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Peripheral neuropathy as a rare syndrome related to metronidazole usage: Metronidazole may lead to persistent neuropathy

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Abstract

Metronidazole is a potent drug used against some protozoa like Entamoeba histolytica, Giardia lamblia, Trichomonas vaginalis and Balantidium coli, and anaerobic bacteria. It is used for the treatment of alcoholism, Crohn's disease, exophthalmos, rheumatoid arthritis, rosea and acne as well. It is a well-tolerated drug with some kinds of side effects like abdominal pain, headache, nausea and metallic taste. Rarely but severely, pseudomembranous colitis, epileptic seizure, encephalopathy and peripheral neuropathy might be seen. These side effects are generally self-limited. Drug administration should be stopped immediately in case of these side effects' existence. In this article, we presented a case which used metronidazole for hepatic ameobiasis for 18 weeks and developed peripheral neuropathy

Key words: ameobiasis, metronidazole, peripheral neuropathy

Introduction

Metronidazole is a 5-nitroimidazole (Fig 1) compound as potent compound as potent drug used against protozoa (1). It is admitted that metronidazole easily penetrates into cerebrospinal fluid and central nervous system. Neurological symptoms generally occur when it is administered above 2gr. per day (2).

It is also used for the treatment of alcoholism, Crohn's disease, exophthalmos, rheumatoid arthritis, rosea and acne as well. Headache, vertigo, syncope, sleep disturbance, confusion and depression are some of the side effects. Peripheral neuropathy is a rare side effect (3-7). These side effects are generally self-limited but may last for a long time. In this article, we aimed to present a case which used metronidazole for the treatment of hepatic ameobiasis and developed peripheral neuropathy

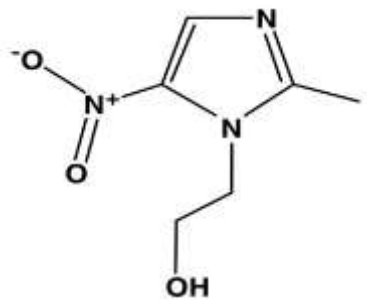

Figure 1: The molecular structure of 5-nitroimidazole

Case

39 years-old male patient with the signs of night sweats, coughing and fever for 6 months, have been referred to internal medicine outpatient clinic. Systemic examination was normal except the hepatomegaly. The patient had a normal anamnesis.

Hepatic ameobiasis cysts were diagnosed via abdominal ultrasonography then metronidazole treatment was prescribed. Aspartate Aminotransferase (AST) level was 70U/L, Alanine Aminotransferase (ALT) level was 140U/L, Immunoglobulin E (IgE) level was 707IU/ml. The patient continued the treatment for 18 weeks. AST level was 54U/L,ALT level was 82U/L, IgE level was 260IU/ml. after treatment (Table 1).

Infectious complaints regressed but bilateral lower extremity formication and burning sensation persisted after 2 months of metronidazole treatment. Peripheral neuropathy was suspected due to the persistence of the signs, then the patient was consulted to the neurology clinic and metronidazole medication was ceased. After ceasing the metronidazole treatment, partial loss of symptoms was observed.

Neurological examination showed that bilateral Achilles deep tendon reflexes (DTR) were absent, bilateral patellar DTRs were hypoactive. Socks type hypoesthesia was examined at both lower extremities. Other neurological findings were normal.

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Table 1: Patient biochemistry table before treatment and after treatment. AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, IgE: Immunoglobulin E

Parameter	Referance Value	Before treatment	After treatment
AST	0 – 35 U/L	70	54
ALT	0 – 34 U/L	140	82
IgE	1-100 IU/mL	707	260

As a result of the electromyography (EMG), symmetrical sensorial axonal peripheral neuropathy of bilateral lower extremities was determined. Following the control examinations, regression of the symptoms and EMG findings were observed.

Discussion

Metronidazole is frequently prescribed in the gastroenterology and gynaecology clinics. It has not been thought to be neurotoxic so far although some case reports present that metronidazole may cause neuropathy (8,9). Metronidazole is administered for hepatic ameobiasis abscess for 7-14 days, and for some other diseases it may be used for a long time period (9).

Cumulative neurotoxic dose of metronidazole reported in the literature is between 13,2 and 228 gram. Development duration of neurological symptoms may vary between 11 days and 6 months (10-12).

In our case, treatment duration was 4 and a half months as there was not a recovery from the disease and neurological symptoms started 2 and a half months ago. Mechanism of the neuropathy is unknown yet but it causes axonal type sensory-motor neuropathy (9), likewise we have stated axonal type sensorial neuropathy in the EMG results.

In another case report which studied the neuropathic side effects of metronidazole, 13 patients between the ages of 12 and 22 were administered metronidazole per os for a period of 4-11 months. The follow-ups presented that 11 patients had neurological symptoms and peripheral neuropathy with decelerated neuronal transmission. Consequently, treatments of 9 patients were suspended then it was observed that 5 of them fully recovered 3 of them almost recovered and peripheral neuropathy of one patient persisted (13).

Turan et al. (14) reported a case with the diagnoses of acute myelocytic leukaemia and vulva abscess that was given metronidazole and developed peripheral neuropathy

Some occasions convinced us that the peripheral neuropathy of the case was a side effect of metronidazole as our case developed peripheral neuropathy without any other diseases, etiological factors or any other medications with side effects those may cause peripheral neuropathy; before the metronidazole treatment there were not any complaints pointing out peripheral neuropathy; complaints started after metronidazole treatment and ceased after suspension of the treatment

Conclusion

As a result, medications of the patients should be primarily checked while searching for the reasons of the peripheral neuropathy. With this case report which developed metronidazole induced peripheral neuropathy, we aimed to state the importance of early diagnosis and treatment because drug induced peripheral neuropathy may be persistent

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of Research/Case, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was completed due to defined rules by the Local Ethics Commission guidelines and audits.

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