

## NMS case reports associated with SGAs

Source	Patient age/ gender	Diagnosis	NMS history	Other medications	Dose when NMS developed	Presentation/sequelae/ atypical features
<b>Aripiprazole</b>						
Chakraborty N et al. <sup>1</sup>	42/M	Schizophrenia	--	Yes	15 mg	Previously the patient was prescribed other atypicals without benefit. No fever or autonomic instability
Rodriguez OP et al. <sup>2</sup>	--	--	--	--	--	NMS without fever
<b>Clozapine</b>						
Franzen D et al. <sup>3</sup>	62/M	--	--	--	--	NMS developed after 30 years stable treatment with clozapine. Rechallenging the patient after 14 days from recovery was unsuccessful
Brown TM et al. <sup>4</sup>	17/M	Cognitive disability and agitation		Lithium	200 mg/d	The patient had "severe truncal ataxia, difficulty with head control, features of athetosis and hemiballismus as well as dystonia, severe dysmetria and past pointing." NMS developed 15 days after the last dose increase
Gambassi G et al. <sup>5</sup>	77/M	Dementia	No	Paroxetine	25 mg/d	Clozapine had previously been well tolerated by the patient before he discontinued it. NMS symptoms appeared when clozapine, 25 mg/d, was added to paroxetine
Huang TL <sup>6</sup>	34/F	Schizophrenia	--	No	250 mg/d	Induced NMS with long-term use of clozapine. The clozapine rechallenge was successful. Dose was slowly increased to 250 mg/d over 18 days
Baciewicz A et al. <sup>7</sup>	35/M	Bipolar disorder		Valproate sodium	150 mg/d	Normal creatine kinase levels, no rigidity
Karagianis JL et al. <sup>8</sup>	--	--	--	--	--	Fever, rigidity, and elevated creatine kinase were less prominent than in NMS associated with first-generation neuroleptics
Amore M et al. <sup>9</sup>	F	--	No	--	--	Patient had no history of NMS
Chatterton R et al. <sup>10</sup>	Middle aged/M	Schizophrenia	--	No		NMS occurred on a steady state dosage of clozapine monotherapy
Goates MG et al. <sup>11</sup>	--	--	--	--	--	No extrapyramidal symptoms
Vetter P et al. <sup>12</sup>				No		Benign hyperthermia in the post-NMS period
Illing M et al. <sup>13</sup>	M	Schizophrenia, paranoid	Yes	No	--	--
Ganelin L et	42/M	Schizophrenia	--	--	--	Typical NMS presentation.

