ORIGINAL ARTICLE

Methamphetamine Related Radiculopathy: Case Series and Review of Literature

MOHSEN FOROUGHIPOUR, MOHAMMAD TAGHI FARZADFARD*, MEISAM AGHAEE, ALI GHABELI-JUIBARY, FARIBORZ REZAIETALAB

Department of Neurology, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

Background: Peripheral nervous injury and neuromuscular complications from methamphetamine abuse has not been reported. The mechanism is not yet identified.
Methods: Eight patients with lower extremity weakness following methamphetamine abuse were reported during December 2009 to May 2010.
Results: Patients presented with lower extremity weakness. All patients were co-abusers of methamphetamine and opioids. Other clinical manifestations comprised of distal paresthesia of the lower extremities with progression to proximal portions, with minimal sensory involvement in the distal of the lower extremities. Electrodiagnostic findings were consistent with lumbosacral Radiculopathy. Vital signs were unremarkable and all laboratory tests were within normal limits. Follow-up examination after three months showed improvement of weakness in 3 patients.
Conclusion: For patients with a history of illicit drug abuse and acute neuromuscular weakness, methamphetamine or heroin toxicity should be taken into account. Hence, urine morphine and amphetamine/ methamphetamine tests should be performed and serum lead and thallium levels should be evaluated. In addition, rhabdomyolysis and myoglobinuria should be worked up.

Keywords: Methamphetamine; Heroin; Radiculopathy; Neuropathy

INTRODUCTION

Amphetamine-like drugs are potent psychostimulants capable of producing prompt neuropsychiatric effects (1,2). While amphetamine abusers are seeking euphoria, sensual enhancement, greater physical endurance and visual illusions as desired effects; headache, nausea, tachycardia, hyperthermia, agitation, anxiety, insomnia and several neurologic complications may develop as side effects (1-3). Recreational abuse of these drugs has shown an increasing trend during recent decade in Iran (3).

Methamphetamine or N-methyl-O-phenyliso-propylamine is a lipid soluble compound which has been shown to be a powerful neurotoxin (1,4). It is available mostly in tablet form in the illicit drug market in Iran and is commonly called shisheh (/shishə/ means “glass” in English). Methamphetamine abusers strive to increase the neurologic effects of the drug and want to experience an upsurge in their euphoria overtime. Therefore, abusers increase their dose either suddenly and subsequently risk acute overdose, or gradually and develop chronic complications (3-26). Expected acute neurologic complications of amphetamine abuse include seizures and ischemic or hemorrhagic cerebral accidents. The most frequent long-term complications include cognitive impairments, psychosis and Parkinsonism (Table 1).

Lumbosacral radiculopathy following methamphetamine abuse has not been reported in peer reviewed literature so far. Clinical presentation of this disorder usually consists of flaccid paraparesis or paraplegia with sensory loss in the legs and lower thoracic dermatomes along with urinary sphincter disturbances in some occasions. In this study, we described a series of eight patients who developed lumbosacral radiculopathy following methamphetamine abuse.

METHODS

During December 2009 to May 2010, 8 methamphetamine abusers who presented with lumbosacral radiculopathy were admitted to Ghaem Hospital, Mashhad Medical University of Medical Sciences. Clinical manifestations, laboratory tests (serum electrolytes, complete blood count, lipid profile, immunologic tests, serum antibodies against herpes simplex virus and varicella zoster virus, and serum B12 level), electromyography (EMG) and nerve conduction velocity (NCV) were collected from all patients. EMG and NCV were performed using Medelec MS92 (Medelec, San-ei, Tokyo, Japan) and Toennies Multiliner E (Jaeger/Toennies, Höchberg, Germany) respectively. Diagnosis was made based on history and clinical findings. All Patients declared that they have abused methamphetamine (shisheh) for at least a period of time and especially prior to admission. All of them admitted that they have abused other types of illicit drugs, especially opioids.

