

· 病例报告 ·

## 复发性抑郁障碍进展为谵妄性躁狂1例并文献复习

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[关键词] 复发性抑郁障碍;谵妄性躁狂

[中图分类号] R749.4

[文献标志码] B

[文章编号] 1007-4368(2024)03-440-05

doi:10.7655/NYDXBNSN230662

### A case report of diagnostic conversions from recurrent major depressive disorder into delirious mania and a brief literature review

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[Key words] recurrent major depressive disorder; delirious mania

[J Nanjing Med Univ, 2024, 44(03): 440-444]

谵妄性躁狂(delirious mania, DM)是一种极易被忽视、潜在致死的严重神经精神综合征,表现为极度兴奋躁动,可有短暂、片段的幻听,思维散漫,行为紊乱,伴有冲动行为;也可出现短暂意识障碍,有错觉、幻觉及思维不连贯等症状<sup>[1-2]</sup>。尽管最初认为DM发病率极罕见,但有研究显示,在所有急性躁狂发作病例中,DM占比可高达15%<sup>[3]</sup>。一旦该疾病未被及时识别或未恰当给予治疗,其可快速进展,进而可能威胁生命健康。临床上关于DM的病例报告有限,本文报道1例复发性抑郁障碍进展为DM的患者,以期为DM的早期诊断、治疗提供借鉴和启发。

#### 1 病例资料

患者,男,35岁,无业,离异。因“间断情绪低落、自伤9年,复犯2月余”于2022年9月首次入住上海市精神卫生中心治疗。2013年因目睹家人突

发急性心肌梗死去世,开始睡眠欠佳,情绪尚可自行调节。2015年因父母逼迫其结婚,婚后出现闷闷不乐,情绪低落,自我评价低,前往当地医院就诊,诊断为“中度抑郁障碍”,予以度罗西汀、舒必利治疗,具体剂量及服药时长不详,门诊规律治疗后,情绪症状控制尚可。2016年患者体检时查出腹部血管瘤,于手术切除后开始出现自卑,自觉不如别人,情绪低落,症状出现波动,当地医院门诊治疗,先后予以度罗西汀、舒必利、奥氮平、米氮平、疏肝解郁胶囊等治疗,具体剂量不详,病情平稳,能胜任工作。2021年底患者自觉病情好转,自行停药。停药后再次出现情绪低落,不愿出门,自我评价低,无精打采,兴趣减退,有消极想法,跟家人说“不如死了算了”,再次服药后病情改善不明显,具体药物种类及剂量不详。2022年7月无明显诱因下患者独自徘徊在窗口有自杀想法,并出现用头撞击墙壁等行为,被家人强行送至当地医院精神科治疗,诊断为“复发性抑郁障碍,不伴有精神病性症状的重度抑郁发作”,予以米氮平45 mg/d、度罗西汀20 mg/d、喹硫平200 mg/d,联合改良电抽搐治疗(modified electric convulsive treatment, MECT)及经颅磁刺激治疗后出院,病情改善不彻底,仍出现兴趣减退,闭门不

[基金项目] 国家自然科学基金(82201678);上海市科委(18411961500, 22YF1439100);上海市卫生健康委员会(202040366)

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出。某天家人让其做核酸时,再次出现用头撞墙壁、扇自己巴掌等行为,家人见其病情严重,治疗困难,故送入上海市精神卫生中心。既往史:患者有脾脏肿瘤切除、腹部血管瘤切除手术史。个人史和家族史均无特殊。

入院体格检查和辅助检查:生命体征平稳,神经系统检查未见明显异常;血常规、电解质、肝肾功能、心功能、尿常规、粪常规、肝炎、梅毒、人免疫缺陷病毒及滥用药物筛查等实验室检查无明显异常;心电图、胸部CT、腹部B超、头颅磁共振(magnetic resonance, MR)结果均未见明显异常,脑电图轻度异常(需排除药物影响)。