al. <sup>14</sup>						Severe serum creatine kinase elevation (25,000 U/L).
Sachdev P et al. <sup>15</sup>	33/M	Schizophrenia	--	--	100 mg/d	No muscle rigidity was noted. Low serum phosphorus (0.26 mmol/liter) and platelet levels (36,000/ml)
	36/M	Schizophrenia	No	--	150 mg/d	No rigidity or catatonia was noted
	14/M	Schizophrenia	--	No	375 mg/d	No rigidity or disorientation noticed initially
	36/M	Schizophrenia	Yes (trifluoperazine)	--	--	Patient was treated with 8 unilateral ECT sessions. Complete recovery of NMS occurred over 12 days. Clozapine challenge was unsuccessful. Mild receptive dysphasia and a moderate degree of expressive dysphasia
	15/M	Schizophrenia, mild mental retardation	Yes (chlorpromazine)	Lithium	200 – 300 mg/d	Challenged with clozapine after recovery from previous NMS was unsuccessful. Rechallenge with clozapine several weeks later caused possible NMS. Clozapine was stopped. The third rechallenge with clozapine 150 mg/d four weeks later produced no symptoms
Tsai G et al. <sup>16</sup>	--	--	--	--	--	--
Muller T et al. <sup>17</sup>	M	--	--	Carbamazepine	--	--
Reddig S et al. <sup>18</sup>	Adult/M	--	No	No	--	The patient had classic NMS with lead-pipe rigidity
Burrell MF et al. <sup>19</sup>	Adult/M	Schizophrenia	--	--	--	--
DasGupta K et al. <sup>20</sup>	30/M	--	--	--	25 mg x 3 doses	NMS happened after three doses
Miller DD et al. <sup>21</sup>	Middle aged/M	Schizophrenia	Yes	--	--	--
Bottlender R et al. <sup>22</sup>	Middle aged/F	Schizophrenia	Yes	--	--	Patient had three episodes of NMS with clozapine, risperidone, and amisulpride
Pope HG Jr et al. <sup>23</sup>	Adult/M	Bipolar disorder	Yes (fluphenazine)	Lithium	--	NMS reappeared after about 3 weeks of treatment. The first report of apparent NMS with clozapine
<b>Olanzapine</b>						
Mendhekar DN et al. <sup>24</sup>	16/M	Schizophreniform disorder	--	--	7.5 mg/d po	Retrograde amnesia about the events surrounding the NMS. Anterograde amnesia with deficits in learning new verbal information
Norgard NB et al. <sup>25</sup>	66/F	Paranoid schizophrenia	--	Several other psychiatric drugs	--	--
Supe S et al. <sup>26</sup>	36/F	Chronic schizophrenia	Yes	Flufenazine	--	Generalized tonic-clonic seizures preceded the acute onset of recurrent NMS
Fernandez M et al. <sup>27</sup>	73/F	Depressive syndrome	No	Citalopram	5 mg/d	Patient had multiple other medical diagnoses prior to having NMS
Skarpathiotaki	16/M	Schizophrenia	--	Oxcarbamazepine		NMS developed at a low dose

s M et al. <sup>28</sup>						(12.5 mg/d po) within 8 hours of initiation of treatment
Hall RC et al. <sup>29</sup>	79/M	--	--	Phenytoin, Lorazepam	10 – 40 mg/d	Patient presented with fevers of unknown origin
Hanft A et al. <sup>30</sup>	17/M	Psychotic symptoms	No	Divalproex sodium	10 mg/d	NMS appeared after 2 days of olanzapine treatment. Clozapine was started after recovery under close observation
Nielsen J et al. <sup>31</sup>	Adult/F	Delirium. pneumonia	--	--	--	Fluctuating hyperthermia and autonomic instability during a month before admission. Slight rigidity was present. Creatine kinase was not elevated
Tofler IT et al. <sup>32</sup>	Middle-aged/M	--	--	Fluphenazine		NMS developed while on combination drug therapy
Kontaxakis VP et al. <sup>33</sup>	Middle aged/F	--	--	Paroxetine		NMS developed after addition of paroxetine to olanzapine
Horni G et al. <sup>34</sup>	52/M	--	--	SSRI	--	NMS developed after long and stable treatment (2.5 years)
Kopf A et al. <sup>35</sup>	49/F	Psychotic disorders	Yes (haloperidol, clozapine)	--	--	Patient received olanzapine (20 mg/d) for 11 months after the first NMS episode without adverse effects. NMS developed 12 days after olanzapine re-exposure. Patient was treated with a course of unilateral and bilateral ECT
Suh H et al. <sup>36</sup>	86/M	Dementia with paranoid delusion	Yes	--	5 mg/d	After patient recovered from initial NMS episode, NMS recurred after olanzapine was restarted. He was treated with quetiapine, 25 mg/d, for several days with no signs of NMS
Berry N et al. <sup>37</sup>	16/M	Bipolar disorder	--	Lithium	--	Classic NMS was diagnosed in this patient receiving combination therapy with lithium
Goveas JS et al. <sup>38</sup>	75/M	Bipolar disorder	Yes (haloperidol)	Paroxetine, lamotrigine, lorazepam	10 mg/d	NMS developed on stable dose for approximately 5 months
Arnaout MS et al. <sup>39</sup>	30/M	Schizophrenia	--	--	--	NMS was associated with extremely elevated levels of serum sodium. (190 meq/l)
Hall KL et al. <sup>40</sup>	Adult/F	--	--	No	--	--
Aboraya A et al. <sup>41</sup>	18/M	Schizophrenia	No	Risperidone	--	Patient was treated with 8 days of risperidone followed by 5 days of olanzapine
Reeves RR et al. <sup>42</sup>	53/M	--	--	Levomepromazine	--	NMS without rigidity. Failed rechallenge attempt with olanzapine
Malyuk R et al. <sup>43</sup>	64/F	Bipolar disorder	Yes, twice	Lithium	10 mg/d	NMS developed 18 weeks after initiating olanzapine. Significant medical history
Philibert RA et al. <sup>44</sup>	52/M	Bipolar disorder, Parkinson's disease	--	--	--	Before NMS developed, risperidone and selegiline were discontinued. Olanzapine was added
Stanfield SC et al. <sup>45</sup>	42/M	Schizophrenia	--	--	--	NMS developed after 3 weeks of treatment
Jarventausta K	78/F	Chronic	--	Levomepromazine	--	Patient's medication had been