RESULTS

During a 5 month period, 8 methamphetamine abuser subjects who presented with lumbosacral radiculopathy were

*Correspondence to: Mohammad Taghi Farzadfard, MD. Assistant Professor, Department of Neurology, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran.
Tel:+98 511 801 2306, E-mail: Farzadfardmt@mums.ac.ir
Received 29 March 2013; Accepted 12 May 2013

Table 1. Neurologic complications following abuse of amphetamine-like drugs

Neurologic Complications	Reference
Seizure	3,5,7-9
Cerebral Ischemia (Stroke),	3,5,7-14
Cerebral hemorrhage (ICH, SAH)	7,9,10,15
Serotonin Syndrome	16
Bruxism	3
Optic nerve atrophy (peripheral neuropathy)	17
Transient ischemic attack	7
Spinal cord infarctions	7
Radiculopathy	Present study,18,19
Chorea athetoid and Dyskinesia	3,7,8
Cognitive impairment	6,9,20-23
Parkinson's Disease	5,6,9,24-26
Psychosis	5-9
Rhabdomyolysis	7

admitted. The median age of patients was 26 years and five patients were male. All patients abused methamphetamine via ingestion of tablets in the past 12 months prior to admission to the hospital. No patient had a history of disc herniation or spinal trauma.

Clinical manifestations comprised of distal paresthesia of the lower extremities with progression to proximal portions, with minimal sensory involvement in the distal of the lower extremities. On physical examination, deep and superficial sensory loss was observed. Achilles tendon and patellar tendon stretch reflex were diminished or absent in all patients. Weakness of hip extension, knee flexion and plantar flexion were also evident. Decreased forces of the lower extremities with prominence of distal muscles were observed. Laboratory profiles of all patients were within normal limits. Lumbosacral magnetic resonance imaging was performed for all patients and showed unremarkable findings. EMG/NCV in all patients showed variable degrees of lumbosacral radiculopathy. Sensory nerve conduction studies were normal. Compound motor action potentials were normal except in two patients with severe damage showing diminished amplitude. F waves were normal in all patients.

At a three month follow up after discontinuation of methamphetamine, plexopathy in three patients subsided and they were able to walk. The other 5 patients showed some degrees of disability on follow-up.

DISCUSSION

Radiculopathy, as a subset of neuropathic disorders, is a condition in which nerve roots are adversely affected. In a majority of cases, the disorder is caused by nerve root compression as a result of disk herniation or degenerative spondylosis (27). However, radiculopathy in our patients was probably due to the neurotoxic effects of methamphetamine. The exact mechanism of neurotoxicity has not been completely identified. Possible causes might be direct neuronal damage or vasoconstriction due to methamphetamine (7,28). There are safety reports of patients who developed radiculopathy following methamphetamine abuse while concomitantly being treated with carboplatin or Advair Diskus 250/50 (18,19). Nevertheless, it is not clearly known whether radiculopathy in these cases was caused by the neurotoxic properties of methamphetamine or caused by deleterious interactions between methamphetamine and carboplatin or Advair Diskus 250/50. Another possible theory would be the adverse effects of the aforementioned medicines.

Apart from methamphetamine, neuropathic disorders following abuse and overdose of other illicit drugs including heroin and cocaine were reported in several articles (Table 2). There were many reports regarding heroin associated plexopathy and radiculopathy (29-37). In most of these reports, brachial or lumbosacral plexopathy was accompanied by rhabdomyolysis (29,31-37). In this regard, Diaz Guzman et al. suggested the term rhabdomyolysis-lumbosacral plexopathy (RLPS) to describe lumbosacral plexopathy along with rhabdomyolysis developing shortly after intravenous heroin administration (31). The sensory and motor deficit levels may extend to the cervical region in heroin-induced radiculopathy (42,43). The prognosis is generally poor, with residual spastic paraparesis and sensory deficits, and in some patients, death may occur. Electrodiagnostic studies assist in localizing the lesions and provides a more accurate diagnosis (34,44). Almost all reported cases of neuromuscular complications have occurred following intravenous injections of heroin rather than other methods of abuse. Unsafe non-sterile injections of heroin and the use of a mixture of various substances may also be related to this pathology. Notwithstanding, some studies reported these complications after heroin was taken orally or intranasally (29,32). This suggests a systemic mechanism

Table 2. Neuropathy due to illicit drug abuse

Substance	Neuropathic features	No. cases (Reference)
Heroin		
	Brachial plexopathy	1 (29), 1 (30)
	Rhabdomyolysis + brachial/lumbosacral plexopathy	3 (29), 1 (31), 5 (32), 1 (33), 1 (34), 4 (35), 2 (36), 1 (37)
	Rhabdomyolysis + Myelopathy	2 (35), 1 (37), 1 (38)
	Peripheral neuropathy	97 (39), 1 (40)
	Rhabdomyolysis + Distal axonal sensorimotor neuropathy	2 (29)
Amphetamine-like drugs		
	Radiculopathy	8 (*), 21 (18), 23 (19)
Cocaine		
	Multiple mononeuropathy	1 (41)

* Present study

as a cause of radiculopathy rather than a local trauma.

