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CASE REPORT

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A case report of toxic leukoencephalopathy induced by metronidazole in a woman with surgical site infection

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Abstract

Metronidazole may rarely cause encephalopathy and neuropathy. In this study, we report a 30-year-old post-partum, ex-addicted female with leukoencephalopathy due to metronidazole.

KEYWORDS

metronidazole, neuropathy, toxic leukoencephalopathy, toxicity

1 | INTRODUCTION

Metronidazole may rarely cause encephalopathy and neuropathy. In this study, we report a 30-year-old post-partum, ex-addicted female with leukoencephalopathy due to metronidazole.

Metronidazole is an antimicrobial agent used to treat various infections such as pseudomembranous colitis resulting from Clostridium difficile, amebiasis, giardiasis, trichomonas vaginitis, and serious anaerobic bacterial infections.[1] Metronidazole may cause various neurological side effects including peripheral neuropathy, cerebellar dysfunction, visual impairment, vestibulotoxicity, cochleotoxicity, ataxic gait, dysarthria, seizures, and encephalopathy.[2–4] In this study, we report a case of metronidazole-induced leukoencephalopathy.

2 | CASE PRESENTATION

A 30-year-old woman who had given birth two weeks ago was admitted to a regional hospital due to fever, palpitation, erythema, inflammation, and secretion around the cesarean wound. Her vital signs were as follows: T:37.3Cº BP:110/70 mmHg PR:89. Initial laboratory findings revealed R.B.C: 4.4 × 106/µl, Hb: 11.6 g/dl, Hct: 36%, W.B.C: 11.6 × 103/µl, Plt: 213 × 103/µl, neutrophil: 73%, lymphocyte: 18%, monocyte: 5%, and eosinophil: 5%. So Primary diagnosis set for wound infection. Because of infection cefazolin (1 gr IV for 9 doses), gentamicin (80 mg IM for 6 doses) and metronidazole (500 mg IV 7 doses) were administered to the patient. After 5 days, she complained of hearing loss so gentamicin was stopped. She was also ex-addicted and taking methadone during abstain.

At day 9 of admission, she developed neural complications including nausea, vomiting, aphasia, loss of consciousness, hearing disturbances, extreme rigidity, and gazed eyes so she was referred to Alborz hospital. There initial laboratory tests were as follows: RBC: 4.7 × 106/μl, Hb:13.5 g/dl, HCT: 41.3%, PLT: 213 × 103/μl, WBC: 15.4 × 103/μl (neutrophil: 92% and lymphocyte: 8%), AST: 29 IU/L, ALT: 18 IU/L, sodium: 136 mEq\L, potassium: 4.4 mEq/L, CRP: 33, PH:7.307, PCO2: 26.9, HCO3: 13.2, PO2: 185.8, SO2: %99.2, urea 28, and Cr: 1 mg\dl. There were evidences proving inflammation existence, So HBsAg, HCVAb, HIVab, and blood culture performed which all were negative. Isoelectric focusing of CSF & Serum was done, and OCB was negative. CSF culture, fluid examination, and oligoclonal banding test did not show any abnormality (Tables 1, 2, and 3).

Brain MRI performed in axial T1, T2, FLAIR, DW and sagittal and coronal T2 sequences to examine the brain. Diffuse white matter T2 increased signal changes observed in periventricular regions on both sides and as well in the corpus callosum (Figure 1). These findings are non-specific and could be due to inflammatory-infective causes such as ADEM, HIV, PRES, or vascular causes such as CADASIL, so her CSF sample was referred to molecular detection section for CSF pathogen panel. CSF viral pathogen panel was negative for EBV, CMV, HSV1, HSV2, VZV, HHV 6, HHV7, Parvovirus B19, and Human enterovirus.

At the entrance to Alborz hospital (9 days after first admission), she was hospitalized in ICU and received methylprednisolone 1gr/day for 5 days, which was not effective, after that, plasmapheresis was done for 7 times by the amount of 2–2.5 L with the substitution of FFP and albumin which was also ineffective. In the next step, IVIG was administered for her at a dose of 130 gr IVIG in divided doses in 5 days.

