Journal of Infectious Diseases

Review Article

A Case of Prochlorperazine-Induced neuroleptic agent Malignant Syndrome: A Case Report and Literature Review

Sackline Preitas Brilhante de São
Federal University of Espírito Santo, Maruípe, Vitória-ES, Brazil

Corresponding Author

Sackline Preitas Brilhante de São
Federal University of Espírito Santo, Maruípe, Vitória-ES, Brazil,
Email: sacklinebrilhante@yahoo.com

Received Date: Jan 24, 2022
Accepted Date: Jan 26, 2022
Published Date: Feb 27, 2022

Abstract

Neuroleptic malignant syndrome (NMS) could be a medical emergency related to the employment of neuroleptics and antiemetics. NMS is characterised by a particular clinical syndrome of altered mental standing, rigidity, hyperthermy, and involuntary pathology. NMS happens as a results of changes in presynaptic or postsynaptic Intropin communication. Central D2 receptor blockade within the neural structure, nigrostriatal pathways, and neural structure ends up in increased muscular rigidity and tremor via extrapyramidal pathways. neural structure D2 receptor blockade leads to Associate in Nursing elevated temperature point and impairment of heat-dissipating mechanisms. The rumored mortality rates for NMS vary between five to twenty % and also the prevalence of medical complications and illness severity ar the strongest predictors of mortality. this can be a case of a fifty one year previous Caucasian feminine WHO conferred with altered mental standing, temperature of 109°F, diffuse muscular rigidity and involuntary pathology manifested as labile vital sign, tachypnea, hypoxemia and arrhythmia once intense eighteen tablets of major tranquilliser over 3 days for channel upset. Her clinical presentation and laboratory physical exercise were per NMS and he or she developed fatal complications and multi-organ pathology secondary to Prochlorperazine-induced ataractic drug malignant syndrome.

Keywords

ataractic drug malignant syndrome, 5-hydroxytryptamine syndrome, deadly catatonia, autosomal dominant disease, cholinergic crisis, rigidity, dysautonomia, dantrolene, bromocriptine, amantadine, creatin enzyme, major tranquilliser, antipsychotic agent, antiemetic, seizure, dopamine, d2 receptor, dystonia, dyskinesia, benzodiazepines, electroshock, ect, neural structure, extrapyramidal

Introduction

Neuroleptic malignant syndrome (NMS) could be a medical emergency related to the employment of antipsychotics (Neuroleptics) and anti-emetics. NMS is characterised by a particular clinical syndrome of mental standing alteration, muscular rigidity, hyperthermy and involuntary pathology. The syndrome was 1st represented by Delay and colleagues in 1960, in patients treated with high-potency antipsychotics and it absolutely was named (Akinetic hypertonic syndrome) [1]. Incidence rates for ataractic drug malignant syndrome vary from zero.07 to 2.2 % among patients taking antipsychotic agent agents [2]. Mortality has declined from the earliest reports within the Sixties of seventy six % to ten – twenty % [3,4].

NMS happens as a results of changes in Intropin communication. the foremost accepted mechanism by that NMS happens is Intropin D2 receptor antagonism. during this mechanism, central D2 receptor blockade within the neural structure, nigrostriatal pathways, and neural structure ends up in increased muscular rigidity and tremor via extrapyramidal pathways. neural structure D2 receptor blockade leads to Associate in Nursing elevated temperature point and impairment of heat-dissipating mechanisms. Peripherally, antipsychotics result in increased atomic number 20 unharness from the sarcoplasmic reticulum, leading to increased ability, which might worsen the hyperthermy, rigidity, and vegetative cell breakdown.

Symptoms typically develop throughout the primary period of time of ataractic drug medical care, but the association of the syndrome with drug use is individual, which implies that NMS will occur once one dose, or once treatment with identical agent at identical dose for several years.

Physicians ar suggested to own a high index of suspicion for NMS and think about different connected conditions like 5-hydroxytryptamine syndrome, autosomal dominant disease, acute deadly catatonia, and central system infection (meningitis/encephalitis) within the medical diagnosis and clinical workup.

