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Metronidazole Induced Encephalopathy and Sudden Hearing Loss – A Case Report

Metronidazol Kaynaklı Ensefalopati ve Ani İşitme Kaybı - Bir Vaka Raporu

Acil Tıp

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Özet

İlaç kullanımı sonrasında hastalar nörolojik semptomlarla acil servise başvurabilirler. Bu vakada, metronidazol kullanımından sonra ani işitme kaybı, denge kaybı ve konuşma bozukluğu olan bir hastayı sunmayı amaçladık. Bu vakanın sunulma nedeni, literatürdeki diğer vakalardan farklı olarak, ilk kez bir hastanın klinik iyileşmesi ile birlikte manyetik rezonans görüntüleme (MRG) bulgularının gerilediğini gösteren bir vakadır. 65 yaşındaki erkek hasta, metronidazol kullanımından 3 gün sonra gelişen ani işitme kaybı ve bunu takiben gelişen konuşma ve denge bozuklukları ile acil servise başvurdu. MRG ile corpus callosumda difüzyon kısıtlılığı gözlendi ve bu düzeyde fluid-attenuated inversion recovery (FLAIR) serisinde hiperintens sinyal değişimi gözlendi. Metronidazol kesildikten kısa süre sonra hastanın klinik durumu düzelmeye başladı. Önceki bulguları sonraki kontrol MRG'de gerileyen hastanın taburcu edildiği görüldü. Nörolojik semptomlarla başvuran hastalarda ilaç kaynaklı toksisite akılda tutulmalıdır.

Anahtar kelimeler: *Metronidazol*, *ensefalopati*, *ototoksisite*

Abstract

After using medication, patients can apply to the emergency department with neurological symptoms. In this case, we aimed to present a patient with sudden hearing loss, imbalance and speech disorder after metronidazole use. The reason for presenting this case is that unlike other cases in the literature, this is the first case showing that MRI findings regressed with clinical improvement of the patient. A 65-year-old male patient was admitted to the emergency service with sudden hearing loss three days after metronidazole use, followed by speech and balance disorders. Diffusion restriction was observed in the corpus callosum in the magnetic resonance images (MRI), and a hyperintense signal change was observed at this level in the fluid-attenuated inversion recovery (FLAIR) series. Shortly after metronidazole was discontinued, the patient's clinical condition started to improve. The patient, whose previous findings regressed on the subsequent control MRI, was discharged. Drug induced toxicity should be kept in mind in patients presenting with neurological symptoms.

Keywords: *Metronidazole*, *encephalopathy*, *ototoxicity*

Introduction

Metronidazole is an antimicrobial agent of the nitroimidazole group used in the treatment of infections caused by anaerobic bacteria and protozoa. Development of neuropathy is known after metronidazole use[1]. While encephalopathy is a less frequently reported side effect, sudden hearing loss has been reported even more rarely[2–3]. We aimed to discuss the literature with a patient who presented with symptoms of sudden hearing loss, speech impairment, imbalance, and difficulty walking.

Case Report

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A 65 year old male patient was admitted to the emergency room with sudden hearing loss that started 5-6 days ago, followed by loss of balance while walking and slowing speech, which started 2 days later. It was learned that the patient, who was able to walk with support, do daily tasks and speak normally at home, had not been able to walk with support and had impaired speech, and he applied to the emergency department. He had a history of diabetes mellitus, hypertension, coronary by-pass operations, therefore he used the drugs perindopril, acetylsalicylic acid, metoprolol, gliclazide; it was learned that he used methotrexate orally because of rheumatoid arthritis. It was learned that the patient was started on oral metronidazole and ciprofloxacin 5 days before his admission to the emergency department due to an infected pressure sore in the sacral region. It was learned that our patient developed sudden hearing loss on the third day of this newly initiated treatment and therefore he was admitted to the hospital and steroid and hyperbaric oxygen therapy was also initiated upon detection of bilateral sensorineural hearing loss. Our patient, who did not benefit from the treatments initiated for hearing loss, was admitted to our emergency department after the onset of speech impairment, loss of balance, and difficulty walking.

In the physical examination of the patient: tension arterial: 166/71mmHg, heart rate: 84/min, fever: 36.1°C, SpO2: 95%, capillary glycemia: 128 mg/dL. The eyes were open spontaneously, there was no facial asymmetry, there was no verbal output, did not understand what was said, could be understood with signs, followed the commands. Four extremity muscle strength was detected as 4/5 proximally more prominent. Eye movements were natural in all directions. There was nystagmus hitting the gaze direction in right and left gaze. Deep tendon reflexes could not be obtained. There was no neck stiffness; Hoffman's test was found to be bilaterally negative.