After the patient stabilized, MRI was ordered again in which slight dilatation of the ventricle along with widening of lateral sulcus was noted. Cerebellar hemispheres, vermis, and dentate nucleus were normal. Pathologic signal was not demonstrated in pons and medulla oblongata. Craniocervical junction appears normal. No extra- or intra-axial collection in dura and meninges was observed. Signal void was seen normally in major arteries. Pathologic signal was not visualized in intracranial veins. There was not any space-occupying lesion in basal cisterns. Visualized parts of orbit had normal configuration. Macroadenoma was not seen in hypophysis. Stalk was normal. Suprasellar cistern was free. In DWI images, diffusion restriction and acute infarction were not seen. Severe mucosal thickening was noted at ethmoid complex and also sphenoid sinus and less than severely at mastoid air cells (Figure 2). Finally, after 52 days, she was able to talk and move voluntarily and sodium valproate (Depakin), metoprolol (Metoral), metoclopramide, Gemfibrozil, and Quetiapine prescribed for her.

3 | DISCUSSION

Metronidazole can rarely cause central nervous system toxicity. Although metronidazole-induced encephalopathy (MIE) is mostly reported from the United States and Korea, there have been few case reports worldwide including India, Japan, Australia, Canada, United Kingdom, Belgium, Chile, Germany, Israel, Netherlands, Nigeria, Taiwan, Tunisia, and Turkey. Average time taken to develop complications from treatment initiation is 15 days (range 1–90 days), and the average cumulative dose is 93.4g (range, 0.25-1095g).[5] MIE can be suspected in a patient, which presents cerebellar and brainstem deficits in close relation to metronidazole treatment.[6] T2/FLAIR hyperintense lesions in the dentate

TABLE 1 CSF culture

Test	Result
Gram stain	-
W.B.C	0–1
Epith. Cells	0–1
Bacteria	Not seen
Culture	No growth after 24 h No growth after 48 h No growth after 72 h
Anaerobic culture	No growth

TABLE 2 C.S.F fluid

Test	Result	Unit	Reference range
Appearance	Clear		Clear
Color	Color less		Clear crystal color less
W.B.C	0	mm^3	<5/μlit
R.B.C	2		
Cell differential	-	%	60%–70% lymphocyte 30%–35% monocyte
Glucose	99	mg/dl	>2/3 blood glucose
Protein	202	mg/dl	<500

TABLE 3 Oligo clonal banding

Test	Result	Unit	Reference Range
Albumin Serum	3.5 g/dl	g/dl	3.5−5
CSF Albumin	19 mg/dl	mg/dl	10–35
IgG	1153 mg/dl	mg/dl	800–1700
IgG CSF	3.8 mg/dl	mg/dl	Up to 8 0
IgG index	0.6		3–0.7
Alb index	5.4		<9: intact BBB 9–12: Slight impairment 12–20: Moderate impairment 30–100: Sever impairment >100: Complete impairment

nuclei are the best diagnostic finding. In some cases, lesions of the dentate nuclei were not present initially but revealed on re-imaging.[7,8] The majority of the cases present cerebellar dysfunction (dysarthria, ataxia, dysmetria, and nystagmus) followed by altered mental status and seizures,[5] chorea, myoclonus,[9,10] and pure sensorineural hearing loss are also reported.[11] The patient has also taking methadone, and there are reports of toxic leukoencephalopathy due to methadone.[12]

Toxic leukoencephalopathy should be considered in these patients, and suspected drug should be discontinued.