et al. <sup>46</sup>		schizophrenia				unchanged for more than 2 years. When this combination was restarted later, NMS symptoms reappeared
Nyfort-Hansen K et al. <sup>47</sup>	>80/M	--	--	--	--	--
Gheorghiu S et al. <sup>48</sup>	70/F	Schizoaffective disorder	Yes	Carbamazepine, betahistine	10 mg/d	Patient had been free of antipsychotics for over 6 months before olanzapine was started
Levenson JL <sup>49</sup>	60/F	Schizophrenia, paranoid	Yes	No	10 mg/d	Six days before admission, the patient's haloperidol was changed to olanzapine
Margolese HC et al. <sup>50</sup>	21/M	Mental retardation	Yes, twice	--	12.5 mg/d	Patient had mild to moderate mental retardation
Apple JE et al. <sup>51</sup>	33/M	Severe mental retardation	--	Bupropion	10 mg/d	History of severe mental retardation (Estimated IQ: 33). A later trial of chlorpromazine was unsuccessful
Johnson V et al. <sup>52</sup>	Elderly/M	Schizoaffective disorder	Yes (risperidone)	--	--	NMS developed 2 days after adding olanzapine
Hanel RA et al. <sup>53</sup>	30/M	--	Yes (haloperidol, chlorpromazine)	Orfenadrin, zopiclone	--	--
Burkhard PR et al. <sup>54</sup>	22/M	Schizophrenia, paranoid	Yes (haloperidol, levomepromazine biperidene chlorhydrate)	Clorazepam	10 mg/d	--
Filice GA et al. <sup>55</sup>	67/M	Bipolar disorder	--	--	10 mg/d	After 6 days of treatment, the patient had all major manifestations of NMS.

### Quetiapine

Kobayashi A et al. <sup>56</sup>	68/M	Parkinson's disease	--	--	75 mg/d	Patient had Lewy bodies dementia
Klein JP et al. <sup>57</sup>	30/M	Psychotic depression	--	--	400 mg/d	Both patients had massive elevations of serum creatine kinase associated with quetiapine treatment that disappeared after drug discontinuation. The second case was later treated with olanzapine without complications
	Adult/M	Schizoaffective disorder	--	Lamotrigine, mirtazapine	150 mg/d	
Hatch CD et al. <sup>58</sup>	54/M	--	Yes	--	--	Patient was unsuccessfully challenged with quetiapine after conventional antipsychotic-induced NMS

### Risperidone

Reeves RR et al. <sup>59</sup>	57/M	--	--	Mirtazapine	--	Patient developed NMS within 48 hours of discontinuing haloperidol and adding low doses of risperidone and mirtazapine. He was subsequently treated with olanzapine without adverse effects.
Norris B et	59/F	Bipolar disorder	--	--	2 mg/d	NMS after respirdone restart.