Case Presentation

The patient could be a fifty one year previous Caucasian feminine WHO was transferred to our medical medical aid unit from different hospital ER thanks to epilepsy. She ab initio conferred to the ER with altered mental standing, hyperthermy with a temperature of 109 °F, arrhythmia, tachypnea and cardiovascular disease that was shortly followed by persistent seizures. Her medical record enclosed degenerative arthritis, depression, and history of misuse. Her surgical history enclosed ablation, body part fusion and ablation. Her medications enclosed Pepcid forty mg orally doubly daily, nonsteroidal anti-inflammatory four hundred mg orally thrice daily pro re nata, nontricyclic fifty mg orally once daily, and major tranquilliser (Compazine) five mg orally thrice daily pro re nata. Her family rumored that she took around eighteen tablets of major tranquilliser within the last three days for nausea and channel upset, and this was confirmed by job her pharmacy to verify the last date of refill and doing a manual pill count.

Her initial important signs upon arrival to the primary treating facility were a temperature of 109 °F, pulse rate of
137 beat/minute, rate of twenty five breaths/minute, gas saturation of seventy one on area air and vital sign of 72/32 mmHg. She was actively seizing and hemodynamically unstable, therefore she was intubated within the emergency department of the primary arrival facility, and central blood vessel access was secured to start out endovenous fluids

and broad spectrum antibiotic coverage with antibiotic, cefepime and levofloxacin per infection protocol, this can be additionally to ice packs to decrease her temperature. thanks to severe pathology she was additionally started on carbonate drip and got a complete of three doses of benzodiazepine to abort her seizure.

Initial laboratory physical exercise within the emergency department enclosed complete blood count: (White cell count: four.9 x10^9/L, Hemoglobin: eleven.6 g/dL, Platelets: 279 x10^9/L), complete metabolic profile: (Potassium: five.7 mmol/L, Sodium: 138 mmol/L, Bicarb: ten mmol/L, Creatinine:

1.7 mg/dL, AST: seventy three U/L, ALT: thirty five U/L, Total Protein: 6.6 g/dL), drinkable acid: eighteen.5 mg/dL, blood gas (PH: seven.05, PCO2: twenty nine mm Hg, HCO3: eight meq/L, PO2: fifty five metric linear unit Hg), humour alcohol level: none, Datril level: negative, salt level: negative, excretory product drug screen: negative, excretory product analysis : trace bacterium, troponin-I: two.5 ng/mL.

Initial ECG showed sinus arrhythmia (Figure 1). CAT (CT) of the pinnacle didn't show any acute method. CT chest showed bilateral basal pathology. CT abdomen and pelvis showed no acute method. spinal tap results were (RBCs: 158 cells/µL, WBC: two cells/µL, Glucose: sixty one mg/dL, Protein: twenty eight mg/dL).

The patient didn't show any clinical improvement therefore she was transferred to the next level of care. Upon arrival to our medical aid unit (ICU) she was already intubated and off sedation, her important signs were (T: ninety nine °F, HR: 124 beat/minute, BP: 115/72 mmHg). No signs of bodily trauma. Head atraumatic and normocephalic. Pupils expanded and non-reactive. vas examination discovered tachycardic S1 and S2. metabolism examination discovered bilateral wheezes. Abdominal examination discovered paries rigidity. She already had Associate in Nursing inward Foley tube with cola coloured excretory product within the bag. Her skin was diffusely heat with no visible rash, bruising, haematoma or IV track marks. Central system examination showed Associate in Nursing intubated patient with no response to unwholesome stimulation, but she had vital rigidity within the higher and lower limbs additionally to increased tone. Her deep connective tissue reflexes were diffusely absent.

At our medical aid unit we have a tendency to continuing endovenous fluid revitalization, carbonate drip and broad spectrum antibiotics. Laboratory investigations were perennial to follow the patient clinical response to the initial revitalization measures. Her ABG showed (PH: seven.3, PO2:

286 mm Hg, PCO2: thirty mm Hg, HCO3: fifteen meq/L). Complete blood count (White cell count: nine.5 x 10^9/L, Hemoglobin: twelve.1 g/dL, Platelets: one hundred thirty x10^9/L). excretory product analysis (Bilirubin: massive, Blood: massive, Ketone: Positive, macromolecule >300 mg/dL, Nitrite: Positive, blood corpuscle esterase: Positive). Microscopic excretory product analysis showed (WCC: 5-10 WBCs/hpf, RBC: 5-10 cells/hpf, Casts: Hyaline and Fine granular). Complete metabolic profile (K: three mmol/L, Na: 142 mmol/L, Cl: 117 mmol/L, HCO3: ten mmol/L, BUN: fifteen mg/dL, Cr: 1.84 mg/dL, Ca: 5.6 mg/dL, Albumin: 2.9 g/dL, Protein: 5.3 g/dL, basic phosphatase: fifty three U/L, AST: 502 U/L, ALT: 117 U/L). humour hemoprotein > one thousand mg/dL. creatin enzyme (CK) 28234 U/L. Troponin-I > fifty ng/mL. CRP < .4 mg/L. ESR:

8 mm/hour. Repeat excretory product drug screen was positive for benzodiazepines solely.

Her rate was persistently locomote between 120-140 beat/minute (sinus tachycardia) (Figure 2), force per unit area was labile with multiple hypotensive episodes (Figure 3). Temperature ranged from one hundred – 104 °F (Figure 4). She confiscate once more therefore Levetiracetam (Keppra) was initiated and he or she was placed on continuous graphical record (EEG) that showed a coffee amplitude flat line while not reactivity throughout. She became hypotensive later therefore a vasoconstrictor (norepinephrine) was started. Electrolytes abnormalities were endlessly corrected and monitored per our electrolytes replacement protocol. Dantrolene was given per specialist recommendation.

Few hours later the patient developed inanimate bodily cavity cardiac arrhythmia, therefore emergency procedure (CPR) was initiated with no success reciprocally of spontaneous circulation (ROSC). when multiple cycles of unsuccessful resurgence|CPR|cardiac resuscitation|mouth-to-mouth resuscitation|kiss of life|resuscitation|emergency procedure} the family requested stopping resuscitation measures; and patient ceased. Follow abreast of the initial blood cultures and excretory product cultures finalized as no growth in each.

Discussion

Neuroleptic malignant syndrome (NMS) could be a medical emergency related to the employment of antipsychotics (neuroleptics) and anti-emetics. The syndrome is characterised by a IV of mental standing modification, muscular rigidity, physiological state and involuntary disfunction. The syndrome was initial delineated by Delay and colleagues in 1960, in patients treated with high- efficiency antipsychotics and it absolutely was named (Akinetic hypertonic syndrome) [1]. Incidence rates for major tranquillizer malignant syndrome vary from zero.07 to 2.2 p.c among patients taking antipsychotics [2]. Mortality has declined from the earliest reports within the Nineteen Sixties of seventy six p.c to ten – twenty p.c [3,4,5].

NMS happens as a results of changes in presynaptic or postsynaptic monoamine neurotransmitter sign. the primary mechanism by that antipsychotics cause major tranquillizer malignant syndrome is that of monoamine neurotransmitter D2 receptor antagonism. during this mechanism, central D2 receptor blockade within the neural structure, nigrostriatal pathways, and neural structure ends up in enlarged muscle rigidity and tremor via extrapyramidal pathways. neural structure D2 receptor blockade leads to associate elevated temperature point and impairment of heat-dissipating mechanisms [6,7,8,9]. The second mechanism is reduced monoamine neurotransmitter sign ensuing from unforeseen withdrawal of dopaminergic agents or once the drug indefinite quantity is dead reduced in individuals taking dopaminergic medication like dihydroxyphenylalanine for degenerative disorder [10].

Peripherally, antipsychotics cause enlarged Ca unharness from the sarcoplasmic reticulum, leading to enlarged muscular ability that successively worsens physiological state, rigidity, and rhabdomyolysis [11]. Genetic factors play a job in NMS. Case reports of major tranquillizer malignant syndrome occurring in identical twins similarly as during a mother and 2 of her daughters are according [12]. Genetic studies have shown that the presence of a selected allelomorph of the monoamine neurotransmitter D2 receptor cistron is over-represented in NMS patients [13].

