manifesting as diplopia, dysarthria, dysphagia, and dyspnea. Despite intravenous neostigmine, the patient required plasmapheresis, intubation, and mechanical ventilation. The course was complicated by *Pseudomonas aeruginosa* pneumonia, renal failure necessitating hemodiafiltration and hypothyroidism despite oral substitution of levothyroxine. The patient was mechanically ventilated for 42 days, received plasmapheresis for 5 days and hemodiafiltration for 19 days. His antimicrobial therapy during 32 days was cefuroxime, ceftazidime, clarithromycin and fluconazole. In August 2006 he was dismissed home. Whereas glucocorticoids were given during the whole period, azathioprine was stopped in July 2006 because of the pneumonia. Azathioprine 150 mg/day was resumed in September 2006. Despite increases in the levothyroxine dosage, hypothyroidism persisted. Since late 2006, he developed night sweats and since early 2007 severe lower back pain. His medication in May 2007 was pyridostigmine (480 mg/day), prednisolone (12.5 mg/day), belladonnae, azathioprine (150 mg/day), levothyroxine (0.16 mg/day) and bisoprolol (5 mg/day). He presented with slight double vision and bilateral ptosis and complained about pain in the lower back and hips.

Abnormal blood tests were: hemoglobin 9.8 g/dl (normal 14.0–17.0), lymphocytes 14.2 % (normal 20–40), C-reactive protein 4.6 mg/dl (normal <0.6), TSH 5.3 μU/ml (normal 0.2–3.1) and erythrocyte sedimentation rate 100 mm/h. Spondylodiscitis L5/S1 was clinically suspected, which was supported by magnetic resonance imaging (Fig. 1). Puncture of the vertebrum was tried but only little material without growth of microorganisms could be achieved. Blood cultures were positive for *E. faecalis*. Antibiotic therapy with linezolid was started.

Ten days after admission, the patient complained about dyspnea and leg edema, and endocarditis was suspected. Echocardiography showed an enlarged right atrium and ventricle, vegetations on the tricuspid and aortic valve, and a severe tricuspid regurgitation (Fig. 2).

Antibiotic therapy was changed to sulbactam, ampicillin and gentamycin, and the patient was referred for cardiac surgery. The tricuspid vegetation was removed, the septal cusp quadrangularly resected and an anuloplasty using a 30-mm Kalangos ring was performed. The aortic valve was resected and a Sorin Freedom Solo 25 mm bioprosthesis implanted. *E. faecalis* grew on the vegetations of the aortic as well as tricuspid valves. The patient was dismissed with teicoplanin and ciprofloxacine. Under this therapy and orthotic stabilization, spondylodiscitis regressed, why teicoplanin and ciprofloxacine were replaced by amoxicillin and clavulanic acid after 2 months. Revision of the patient's records disclosed that *E. faecalis* had been already cultivated from several central venous catheter tips, but not in blood cultures at the intensive care unit in 2006, and neither any antibiotic therapy against *E. faecalis* nor follow-up investigations regarding signs of infection had been proposed.

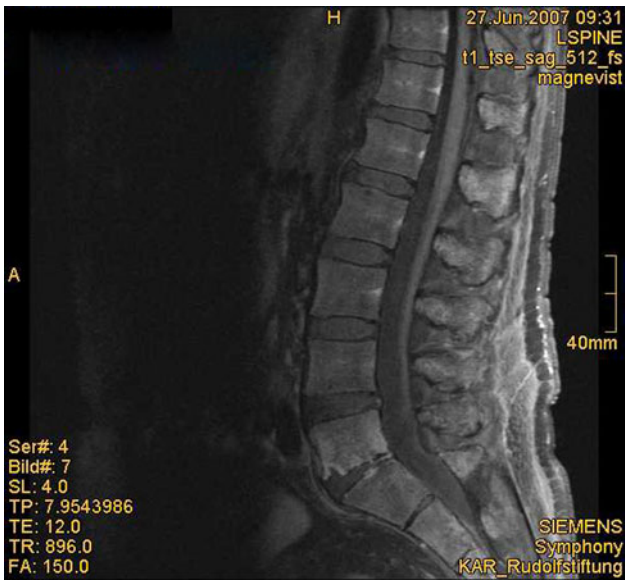

Fig. 1 T1 weighted sagittal magnetic resonance imaging of the lumbar spine. After intravenous application of Gadolinium marked contrast enhancement of the vertebral body of L5 is visible, a finding typical for inflammation