精神检查:意识清晰,定向力完整,衣着适时整洁,年貌相符,表情愁苦,接触交谈合作,对答切题,注意力集中,未引出幻觉、错觉、感知综合障碍,思维连贯,未引出思维形式、思维逻辑、思维内容障碍等,可及情绪低落、兴趣缺乏,并有自责、消极观念、无价值感、绝望感,情感反应协调,意志要求存在,智能检查粗测尚可,自知力部分存在。汉密尔顿抑郁量表评分27分。根据病史、精神检查及国际疾病与相关健康问题统计分类第十版(International Classification of Diseases 10th Revision, ICD-10)诊断标准,诊断为“复发性抑郁障碍,不伴有精神病性症状的重度发作”。

治疗经过:患者否认既往有躁狂样发作,入院时表现为重度抑郁,故予文拉法辛75 mg/d,10 d后增至150 mg/d抗抑郁治疗,富马酸喹硫平0.05 g/d,2 d后增至0.1 g/d,4 d后增至0.15 g/d,10 d后增至0.2 g/d稳定情绪,劳拉西泮(0.5 mg/d)改善睡眠,2周后患者情绪迅速缓解,否认情绪低落、消极观念,诉求稍有增多,对查房内容稍显抵触。治疗约3周后,患者猜疑室友,并与之发生口角,情绪激动,突发捶门,予以约束性保护。隔天再次予以约束保护时,突然出现极度兴奋躁动,思维散漫,行为紊乱,伴有冲动行为,辱骂医护人员,伴有短暂性的缄默、木僵、凝视,夜眠差。考虑患者是否存在器质性疾病所致精神障碍的可能,故立即予以体格检查及神经系统查体,均未发现明显异常。后续血常规、电解质、尿常规、肝肾功能、心功能、血糖、头颅CT等辅助检查结果显示,仅单核细胞升高(8.8%)、尿酸升高(451.0  $\mu\text{mol/L}$ )、总蛋白降低(64.7 g/L)、球蛋白降低(24.8 g/L),余指标均未见明显异常。考虑患者转向躁狂相,故停用文拉法辛,喹硫平逐渐增至750 mg/d,丙戊酸钠逐渐增至1 000 mg/d,劳拉西泮逐渐增至

1.0 mg,并联合MECT控制兴奋行为,患者仍表现为极度兴奋躁动、紊乱,短暂性意识状态朦胧,并伴有时间、地点定向障碍,言谈中可引出言语性幻听、幻视(为恐怖性)。期间反复进行体格检查、神经系统检查、实验室辅助检查等,均未发现明显异常。联合氨磺必利控制症状,并予电解质补液、营养支持等积极对症治疗。2~3 d后患者病情明显好转,定向力逐渐恢复,幻觉、妄想等精神病性症状消失,难以回忆起当时的发病过程,情绪平稳,饮食睡眠可,逐渐停用劳拉西泮。

## 2 讨论

本例患者出现极度兴奋躁动、言行紊乱、幻听、被害妄想等表现,需要与精神分裂症相鉴别,但是患者精神病性症状表现急遽,继发于情感症状之后,且持续时间不足1个月,深入检查仍可发现一定的情感及现实基础,随情感症状的改善而缓解,故精神分裂症诊断依据不充分。此外,该患者出现定向障碍、幻视、意识水平下降等表现,需排除器质性疾病所致的精神障碍以及精神活性物质所致精神和行为障碍,但是患者为青年男性,平素体健,且全面体格检查、神经系统检查及辅助检查均未发现明显异常,故暂不考虑此诊断。本例为复发性抑郁障碍患者,经抗抑郁治疗后,出现定向障碍,可疑错觉、幻觉、关系妄想、被害妄想,极度兴奋躁动,易激惹,难以安静,行为冲动,此过程中还伴有短暂性缄默、木僵、凝视,睡眠需求减少,考虑诊断为DM<sup>[1]</sup>。