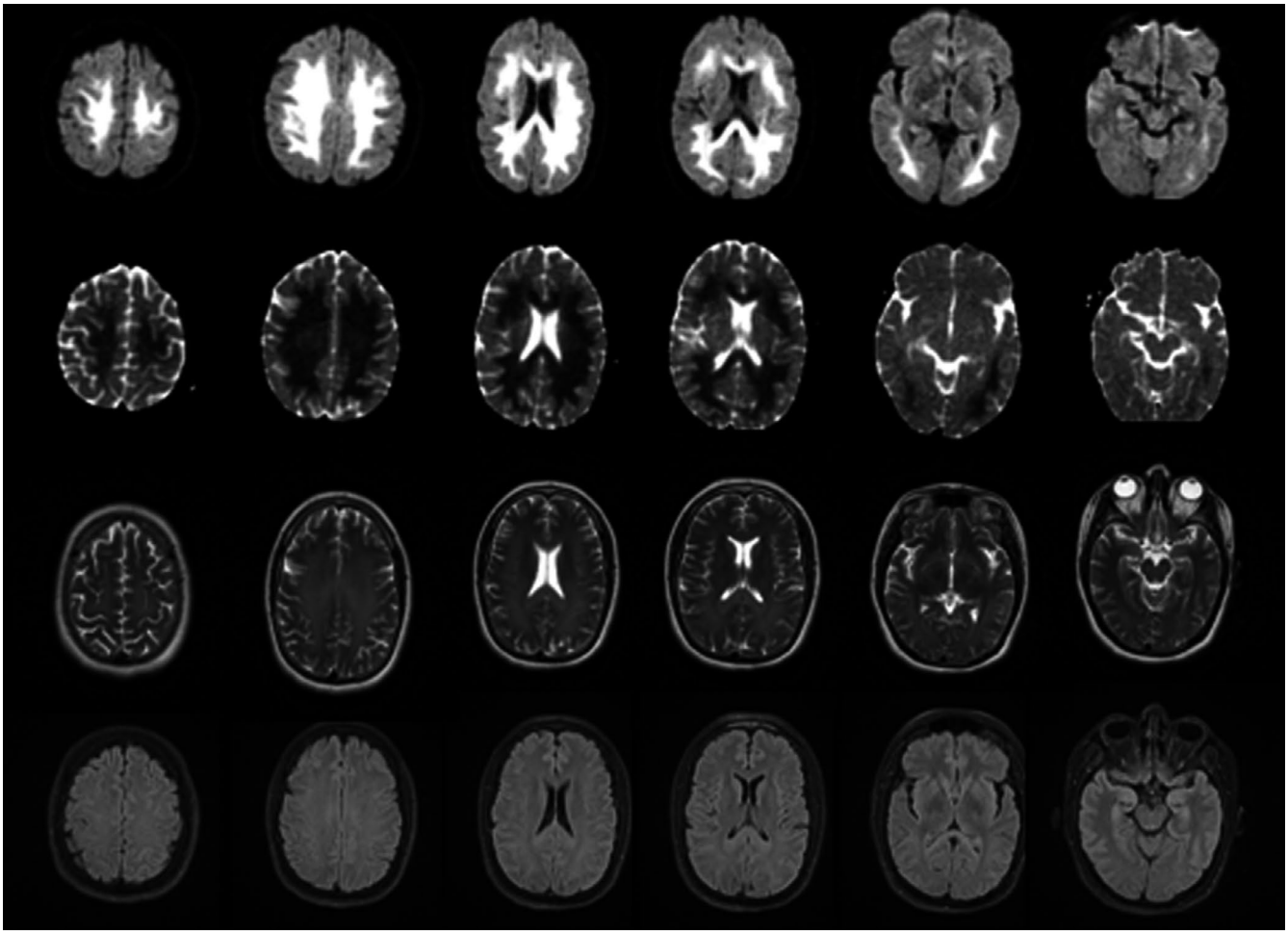

FIGURE 1 Brain MR in axial T1, T2, FLAIR, DW, and sagittal and coronal T2 sequences. Increased signal changes in periventricular regions on both sides and also in the corpus callosum