al. <sup>60</sup>						Patient had taken risperidone for several years prior to this episode and had stopped it for approximately 3 weeks. Patient was initially afebrile and had no muscular rigidity
Zalsman G et al. <sup>61</sup>	16/M 17/M	--	--	--	--	Both patients suffered life-threatening "NMS-like" syndrome associated with risperidone treatment
Bottlender R et al. <sup>22</sup>	59/F	Schizophrenia	Yes	Amitriptyline	4 mg/d	Patient had separate episodes of NMS with clozapine, risperidone, and amisulpride. NMS occurred after restarting risperidone
Hayashi H et al. <sup>62</sup>	Adult/M	--	--	Levomepromazine	--	Patient had chronic renal failure. Massive intestinal bleeding was observed during the NMS episode
Reeves RR et al. <sup>63</sup>	24/F	Psychotic disorder	--	Fluvoxamine	--	Patient had a successful challenge with olanzapine and fluvoxamine without adverse effects
Robb AS et al. <sup>64</sup>	Adolescent/F	--	--	--	--	--
Lee MS et al. <sup>65</sup>	27/M	Schizophrenia	--	--	8 mg/d	Delayed NMS after treatment for 21 months
Webster P et al. <sup>66</sup>	--	--	--	--	--	NMS developed within 12 hours of starting the medication
Bajjoka I et al. <sup>67</sup>	75/M	Dementia	No	No	10 mg/d	NMS developed after 3 weeks of risperidone therapy
Kern JL et al. <sup>68</sup>	M	--	--	Paroxetine, venlafaxine	--	Delayed NMS with a 12-month history of risperidone
Sharma R et al. <sup>69</sup>	Adolescent/M					Patient demonstrated the classic tetrad of fever, generalized skeletal muscle rigidity, altered mental status, and autonomic dysfunction
Meterissian GB <sup>70</sup>	53/F	--	Yes	--	--	NMS developed 4 days after starting treatment with risperidone
<b>Ziprasidone</b>						
Strawn JR et al. <sup>71</sup>	--	--	--	Haloperidol	--	--
Borovicka MC et al. <sup>72</sup>	47/M	Schizoaffective disorder	--	Lithium	80 mg bid plus 20 mg IM on day 6	Absence of muscle rigidity
Zaidi AN <sup>73</sup>	50/M	Chronic paranoid schizophrenia	--	--	40 mg bid	NMS developed after 3 weeks of treatment
Leibold J et al. <sup>74</sup>	15/M	Schizoaffective disorder	--	Thiazoles	80 mg/d	Patient had persistent urinary incontinence. NMS developed after 8 weeks of treatment
Gray NS <sup>75</sup>	52/F	Parkinson's disease	No	Sertraline	40 mg/d	Patient had a history of Parkinson's disease
Murty RG et al. <sup>76</sup>	49/F	Affective disorders, psychotic	--	Venlafaxine	120 mg/d	--

Cases that developed from SGA combinations						
Chungh DS et al. <sup>77</sup>	Child/F	Bipolar disorder	--	Risperidone, olanzapine, quetiapine	--	--
Gram LF <sup>78</sup>	--	--	--	Risperidone, olanzapine	--	
Kontaxakis VP et al. <sup>79</sup>	20/M	Schizophrenia	--	Risperidone, clozapine	--	NMS developed after clozapine (100 mg/d) was added to a regimen of risperidone (16 mg/d). Patient later restarted on clozapine monotherapy without further complications
Emborg C <sup>80</sup>	23/M	--	--	Olanzapine, clozapine	100 mg	The day before onset of NMS, olanzapine was supplemented with 100 mg clozapine
	33/M			Olanzapine, clozapine	25 mg/d	Patient was on olanzapine for 7 months before NMS developed. The day before NMS onset, 100 mg clozapine was added

**References** (Note: Reference numbers used here are independent of those in the printed version of this article.)

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