DM在美国《精神障碍诊断与统计手册》第5版(Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, DSM-5)、ICD-10等诊断系统中并未被明确定义,但大量学者已在临床报告中进行相应阐述<sup>[2-8]</sup>(表1)。1849年Bell<sup>[4]</sup>首次将DM描述为1种短时限但潜在致死的严重综合征,常急性起病,快速进展,可伴有明显的坐立不安和过多的肢体活动、情绪不稳、偏执妄想、荒诞的幻觉及定向障碍等。此后,经过众多学者的斟酌,其概念经较大修订,1980年Bond<sup>[5]</sup>描述了DM的6个诊断标准:急性起病,轻躁狂或躁狂表现,谵妄症状和体征的进展,躁狂症或抑郁症个人史,情感障碍家族史,躁狂针对性治疗有效。本例患者除阳性家族史外,均满足上述各项诊断标准。此外, Jacobowski等<sup>[2]</sup>认为DM需同时满足谵妄表现(如定向障碍、意识状态改变、认知受损等)和躁狂表现(如过度兴奋、思维奔逸、易

激惹、失眠等),亦可伴随紧张症(如动作抑制、活动过多、违拗、模仿言语或模仿动作)及精神病性症状(如幻觉、妄想等),且事后难以回忆起当时的发病过程。该例患者亦符合以上临床特点。事实上,目前关于DM尚无统一的诊断标准,不过一些评估量表可有助于其症状的及早识别,例如布什-弗朗西斯紧张症评定量表评估紧张症<sup>[9]</sup>,ICU意识模糊评估法识别谵妄症状<sup>[10]</sup>,杨氏躁狂量表评定躁狂症状<sup>[11]</sup>。研究表明在所有急性躁狂发作病例中,DM可占较高比例。更为重要的是,早期漏诊或未及时予以恰当治疗,可能会加速DM病情恶化,甚至危及生命。因此,及早正确识别DM症状尤为重要。

鉴于DM潜在的致死风险,亟需针对DM患者进行规范的治疗和系统的病程管理。然而回顾大量关于DM的病例报道,发现针对DM的治疗策略尚无统一标准<sup>[12-15]</sup>(表2)。多项研究报道支持性治疗十分关键,如纠正电解质紊乱、维持酸碱平衡、营养能量支持等,可以尽量避免或者减少躯体并发症。除

支持性治疗外,有病例报道提示,若患者出现高热、心动过速、高血压、明显的紧张症及肌肉僵硬等,则需停用或避免使用抗精神病性药物,尤其是第一代抗精神病药物。针对严重的DM患者(如伴有自主神经系统症状或高热等),Jacobowski等<sup>[2]</sup>建议苯二氮卓类药物和/或MECT可作为一线治疗方案。例如,初始可尝试2~4 mg/d劳拉西洋进行治疗,若症状改善,后续可予6~20 mg/d进行维持治疗,若症状未见改善,可考虑予MECT治疗。也有报道提示,针对轻症DM患者,也可适当联合心境稳定剂和/或第二代抗精神病药物治疗。值得关注的是,目前治疗推荐仅基于病例报告及临床实践,尚缺乏大样本、系统设计的研究进一步评价。

本例为复发性抑郁症患者,在接受抗抑郁治疗后,突然出现谵妄和躁狂症状,虽然DM和双相障碍的关系尚不明确,但DM的发生可能与文拉法辛的使用有关,从而增加了患者的转躁风险。因此,针对伴有转躁高危风险(如早期起病、病程迁延、易激