With a pre-diagnosis of cerebrovascular disease or encephalitis; complete blood count, biochemistry and non-contrast brain computered tomography (CT) and diffusion MRI were planned. Hemorrhagic stroke was not detected in brain CT. In diffusion MRI, diffusion restriction was observed in the genu and splenium in the corpus callosum and in the left parietal subcortical white matter, which also corresponded apparent diffusion coefficient (Figure1). In the FLAIR series, widespread signal increase areas were observed in the white matter at the centrum semiovale and corona radiata levels (Figure1).

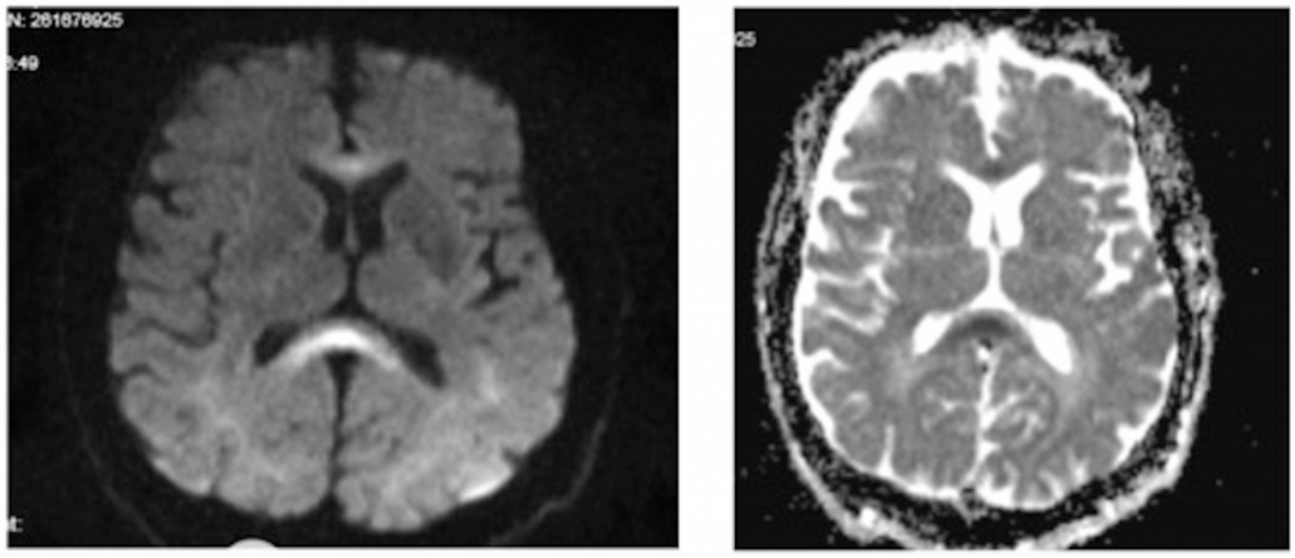

Figure 1
Diffusion restriction was observed in the genu and splenium in the corpus callosum and in the left parietal subcortical white matter, which also corresponded apparent diffusion coefficient (left side) In the FLAIR series, widespread signal increase areas were observed in the white matter at the centrum semiovale and corona radiata levels (right side)

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MR image was interpreted as compatible with encephalopathy due to toxicity.Metronidazole treatment was discontinued in the patient who was admitted to the neurology clinic. Inaddition to the continuation of the other drugs he was using, the patient also received steroid therapy; hyperbaric oxygen therapy was not planned again. After 1 week of clinical follow-up, it was found that there was a significant decrease in the lesions in the brain MRI taken 1 week later (Figure2).