While symptoms typically develop throughout the primary period of major tranquillizer medical aid, the association of the syndrome with drug use is individual which suggests that NMS will occur when one dose or when treatment with constant agent at constant dose for several years [14]. the foremost common anorectic medications square measure antipsychotics and anti-emetics (Table one and Table 2). NMS is most frequently seen with high-potency first-generation tranquilizer agents (e.g neuroleptic, Fluphenazine). However, each category of tranquilizer medication has been involved, as well as the low-potency (eg, Chlorpromazine) and second- generation tranquilizer medication (eg, Clozapine, Olanzapine) similarly as anti-emetic medication (eg, Metoclopramide, Promethazine). NMS is additionally seen in patients treated for encephalopathy within the setting of withdrawal of L-dopa

or monoamine neurotransmitter agonist medical aid, similarly like dose reductions and a switch from one agent to a different [10,15].
The main risk factors for NMS square measure high-potency major tranquillizer use, high-dose major tranquillizer use, fast increase in major tranquillizer dose, depot injectable major tranquillizer use and previous episodes of major tranquillizer malignant syndrome. alternative potential risk factors embrace dehydration, deficiency disease, organic brain syndromes and metallic element use.

The IV of NMS symptoms usually evolves over one to a few days and includes physiological state, muscular rigidity, mental standing alterations and involuntary instability. Mental standing modification is that the initial symptom within the majority of patients [16]. This typically manifests as agitated delirium, confusion, nervous disorder and ultimate coma. involuntary instability usually takes the shape of cardiac arrhythmia, labile force per unit area, tachypnea, sweating, dysrhythmias and hypoxemia [17].
Hyperthermia could be a process symptom, temperatures of quite 38°C area unit typical, however even temperatures larger than 40°C aren't uncommon (40 percent) [5]. Muscular rigidity is usually generalized with associated magnified tone, and delineate as "lead-pipe rigidity".
Physical examination can show signs of involuntary dysregulation as well as physiological state, body process, cardiac arrhythmia, tachypnea, hypoxemia and labile vital sign. Signs of weakened dopaminergic activity as well as muscular rigidity, dystonia and neurological disease. additionally to signs of body process agitation and altered mental standing starting from agitation to temporary state, confusion, and coma.
The syndrome happens among the primary fortnight of medical care initiation. However, ninety p.c of cases occur among ten days. In associate analysis of 340 cases, seventy p.c of patients followed a typical course of mental standing changes showing initial, followed by rigidity, then physiological state, and involuntary disfunction [16].
Multiple laboratory abnormalities are seen in NMS. Complete blood count can show blood disorder and symptom. solution abnormalities like hypocalcaemia, symptom, symptom, symptom, and acidosis area unit often seen. Elevated aminoalkanoic acid enzyme (CK) that is usually quite a thousand international units/L [7,16,17,18]. CK elevation correlates with illness severity and prognosis [18]. Elevations of suck dehydrogenase, base-forming enzyme, and liver transaminases area unit common. an occasional liquid body substance iron concentration is sensitive however not specific marker for NMS among acutely sick medicine patients [17,19]. Myoglobinuric acute kidney disease may end up from rhabdomyolysis and correlates with prognosis.
In patients with doable NMS, brain imaging studies and spinal tap area unit needed to exclude structural encephalopathy and infection. resonance imaging (MRI) and CT (CT) area unit usually traditional. body fluid is sometimes traditional, however a nonspecific elevation in macromolecule may be seen.
Electroencephalography (EEG) could also be done to rule out non-convulsive epilepsy. In NMS patients graphical record might show a generalized slow wave activity.
Physicians area unit suggested to stay in mind alternative medical diagnosis which will have similar signs and symptoms as well as cholinergic crisis, central system infection (meningitis/encephalitis), heat stroke, DTs, tumour, thyroid storm and septic shock. careful anamnesis, comprehensive physical examination, additionally to applicable laboratory testing and imaging will facilitate in narrowing the medical diagnosis. alternative clinical syndromes will mimic NMS and may forever be enclosed within the medical diagnosis of NMS like monoamine neurotransmitter syndrome that is characterised by the triad of altered mental standing, involuntary disfunction, and movement disorder (tremor and abnormal involuntary movement) following exposure to serotonergic agent. The mechanism of monoamine neurotransmitter syndrome is excessive monoamine neurotransmitter (5-HT or serotonin) stimulation. Laboratory findings characteristic of neuroleptic drug malignant syndrome (eg, elevated aminoalkanoic acid enzyme level, liver operate take a look at abnormalities, and low liquid body substance iron level) don't occur in monoamine neurotransmitter syndrome. The monoamine neurotransmitter syndrome may be distinguished from neuroleptic drug malignant syndrome by a close history of medication use, and also the presence of tremor and abnormal movements however the absence of severe rigidity. Treatment includes removal of the offensive drug and substantiating management [20,21,22,23]. deadly catatonia happens in folks with psychosis or throughout frenzied episodes. Neuroleptics would possibly either improve or worsen the symptoms of deadly catatonia. deadly catatonia tends to own a prodroma of pleasure and agitation before the onset of rigidity, whereas neuroleptic drug malignant syndrome tends to start with rigidity
[24,25,26] it's caused by associate chromosome dominant mutation within the ryanodine receptor, that results in excessive atomic number 20 unleash from the sarcoplasmic reticulum in skeletal muscles once potent halogenated inhalational anesthetic agents or muscle relaxant area unit administered. Treatment is substantiating care, use of Dantrolene to decrease atomic number 20 unleash, and future shunning of causative medication [27,28,29,30].
The foremost necessary intervention is to discontinue all antipsychotics and removal of alternative potential contributive psychedelic agents if doable. Maintaining euvolemic state and viscus stability. Alkalization of weewee to assist preventing acute kidney disease and enhance excretion of muscle breakdown product. dominant fever victimisation cooling blankets, ice water, lavage and ice packs, additionally to victimisation benzodiazepines to manage agitation and rigidity.