The following causes have been proposed for heroin induced radiculopathy: (a) an allergic reaction from an unknown substance used in 'cutting' heroin (30,36,37,45); (b) a direct neurotoxic effect of heroin or contaminants (31,32,45); (c) an isolated vasculitis (45); (d) embolism of adulterants (45); (e) systemic hypoxia and hypotension due to border zone infarction or vascular lesion of the spinal cord (45); (f) relative ischemia of spinal column due to hypotension following hypersensitivity reaction to heroin or an adulterant (42); and (g) hyperextension injury of the neck (45). These theories can similarly be proposed for radiculopathy resulting from methamphetamine.

The role of adulterants in causing these idiopathic complications could not be ignored. In Iran, several reports confirmed adulterants in illicit drugs, with lead being the most common culprit (46-48). Lead poisoning has shown to induce radiculopathy in chronic occupational exposure (49).

In this study, patients were treated supportively by reducing pain with analgesics and post discharge physiotherapy. Currently, no specific treatment could be recommended due to the limited information about the mechanism of disease (7,30).

LIMITATIONS

In this study, urine levels of amphetamine/ methamphetamine and morphine were not reported. In addition, serum levels of lead and thallium, which are the most reported adulterants in illicit drug market in Iran, were not screened. Moreover, we could not access any of the ingested substances to chemically analyze the active ingredient. Furthermore, all patients in this study were co-abusers of opioids and methamphetamine. Hence, radiculopathy could not be exclusively attributed to either drug. Correspondingly, Nicholas et al showed that a subset of HIV infected patients with high levels of neuropathy abused significantly higher amount of amphetamines and other illicit drugs in addition to alcohol use and cigarette smoking (50).

CONCLUSION

For patients with a history of illicit drug abuse and acute neuromuscular weakness, methamphetamine or heroin toxicity should be taken into account. Hence, urine morphine and amphetamine/methamphetamine tests should be performed and serum lead and thallium levels should be evaluated. In addition, rhabdomyolysis and myoglobinuria should be worked up. Furthermore, it seems judicious to add methamphetamine and heroin toxicity to the list of differential diagnoses of lumbosacral radiculopathy.

ACKNOWLEDGMENT

The authors are grateful to Dr. M. M. Etemadi for his valuable comments and kind support. We also thank the director of nursing and all nurses of department of neurology, Ghaem Hospital for their kind cooperation.

Conflict of interest: None to be declared
Funding and support: None

REFERENCES

1. Lineberry TW, Bostwick JM. Methamphetamine abuse: a perfect storm of complications. Mayo Clin Proc 2006 Jan;81(1):77-84.
2. Afshari R, Monzavi SM. Illicit Drug Overdose. In: Afshari R, Monzavi SM, editors. Afshari's Clinical Toxicology and Poisoning Emergency Care. 2nd ed. Mashhad: Mashhad University of Medical Sciences Publication; 2012. p.137-74.
3. Brust JC. Acute neurologic complications of drug and alcohol abuse. Neurol Clin 1998 May;16(2):503-19.
4. Davidson C, Gow AJ, Lee TH, Ellinwood EH. Methamphetamine neurotoxicity: necrotic and apoptotic mechanisms and relevance to human abuse and treatment. Brain Res Brain Res Rev 2001 Aug;36(1):1-22.
5. Rusyniak DE. Neurologic manifestations of chronic methamphetamine abuse. Neurol Clin 2011 Aug;29(3):641-55.
6. Itzhak Y, Achat-Mendes C. Methamphetamine and MDMA (ecstasy) neurotoxicity: 'of mice and men'. IUBMB Life 2004 May;56(5):249-55.
7. Neiman J, Haapaniemi HM, Hillbom M. Neurological complications of drug abuse: pathophysiological mechanisms.

