A 55-year-old farmer was admitted to the hospital with low back pain without neurological compromise and nodulopustular skin lesions in the thighs and forearms. The patient reported recurrent episodes of right elbow bursitis as well as right heel pain during the last 8 months.

Past medical history revealed renal transplantation for end stage glomerulonephritis 15 years prior to the admission to the hospital and therapy with immunosuppressive agents since then. During the last 3 years, the patient received methylprednisolone, 4mg per day, and azathioprine, 75mg per day. Moreover, the patient had liver cirrhosis due to chronic hepatitis C viral infection diagnosed at the time of transplantation.

Physical examination and plain radiographs of the lumbar spine showed no abnormalities. The patient was discharged from the hospital with the advice to receive a 2-week treatment with non-steroid anti-inflammatory medications and bed rest for the low back pain and amoxicillin/clavulanic acid for the skin lesions.

Four weeks later, he presented with intense low lumbar pain, numbness of the lower extremities and gait disturbance. Furthermore, there was cervical spine pain, loss of dexterity, and numbness of the hands. The patient had malaise, vertigo, and tinnitus but no fever.

Physical examination revealed a palpable gibbus at the cervical region. Neck motion was decreased. The muscle strength of both lower and upper extremities muscles was mildly decreased (4/5). Deep tendon reflexes of the upper extremities were decreased. Deep tendon reflexes of the lower extremities were normal. There was no clonus.

Imaging evaluation with plain radiographs, computed tomography and magnetic resonance imaging of the spine showed spondylodiscitis at C4-C5, C5-C6, C7-T1, and T1-T2 intervertebral discs (Fig. 1) and spondylodiscitis at L4-L5 associated an epidural mass. Cervical kyphosis was present because of osteolysis with anterior wedged deformity of the C5 vertebra. Posterior C5-C6 spondylolisthesis resulted in compression of the spinal cord at this level. Osteolytic lesions were also shown radiographically at the left elbow (olecranon and radius), the right carpal bones, the distal right fibula, the right calcaneus (Fig. 2), and the right middle and forefoot (the head of the fifth metatarsal and the proximal phalanxes of the fifth, fourth, third and second toes).

What is your diagnosis?
What is your diagnosis?

Blood cultures were negative for common pathogens. Tissue cultures from the skin lesions and fine needle aspiration biopsy of the low lumbar spine showed abundant, acid fast bacilli, identified as Mycobacterium chelonae. The strains were isolated from cultures of specimens in blood, Macokey and L-J media and identified as Mycobacterium chelonae by biochemical tests. The susceptibility testing was performed by the E-test (AB BIODISK) on Muller-Hinton agar with blood. The isolate's MICs (in mg/L) were clarithromycin 2, imipenem > 32, amikacin 12, cefoxitin 32, doxycyclin >256, cotrimoxazole >32, ciprofloxacin >32, and linezolid 0.75.

The patient initiated treatment with oral ciprofloxacin, 750mg every 12 hours and clarithromycin, 500mg every 12 hours for 8 weeks. Amikacin (1gr daily) substituted for ciprofloxacin 4 weeks later. No change of his immunosuppressive regimen was made. A soft neck collar and a thoracolumbar orthosis were prescribed and the patient was ambulatory. Three months after initiation of the chemotherapy, the patient had significant improvement regarding his lower extremities neurological deficits. However, there was only slight neurological improvement of the upper extremities deficits.

No nephrotoxicity was noted. However, the antimicrobial chemotherapy was discontinued for 15 days because of hepatotoxicity (elevated transaminases). During that time, recurrence of the neurological deficits was noticed. The patient was subsequently administered oral ciprofloxacin (750mg every 12 hours) and clarithromycin (500mg every 12 hours), and intravenous imipenem/cilastatin (500mg every 6 hours). Two months later, clinical and imaging improvement was noticed at all affected sites.

Antimicrobial chemotherapy with ciprofloxacin and clarithromycin was then continued for 7 months. Because of no improvement of the neurological deficits of the upper extremities, surgical debridement and decompression of the cervical spinal cord through an anterior approach was done, followed by instrumentation and fusion. The C5 vertebral body, as well as the adjacent intervertebral discs were excised. Cervical spine fusion was done using a titanium cage (PEAK, DePuy International Limited, Leeds, England) and allografts (Grafton DBM, Osteotech, Eatontown, NJ, USA). Anterior stabilization was done using a cervical plate (Orion, Medtronic Sofamor Danek, Memphis, TN, USA). Acid fast staining and cultures of the cervical spine specimens also revealed abundant acid-fast bacilli, identified as Mycobacterium chelonae. Two weeks postoperatively, plain radiographs and magnetic resonance imaging of the cervical spine showed improvement of the spinal deformity and decompression of the spinal cord.

About 15 months after the diagnosis and the initiation of the antimicrobial chemotherapy and 5 months after surgical treatment, the patient discontinued chemotherapy. The patient was at that time pain free and ambulatory, without any neurological deficits of the lower and the upper extremities and without any skin lesions. Neck motion was normal. Plain radiographs and magnetic resonance imaging showed improvement at all sites of mycobacterium osteomyelitis, and solid fusion and decompression of the cervical spinal cord. Unfortunately, one and a half year later, the patient deceased because of uncompensated hepatic failure due to progressive chronic hepatitis C viral infection.