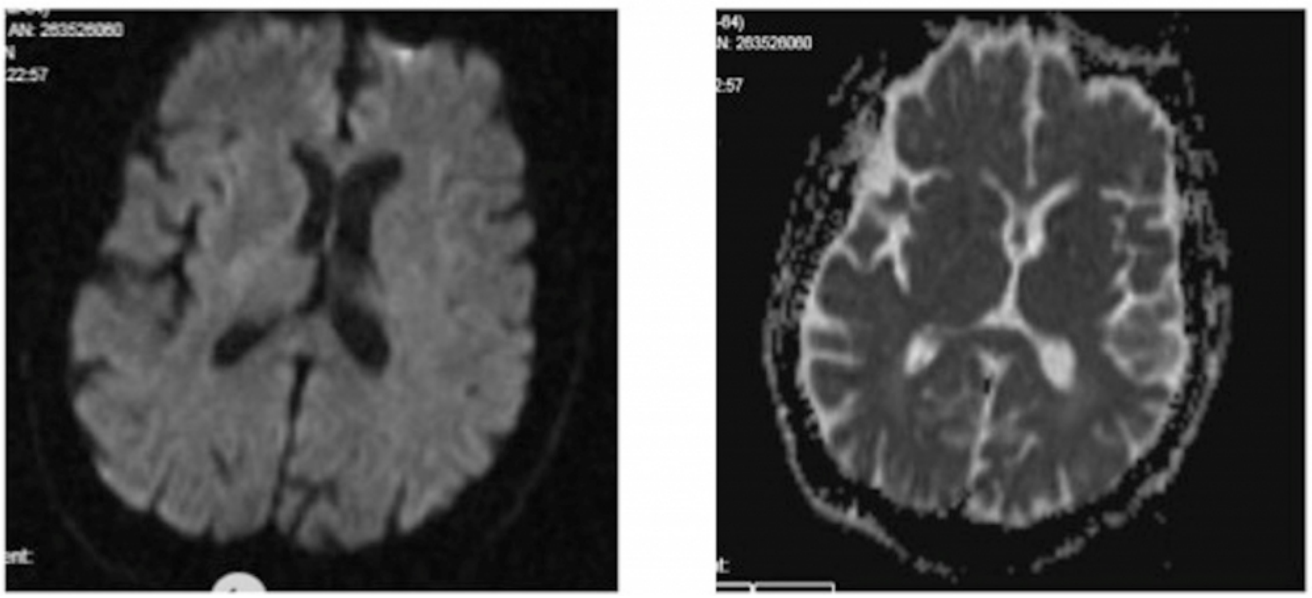

Figure 2
After 1 week of clinical follow-up, it was found that there was a significant decrease in the lesions in the brain MRI taken 1 week later

However, loss of balance and walking difficulty regressed. In the hearing test performed, it was found that there was no significant change and the hearing loss was still continuing. The patient was discharged with a diagnosis of metronidazole-induced encephalopathy (MIE), with outpatient clinical follow-up continuing. It was observed that the neurological complaints of the patient completely regressed in the third month of the outpatient follow-up but the hearing loss continued. Detailed informed consent was obtained from the patient in this study.

Case Discussion

Although the neurotoxic effects of metronidazole are commonly known, metronidazole may be ototoxic in rare cases. Although there are some ideas about the pathophysiology of metronidazole-related encephalopathy, it has not been clearly revealed how these side effects occur[2]. These side effects can mostly be reversed after the drug is discontinued[3]. MIE should be considered in case of speech difficulties, walking difficulties and confusion during the use of this drug, which is widely
prescribed by clinicians[4]. With the study conducted in 2017, the seventh sudden hearing loss due to metronidazole in the literature was defined[5]. While tinnitus was the first symptom in most of the cases in previous studies, the case we reported is the second case in the literature in which encephalopathy was also reported in addition to bilateral hearing loss[5]. Previous studies have shown that brain lesions identified by MRI in MIE patients are typically located in the cerebellar dentate nucleus, dorsal

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medulla, dorsal pons, midbrain, and corpus callosum splenium with bilateral and symmetrical involvement[6]. As well as the brain MRI findings in our case are typical for MIE described in previous studies; the disappearance of the first findings in MRI taken for control purposes was also compatible with previous studies[7]. Studies have reported that hearing loss regresses with early and supportive treatments[8]. In these patients, improvement of neurological findings is typical after discontinuation of
the drug. Especially for ototoxicity, the chance of treatment is higher if the diagnosis is made in the first 2 weeks and treatment is initiated[9]. Our patient leaves the current studies due to the early discontinuation of the drug and the regression of hearing loss despite supportive treatment. In addition, there are still not enough studies to date for the treatment of MIE and hearing loss.

Drug-related toxicities should be considered in patients who come to the emergency department with neurological symptoms, and patients should be evaluated in terms of ototoxicity and neurotoxicity after metronidazole use.

Informed Consent

Hastadan

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