Eur J Neurol 2000 Nov;7(6):595-606.
8. Enevoldson TP. Recreational drugs and their neurological consequences. J Neurol Neurosurg Psychiatry 2004 Sep;75Suppl 3:iii9-15.
9. Büttner A. Review: The neuropathology of drug abuse. Neuropathol Appl Neurobiol 2011 Feb;37(2):118-34.
10. Ho EL, Josephson SA, Lee HS, Smith WS. Cerebrovascular complications of methamphetamine abuse. Neurocrit Care 2009;10(3):295-305.
11. Yen DJ, Wang SJ, Ju TH, Chen CC, Liao KK, Fuh JL, et al. Stroke associated with methamphetamine inhalation. Eur Neurol 1994;34(1):16-22.
12. Ohta K, Mori M, Yoritaka A, Okamoto K, Kishida S. Delayed ischemic stroke associated with methamphetamine use. J Emerg Med 2005 Feb;28(2):165-7.
13. Perez JA Jr, Arsura EL, Strategos S. Methamphetamine-related stroke: four cases. J Emerg Med 1999 May-Jun;17(3):469-71.
14. Rothrock JF, Rubenstein R, Lyden PD. Ischemic stroke associated with methamphetamine inhalation. Neurology 1988 Apr;38(4):589-92.
15. McGee SM, McGee DN, McGee MB. Spontaneous intracerebral hemorrhage related to methamphetamine abuse: autopsy findings and clinical correlation. Am J Forensic Med Pathol 2004 Dec;25(4):334-7.
16. Ener RA, Meglathery SB, Van Decker WA, Gallagher RM. Serotonin syndrome and other serotonergic disorders. Pain Med 2003 Mar;4(1):63-74.
17. Wijaya J, Salu P, Leblanc A, Bervoets S. Acute unilateral visual loss due to a single intranasal methamphetamine abuse. Bull Soc Belge Ophtalmol 1999;271:19-25.
18. Ehealthme. Could Carboplatin, Methamphetamine Hydrochloride together cause Radiculopathy? [Internet]. 2013 [Cited 2013 Apr 1]. Available from: http://www.ehealthme.com/carboplatin-and-methamphetamine-hydrochloride/radiculopathy
19. Ehealthme. Could Advair Diskus 250/50, Methamphetamine Hydrochloride together cause Radiculopathy? [Internet]. 2013 [Cited 2013 Apr 1]. Available from: http://www.ehealthme.com/ advair- diskus-250-50-and-methamphetamine-hydrochloride/radiculopathy
20. Sim T, Simon SL, Domier CP, Richardson K, Rawson RA, Ling W. Cognitive deficits among methamphetamine users with attention deficit hyperactivity disorder symptomatology. J Addict Dis 2002;21(1):75-89.
21. Kalechstein AD, Newton TF, Green M. Methamphetamine dependence is associated with neurocognitive impairment in the initial phases of abstinence. J Neuropsychiatry Clin Neurosci 2003 Spring;15(2):215-20.
22. Scott JC, Woods SP, Matt GE, Meyer RA, Heaton RK, Atkinson JH, et al. Neurocognitive effects of methamphetamine: a critical review and meta-analysis. Neuropsychol Rev 2007 Sep;17(3):275-97.
23. Salo R, Ursu S, Buonocore MH, Leamon MH, Carter C. Impaired prefrontal cortical function and disrupted adaptive cognitive control in methamphetamine abusers: a functional magnetic resonance imaging study. Biol Psychiatry 2009 Apr 15;65(8):706-9.
24. Thrash B, Thiruchelvan K, Ahuja M, Suppiramaniam V, Dhanasekaran M. Methamphetamine-induced neurotoxicity: the road to Parkinson's disease. Pharmacol Rep 2009 Nov-Dec;61(6):966-77.
25. Kuehn BM. Meth use linked to risk of Parkinson disease. JAMA 2011 Aug 24;306(8):814.
26. Callaghan RC, Cunningham JK, Sykes J, Kish SJ. Increased risk of Parkinson's disease in individuals hospitalized with conditions related to the use of methamphetamine or other amphetamine-type drugs. Drug Alcohol Depend 2012 Jan 1;120(1-3):35-40.
27. Tarulli AW, Raynor EM. Lumbosacral radiculopathy. NeurolClin 2007 May;25(2):387-405.