表1 DM的临床特征  
Table 1 Clinical features of DM

Clinical features	Diagnostic criteria
Clinical onset and course	a. Acute onset and rapid progression of symptoms (in hours or days) b. Fluctuating course (delirium, manic features, psychosis, catatonic features) c. Poor or absent recall of events during acute episode once resolved
Criteria met with both delirium and mania	Delirium features in documented cases of DM a. Disorientation b. Fluctuating sensorium, altered consciousness c. Severe cognitive dysfunction Manic features in documented cases of DM a. Intense excitement b. Grandiosity c. Irritability and emotional lability d. Insomnia, decreased sleep requirement e. Marked increases in psychomotor activity f. Disorganized, sometimes rambling speech g. Disorganized thoughts, flight of ideas h. Hypersexuality, inappropriate sexual behavior
Frequent neuropsychiatric complications	Psychosis a. Delusions, including paranoid and/or bizarre delusions b. Hallucinations (predominantly auditory) Catatonia a. Purposeless psychomotor hyperactivity, stereotypies, echopraxia b. Posturing, catalepsy ("waxy flexibility"), motor rigidity c. Immobility/stupor, mutism, negativism, staring d. Incontinence (fecal, urinary)

表2 DM的临床治疗策略

Table 2 Treatment strategy for patients with DM

Therapeutic Category	Treatment strategy
Preliminary evaluation and screening	<ol style="list-style-type: none"> <li>1) Improve relevant examinations to rule out organic underlying causes of delirium, mania, psychosis, catatonia</li> <li>2) Monitor for potential medical complications of DM, especially when catatonia is present                             <ol style="list-style-type: none"> <li>a. Dehydration, malnutrition</li> <li>b. Aspiration (pneumonitis, pneumonia)</li> <li>c. Pulmonary embolus</li> <li>d. Infections (pneumonia, integumentary, urinary)</li> <li>e. Rhabdomyolysis</li> <li>f. Skin ulceration, breakdown</li> <li>g. Urinary incontinence or retention, fecal incontinence or severe constipation</li> </ol> </li> <li>3) If recent exposure to antipsychotic or pro-serotonergic drugs has occurred Monitor for signs of NMS or serotonin syndrome</li> </ol>
Treatment principles for “non-malignant” DM patients	<ol style="list-style-type: none"> <li>1) Strongly consider stopping (or delaying initiation of) antipsychotic drugs</li> <li>2) If antipsychotic drug treatment is required: atypical antipsychotics are preferred over conventional antipsychotics; closely monitor for onset of NMS</li> <li>3) Some patients may respond favorably to mood stabilizers                             <ol style="list-style-type: none"> <li>a. Response more slowly with MECT or benzodiazepines</li> <li>b. Mood stabilizers with/or atypical antipsychotics may be combined with benzodiazepines or MECT</li> </ol> </li> <li>4) Monitoring required for progression to “malignant” DM or development of NMS</li> </ol>
Treatment principles for “malignant” DM patients	<ol style="list-style-type: none"> <li>1) Stop antipsychotic drugs</li> <li>2) Strongly consider admission to intensive care unit for supportive care and specific treatment as indicated</li> <li>3) Benzodiazepines and/or MECT are first-line treatments                             <ol style="list-style-type: none"> <li>a. The initial dose of lorazepam is 2-4 mg/d, which can be increased to 6-20 mg/d if symptoms improve</li> <li>b. If there is no improvement in the treatment with lorazepam, MECT is considered</li> </ol> </li> </ol>

MMS: neuroleptic malignant syndrome.

惹、有自伤行为/想法等)的患者<sup>[16-17]</sup>,尽量避免使用5-羟色胺和去甲肾上腺素再摄取抑制剂类的抗抑郁药(如文拉法辛等),或者待抗抑郁治疗稳定后,逐渐减量或及时联合治疗剂量的心境稳定剂。同时,本例患者既往采用多种抗抑郁药足量、足疗程治疗疗效均欠佳,且反复存在自伤行为/想法,本次入院后仅2周症状即快速缓解,因此精神

科医生在诊疗此类患者时,需提高对软双相症状识别的敏感性<sup>[18]</sup>。此外,在情感障碍疾病的诊疗过程中,注意及早甄别精神症状(抑或入院已存在,由于患者掩饰,没能及时识别)、谵妄症状的出现,及早予以对症处理。综上所述,希望该病例能为精神科医生早期识别、治疗及临床管理DM提供思考和启发。



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[收稿日期] 2023-07-06

(本文编辑: 陈汐敏)