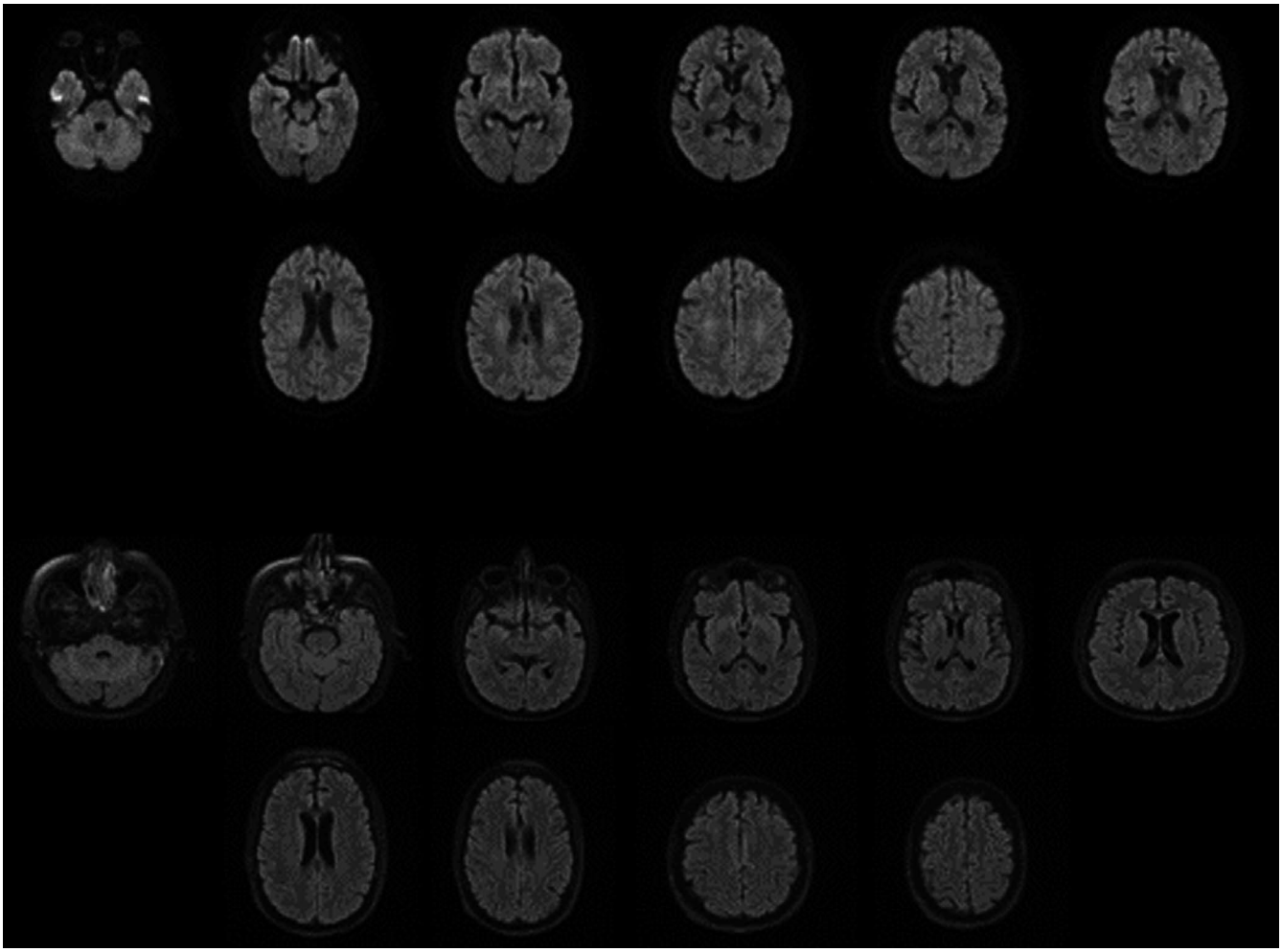

FIGURE 2 Brain MRI without contrast. Mild dilation of ventricle along with widening of lateral sulcus, severe mucosal thickening at ethmoid complex and also sphenoid sinus and less than severely at mastoid air cells

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None.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Dr. Hoorvash Faraji Dana was responsible for management of the patient. Dr. Lida Shojaei Arani was responsible for consultation and also patient management. Dr. Ali Faraji collected the data and drafting the case presentation section. Dr. Kiumars Bahmani involved in drafting the manuscript and reviewed the literature.

ETHICAL APPROVAL

All procedures performed in this case report have been carried out in accordance with the rules of ethics in research, and permission has been obtained from the patient to use the data.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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