1. Dantrolene could be a direct-acting striated muscle relaxant and is effective in treating autosomal dominant disorder (MH). Doses of one to a pair of.5 mg/kg IV area unit usually utilized in adults and might be perennial to a most dose of ten mg/kg/day. effectivity includes reduction of warmth production in addition as rigidity, and effects area unit rumored among minutes of administration. there's associated risk of hepatotoxicity, and Dantrolene ought to most likely be avoided within the setting of abnormal liver operate tests. Common aspect effects embody headache, nausea, vomiting, confusion and hallucinations.
2. Bromocriptine could be a Dopastat agonist prescribed to revive lost dopaminergic tone. it's suggested to be continuing for ten days when NMS is controlled then tapered slowly. Common aspect effects embody nausea, headache, coryza and lightheadedness.
3. Amantadine has dopaminergic effects and is employed as another to bromocriptine. associate initial dose is 100 mg orally or via stomachic tube and is titrated upward PRN to a most dose of two hundred mg each twelve hours. Common aspect effects embody hallucinations, dizziness, postural hypotension, pre-syncope and syncope.

A reasonable approach is to start out with benzodiazepines (Lorazepam or Diazepam) beside Dantrolene in moderate or severe cases, followed by the addition of Bromocriptine or Amantadine [31].

The role of shock treatment in NMS:
In patients with neuroleptic drug malignant syndrome, shock treatment (ECT) helps with the alteration of temperature and level of consciousness. {ect|electroconvulsive medical care|electroshock|electroshock therapy|ECT|shock therapy|shock treatment} ought to be thought of in patients not responding to medical therapy within the initial week, those in whom residual catatonia persists when alternative symptoms have resolved, and people in whom deadly catatonia is suspected as another or concomitant disorder [32,33,36,37,38]. during a case series study of fifteen patients UN agency had neurocognitive or psychosis spectrum

disorders and developed NMS when exposure to multiple antipsychotic drug medicine. All patients received bi-temporal electroshock therapy when failing pharmacotherapy for NMS. shock treatment resulted during a remission rate of seventy three.3%. Patients showed early initial response to electroshock therapy (mean of four.2 treatments), however a median of seventeen.7 treatments was necessary to attenuate repetition of tonus signs [36].

ECT is usually safe, however, serious treatment-related complications as well as pathology and fibrillation are rumored [32-38].

Conclusion

Neuroleptic malignant syndrome could be a medical emergency related to the utilization of neuroleptic drug agents and characterised by a particular clinical syndrome of mental standing amendment, rigidity, physiological state and dysautonomia. the foremost common motivating medications area unit antipsychotics and anti-emetics. NMS will occur when one dose or when treatment with an equivalent agent at an equivalent dose for several years. it's not a dose-dependent development, however higher doses area unit a risk issue. Physicians area unit suggested to own a high index of suspicion and take into account alternative connected medical diagnosis within the clinical workup, as early recognition and treatment is of important importance to scale back morbidity and mortality of this fatal entity.