Teaching points
- The most noteworthy point of our case that expands the relevant literature is that Mycobacterium chelonae caused multi-focal spinal and extra-spinal infection mimicking Metastatic carcinoma in our immunocompromised patient, a 55-year-old renal transplant recipient. It should be emphasized that rapidly growing mycobacteria, including Mycobacterium chelonae, may be misidentified with the use of traditional microbiological. Thus, the major limitation of our case report is that we did not perform molecular microbiological studies for the identification and speciation of the isolated pathogen.
- Non-tuberculous mycobacteria usually affect immunosupressed patients and the infections are usually located in the lungs, the lymph nodes, the subcutaneous tissue, and the skin. Infections of the bone and joints, and particularly the spine, by non-tuberculous mycobacteria are extremely rare, and usually are misdiagnosed. Disease due to Mycobacterium chelonae usually occurs in immunosuppressed patients, patients under corticosteroid therapy, and patients with organ transplantation, rheumatoid arthritis, or autoimmune disorders. The disease is often a disseminated cutaneous infection.1.3 Mycobacterium chelonae osteomyelitis is extremely rare and whenever has been reported it was localized.1.2 The portal of entry of the mycobacterial infection in our patient was not clear.
- According to the Duke University classification,4 disseminated infections caused by rapidly growing mycobacteria are classified into three groups. Group 1 includes patients with none identified immune defect, organ transplantation, collagen vascular diseases or chronic renal failure; patients usually present with skin involvement and respond well to antimicrobial therapy. In this group, survival rate is approximately 90%. Group 2 includes patients with cell-mediated immune deficiency, lymphomas, or leukemia; the patients usually present with widespread multiorgan involvement and severe illness. The survival rate is only 10%. Group 3 includes patients with other underlying diseases, intermediate illness and modest response to therapy.
- In line with the literature,1,5,6 our experience with this case suggests that surgical intervention may be invaluable for the treatment of patients with Mycobacterium chelonae infection. Surgery provides tissue specimens for accurate pathological diagnosis and antimicrobial susceptibility tests. In addition, surgical treatment is used as adjuvant to antimicrobial chemotherapy and reduces mycobacterial load in cases of multidrug resistant infections. Also, it restores vertebral column deformity associated with instability and/ or neurological compromise.
- Although some authors have expressed concerns regarding the risk of introducing a foreign body in an actively infected spinal site, surgical treatment is indicated in patients with vertebral column deformities associated with instability.
and/or neurological compromise. However, since there is poor adherence of the Mycobacterium tuberculosis to the stainless steel and only little biofilm production there are no cases of persistence or recurrence of infection after instrumentation surgery. Yilmaz et al reported no recurrence of tuberculosis during an average of 2.5 years follow up after anterior spinal fusion and instrumentation in patients with spinal tuberculosis. Thus, surgical site relapse of tuberculosis after placement of prosthetic material is rare.

- Combined with chemotherapy, early stabilization of the spinal column has an important role in the management of spinal tuberculosis. Jin et al reported that in selected patients, one stage anterior interbody fusion with autologous grafting and spine instrumentation is more advantageous since it can provide sufficient segmental stability of the affected spine, adequate correction of the kyphotic deformity and promotion of fusion. Posterior fusion should be supplemented in children with severe spinal tuberculosis to prevent progressive kyphosis following this procedure.

- Chemotherapy for Mycobacterium chelonae has been problematic, due to the paucity of effective oral antimicrobial agents. Fewer than 25% of the mycobacterium isolates are susceptible to macrolides, doxycycline, minocycline, sulfonamides and ciprofloxacin. Combined chemotherapy agents are strongly recommended, and linezolid, telithromycin and tigecycline are recently described to have promising results. Clarithromycin is considered the drug of choice for the treatment of Mycobacterium chelonae disease. However, clarithromycin should not be considered as monotherapy. The duration of treatment is not well established. Depending on the host's immunocompetence, the extend of the disease and the possibility of surgical treatment, chemotherapy of cutaneous and soft tissue Mycobacterium chelonae infections is reported to last from weeks to several years. Based on the in vitro susceptibility pattern of the isolate in our patient, linezolid could have been another antimicrobial agent to be used in the therapeutic regimen.

- In conclusion, Mycobacterium chelonae infection may be manifested with multi-focal spinal and extra-spinal skeletal in immunocompromised patients, such as renal transplant recipients. Aggressive management including the early use of invasive tests is recommended for transplant patients with multi-focal infections. Combined curing our patient with this rare infection.

Acknowledgements

This case report was accepted for publication in the journal "Transplant Infectious Diseases" (authors: Demetrios S. Korres, Panayiotis J. Papagelopoulos, Konstantinos A. Zahos, Maria D. Kolia, Garyphalia G. Poulakou, Matthew E. Falagas).

References