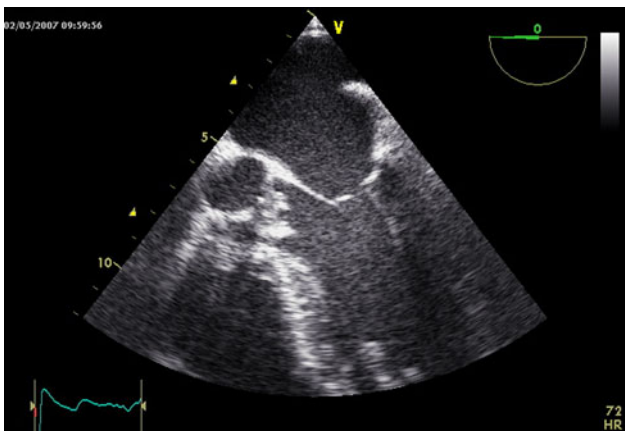

Fig. 2 Transesophageal echocardiographic image, showing large vegetations on the aortic cusps

Discussion

Enterococcus faecalis, a colonizer of the intestinal tract, is known to cause bacteremia, urinary tract infections and

bacterial endocarditis. *E. faecalis* has been identified in up to 15 % of all cases, and is the third frequent microorganism causing bacterial endocarditis (Hill et al. 2007; Hoen et al. 2002). Enterococcal infective endocarditis is nosocomial in up to 39 % of the cases (Anderson et al. 2004). *E. faecalis* endocarditis is known to occur in patients after intensive care (Sijpkens et al. 1995). The ability of *E. faecalis* to colonize vascular tissue is thought to be by adhesin–ligand interactions between its surface determinants and host proteins at the sites of endovascular injuries (Mohamed et al. 2004; Nallapareddy and Murray 2006). *E. faecalis* endocarditis isolates produce biofilm more often than *E. faecalis* isolates from nonendocarditis sources (Mohamed et al. 2004) The *esp* gene, which encodes an enterococcal surface protein, is important in biofilm formation and has been identified more often among *E. faecalis* isolates that cause endocarditis and other bloodstream infections than in *E. faecalis* fecal isolates (Mohamed et al. 2004).

Most probably, the *E. faecalis* infections of the catheters during the intensive care 11 months earlier may have played a role in the development of endocarditis and spondylodiscitis, although no bacteremia had been found at that time. However, it cannot be ruled out that he had acquired the infection earlier, possibly as a consequence of the recurrent diarrheas, and that already the infection has been responsible for the myasthenic crisis in June 2006. Infection was favored by immunosuppression with glucocorticoids, azathioprine and hypothyroidism (Masek et al. 2003). Immunosuppression has been identified as a predisposing factor for infective endocarditis with an increasing prevalence during the last decades (Cabell et al. 2002). Compared with the overall population, patients after solid organ transplantation have a 171-fold risk to develop endocarditis (Ruttmann et al. 2005).

Spondylodiscitis may be associated with endocarditis, especially in patients with enterococcal endocarditis (Cone et al. 2008; Mulleman et al. 2006; Vlahakis et al. 2003). It remains speculative, whether the one or other infection is causative. It can be argued that spondylodiscitis occurred before endocarditis because all the reported patients were referred with a history of back pain, whereas heart failure was initially present in only few of them (Mulleman et al. 2006; Vlahakis et al. 2003). That *E. faecalis* had not been cultivated from the vertebral biopsy does not exclude it as a causative agent, since cases with *E. faecalis* endocarditis and spondylodiscitis show only positive blood cultures but negative biopsy results (Mulleman et al. 2006).

This case shows that patients with myasthenia gravis require close follow ups, including infection parameters, especially when they receive immunosuppressive therapy and when microorganisms known to cause endocarditis, are identified. To prevent myasthenic crises parasympathomimetics and immunosuppressants should be adequately adapted and drugs known to worsen myasthenic manifestations avoided.

Conflict of interest The authors declare that they have no conflict of interest.

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