References

1. Delay J., Pichot P., Lemperiere T., Elissalde B., Peigne F. nonphenothiazine and non-reserpine major neuroleptic, haloperidol, in the treatment of psychoses. Ann. Med. Psychol. (Paris) 1960; 118(1): 145-152.

2. Gelenberg AJ; Bellinghausen B; Wojcik JD; Falk WE; Sachs GS. A prospective survey of neuroleptic malignant syndrome in a short-term psychiatric hospital. Am J Psychiatry. 1988; 145(4): 517-8.

3. Shalev A, Hermesh H, Munitz H. Mortality from neuroleptic malignant syndrome. J Clin Psychiatry. 1989; 50(1): 18.

4. Modi S, Dharaiya D, Schultz L, Varelas P. Neuroleptic Malignant Syndrome: Complications, Outcomes, and Mortality. Neurocrit Care. 2016; 24(1): 97.

5. Caroff SN, Mann SC. Neuroleptic malignant syndrome. Med Clin North Am. 1993; 77(1): 185.

6. Henderson VW, Wooten GF. Neuroleptic malignant syndrome: a pathogenetic role for dopamine receptor blockade?. Neurology. 1981; 31(2): 132.

7. Adnet P, Lestavel P, Krivosic-Horber R. Neuroleptic malignant syndrome. Br J Anaesth. 2000; 85(1): 129.

8. Gurrera RJ. Is neuroleptic malignant syndrome a neurogenic form of malignant hyperthermia?. Clin Neuropharmacol. 2002; 25(4): 183.

9. Jauss M; Krack P; Franz M; Klett R; Bauer R; Gallhofer B; Dorndorf W. Imaging of dopamine receptors with [123I] iodobenzamide single-photon emission-computed tomography in neuroleptic malignant syndrome. Mov Disord. 1996; 11(6):726-8.

10. Keyser DL, Rodnitzky RL (1991). "Neuroleptic malignant syndrome in Parkinson's disease after withdrawal or alteration of dopaminergic therapy". Archives of Internal Medicine. 151(4): 794-6.

11. Strawn JR, Keck PE, Caroff SN (2007). "Neuroleptic malignant syndrome". The American Journal of Psychiatry. 164 (6): 870-6.

12. Otani K; Horiuchi M; Kondo T; Kaneko S; Fukushima Y. Is the predisposition to neuroleptic malignant syndrome genetically transmitted?. Br J Psychiatry. 1991; 158:850-3.

13. Mihara K, Kondo T, Suzuki A, Yasui-Furukori N, Ono S, Sano A, Koshiro K, Otani K, Kaneko S. Relationship between functional dopamine D2 and D3 receptors gene polymorphisms and neuroleptic malignant syndrome. Am J Med Genet B Neuropsychiatr Genet. 2003; 117B(1): 57.

14. Pope HG Jr, Aizley HG, Keck PE Jr, McElroy SL. Neuroleptic malignant syndrome: long-term follow-up of 20 cases. J Clin Psychiatry. 1991; 52(5): 208.

15. Wu YF, Kan YS, Yang CH. Neuroleptic malignant syndrome associated with bromocriptine withdrawal in Parkinson's disease--a case report. Gen Hosp Psychiatry. 2011 May; 33(3): 301. e7-8. Epub 2011 Jan 8.

16. Velamoor VR, Norman RM, Caroff SN, Mann SC, Sullivan KA, Antelo RE, Progression of symptoms in neuroleptic malignant syndrome. J Nerv Ment Dis. 1994; 182(3): 168.

17. Rosebush P, Stewart T. A prospective analysis of 24 episodes of neuroleptic malignant syndrome. Am J Psychiatry. 1989; 146(6): 717.

18. Hermesh H, Manor I, Shiloh R, Aizenberg D, Benjamini Y, Munitz H, Weizman A. High serum creatinine kinase level: possible risk factor for neuroleptic malignant syndrome. J Clin Psychopharmacol. 2002; 22(3): 252.