28. Davidson C, Gow AJ, Lee TH, Ellinwood EH. Methamphetamine neurotoxicity: necrotic and apoptotic mechanisms and relevance to human abuse and treatment. Brain Res Brain Res Rev 2001 Aug;36(1):1-22.
29. Dabby R, Djaldetti R, Gilad R, Herman O, Frand J, Sadeh M, et al. Acute heroin-related neuropathy. J Peripher Nerv Syst 2006 Dec;11(4):304-9.
30. Evans PA, Millington HT. Atraumatic brachial plexopathy following intravenous heroin use. Arch Emerg Med 1993 Sep;10(3):209-11.
31. Diaz Guzman J, Pastor Valverde C, Gil Grande R, Alonso Ortiz A, Trueba Gutierrez JL. Rhabdomyolysis and lumbosacral plexopathy in intravenous drug addict: report of a case. (Article in Spanish) An Med Interna 1996 Feb;13(2):84-6.
32. Hecker E, Friedli WG. Plexus lesions, rhabdomyolysis and heroin. (Article in German) Schweiz Med Wochenschr 1988 Dec 31;118(52):1982-8.
33. Riggs JE, Schochet SS Jr, Hogg JP. Focal rhabdomyolysis and brachial plexopathy: an association with heroin and chronic ethanol use. Mil Med 1999 Mar;164(3):228-9.
34. Stamboulis E, Psimaras A, Malliara-Loulakaki S. Brachial and lumbar plexitis as a reaction to heroin. Drug Alcohol Depend 1988 Dec;22(3):205-7.
35. Bernasconi A, Kuntzer T, Ladbon N, Janzer RC, Yersin B, Regli F. Peripheral nerve and spinal cord complication in intravenous heroin addiction. (Article in French) Rev Neurol (Paris) 1996 Nov;152(11):688-94.
36. Delcker A, Dux R, Diener HC. Acute plexus lesions in heroin dependence. (Article in German) Nervenarzt 1992 Apr;63(4):240-3.
37. deGans J, Stam J, van Wijngaarden GK. Rhabdomyolysis and concomitant neurological lesions after intravenous heroin abuse. J Neurol Neurosurg Psychiatry 1985 Oct;48(10):1057-9.
38. Goodhart LC, Loizou LA, Anderson M. Heroin myelopathy. J Neurol Neurosurg Psychiatry 1982 Jun;45(6):562-3.
39. Warner-Smith M, Darke S, Day C. Morbidity associated with non-fatal heroin overdose. Addiction 2002 Aug;97(8):963-7.
40. Gille M, Delbecq J, Depré A, van den Bergh P. Painful sciatic neuropathy after heroin overdose. J Neurol 1995 Jul;242(7):478-80.
41. Beniczky S, Tfelt-Hansen P, Fabricius M, Andersen KV. Multiple mononeuropathy following cocaine abuse. BMJ Case Rep 2009;2009. pii: bcr07.2008.0446. doi: 10.1136/bcr.07.2008.0446.
42. Richter RW, Pearson J, Bruun B, Challenor YB, Brust JC, Baden MM. Neurological complications of addiction to heroin. Bull N Y Acad Med 1973 Jan;49(1):3-21.
43. Amnueilaph R, Boongird P, Leechawengwongs M, Vejjajiva A. Heroin neuropathy. Lancet 1973 Jun 30;1(7818):1517-8.
44. Kaku DA, So YT. Acute femoral neuropathy and iliopsoas infarction in intravenous drug abusers. Neurology 1990 Aug;40(8):1317-8.
45. Hall JH 3rd, Karp HR. Acute progressive ventral pontine disease in heroin abuse. Neurology 1973 Jan;23(1):6-7.
46. Afshari R, Mégarbane B, Zavar A. Thallium poisoning: one additional and unexpected risk of heroin abuse. Clin Toxicol (Phila) 2012 Sep;50(8):791-2.
47. Afshari R, Emadzadeh A. Short communication: case report on adulterated opium-induced severe lead toxicity. Drug Chem Toxicol 2010 Jan;33(1):48-9.

48. Khosrojerdi H, Sarabadani J. Bluish Discoloration of Periodontal Tissue. Asia Pac J Med Toxicol 2012 Dec;1(1):38-40.
49. Nora DB, Gomes I, Said G, Carvalho FM, Melo A. Modifications of the sympathetic skin response in workers chronically exposed to lead. Braz J Med Biol Res 2007 Jan;40(1):81-7.
50. Nicholas PK, Voss JG, Corless IB, Lindgren TG, Wantland DJ, Kemppainen JK, et al. Unhealthy behaviours for self-management of HIV-related peripheral neuropathy. AIDS Care 2007 Nov;19(10):1266-73.