19. Lee JW. Serum iron in catatonia and neuroleptic malignant syndrome. Biol Psychiatry. 1998; 44(6): 499.

20. Boyer EW, Shannon M. N Engl J Med. 2005; 352(11): 1112. The serotonin syndrome.

21. Birmes P, Coppin D, Schmitt L, Lauque D. Serotonin syndrome: a brief review. CMAJ. 2003; 168(11): 1439.

22. Bodner RA, Lynch T, Lewis L, Kahn D. Serotonin syndrome. Neurology. 1995;45(2):219.

23. Mason PJ, Morris VA, Balcezak TJ. Serotonin syndrome. Presentation of 2 cases and review of the literature. Medicine (Baltimore). 2000; 79(4): 201.

24. Fleischhacker WW, Unterweger B, Kane JM, Hinterhuber H. The neuroleptic malignant syndrome and its differentiation from lethal catatonia. Acta Psychiatr Scand. 1990; 81(1): 3.

25. Castillo E, Rubin RT, Holsboer-Trachsler E. Clinical differ-

entiation between lethal catatonia and neuroleptic malignant syndrome. Am J Psychiatry. 1989; 146(3): 324.

26. Julia Park, Josh Tan, Sylvia Krzeminski, Maryam Hazeghazam, Meghana Bandlamuri and Richard W. Carlson, Malignant Catatonia Warrants Early Psychiatric-Critical Care Collaborative Management: Two Cases and Literature Review, Case Reports in Critical Care, 2017, (1), (2017).

27. Caroff SN, Rosenberg H, Fletcher JE, Heiman-Patterson TD, Mann SC. Malignant hyperthermia susceptibility in neuroleptic malignant syndrome. Anesthesiology. 1987;67(1):20.

28. Denborough M. Malignant hyperthermia. Lancet. 1998; 352(9134): 1131.

29. MacLennan DH, Phillips MS. Malignant hyperthermia. Science. 1992; 256(5058): 789.

30. Wappler F. Malignant hyperthermia. Eur J Anaesthesiol. 2001; 18(10): 632.

31. Pileggi DJ, Cook AM. Neuroleptic Malignant Syndrome. Ann Pharmacother. 2016; 50(11): 973.

32. Addonizio G, Susman VL. ECT as a treatment alternative for patients with symptoms of neuroleptic malignant syndrome. J Clin Psychiatry. 1987 Mar; 48(3): 102-5.

33. Caroff SN, Mann SC, Keck PE Jr, Francis A. Residual catatonic state following neuroleptic malignant syndrome. J Clin Psychopharmacol. 2000; 20(2): 257.

34. Trollor JN, Sachdev PS. Electroconvulsive treatment of neuroleptic malignant syndrome: a review and report of cases. Aust N Z J Psychiatry. 1999; 33(5): 650.

35. Davis JM, Janicak PG, Sakkas P, Gilmore C, Wang Z. Electroconvulsive Therapy in the Treatment of the Neuroleptic Malignant Syndrome. Convuls Ther. 1991;7(2):111.

36. Morcos N, Rosinski A, Maixner DF. Electroconvulsive Therapy for Neuroleptic Malignant Syndrome: A Case Series. J ECT. 2019 Apr 22.

37. Harley JA, Peebles C, Porter RJ. Electroconvulsive therapy for catatonia secondary to neuroleptic malignant syndrome in a patient with multiple sclerosis. Aust N Z J Psychiatry. 2019 Jul; 53(7):703-704.

38. González-Romero MF, Avina-Galindo AM, Elbe D, Friedlander R, Vila-Rodriguez F. Lifesaving Electroconvulsive Therapy for a Child With Autism Spectrum Disorder, Severe Self-Injurious Behavior, and Neuroleptic Malignant Syndrome. J ECT. 2019 Apr 22.

39. Tural U, Onder E. Clinical and pharmacologic risk factors for neuroleptic malignant syndrome and their association with death. Psychiatry Clin Neurosci. 2010 Feb; 64(1): 79-87.

40. Nakamura M, Yasunaga H, Miyata H, Shimada T, Horiguchi H, Matsuda S. Mortality of neuroleptic malignant syndrome induced by typical and atypical antipsychotic drugs: a propensity-matched analysis from the Japanese Diagnosis Procedure Combination database. J Clin Psychiatry. 2012; 73(4): 427.