Panic Disorder and Bipolar Disorder Among Military Servicemen - Comorbid or a Prodrome?

Captain (Dr) Sylas Sebastian & Colonel (Dr) Siti Nordiana Dollah,

Psychiatric Department, Tuanku Mizan Armed Forces Hospital, Kuala Lumpur

ABSTRACT:

Objective: This case series aims to describe three military personnel who presented with Panic Disorder (PD) subsequently develop Bipolar Disorder (BD) many years later. Methods: We identified three male personnel, presented to our psychiatric clinic with diagnosis conversion from PD to BD from 2016 to 2019. Age ranged from 25 - 33 during the first onset of symptoms. Results: All personnel seek psychiatric care outside the military health services. The mean duration between onset of symptoms and treatment was 5.5 years. Case 1 and 2 defaulted their follow up after a short course of treatment and returned with worsening symptoms and functioning. The mean time between PD diagnosis and the diagnostic shift to BD was 4.3 years. Case 3 was referred to a military psychiatrist one year after the first presentation to psychiatry services, showed better compliance with treatment and follow-up. This serviceman relatively had an earlier revision of diagnosis to BD as compared to Case 1 and 2. Case 1 and 2 showed more deterioration in symptoms and functioning, whereas Case 3 maintained his function with treatments. Conclusions: Psychiatrist and other mental health practitioners in the military need to be aware and routinely assess the possibility of panic attacks and anxiety symptoms to be prodromal of BD. Earlier recognition and revision of diagnosis will ensure a timely intervention delivered for better outcome and restoration of functioning in military personnel with BD.

KEYWORDS: Military personnel, Bipolar Diorders, Panic Disorders, Prodromal, Comorbidities

Introduction

Bipolar disorder (BD) is a common psychiatric illness, highly recurrent with high degrees of interpersonal and social impairment, ranked among the top ten cause of medical disability ¹⁻². The typical age of onset is adolescence to early adulthood ³. One of the factors that contribute to the burden of the disease is a significant delay in diagnosing the illness and initiation of appropriate treatment. A study found that the delay may be up to 9 years ⁴. Longitudinal studies show that illness tends to worsen with time, but with early intervention, it can improve long-term outcome ⁵. The most crucial step is making an accurate diagnosis so that effective treatment could be commenced early.

This case series describes 3 cases of male military personnel who were given an initial diagnosis of PD finally shifted to BD diagnosis, including the initial symptoms at onset, treatment delay and the outcomes. The anxiety symptoms were found to the initial presentation with erratic respond to typical treatment. We hypothesize that presentations of PD in these cases may be prodromal symptoms of BD, as cited in the literature.

<u>Case 1</u>

MFS, is a 34 years old, married, ranked leading seaman (a junior non-commissioned officer) from the Royal Navy, was first seen by a private psychiatrist in 2014 at the age of 28 with a history of frequent panic attacks for 2 months duration. He had difficulties coping with the assigned task, irritability, poor sleep and prominent anxiety symptoms with panic attacks. He was diagnosed with PD disorder and was started on tablet Escitalopram, an antidepressant. He responded with a short course of treatment in which he believed his capabilities in coping with his problems improved. He subsequently defaulted his treatment and follow-ups.

Four years later, he presented back with panic attacks with worsening anxiety symptoms, persistent irritability and poor sleep, greatly interfering with his work. He was started back on an antidepressant but did not show much improvement. He was subsequently referred to the military psychiatrist for further management. He was first seen in March 2018.

During the first 6 years of his military service, he was described as a dedicated, hardworking sailorman, full of energy, motivation, and enthusiasm for creative ideas. Throughout 4 years of illness, despite no significant mood symptoms, he manifested significant deterioration of performance. His superior regarded his deterioration is due to his manipulative behaviour. Subsequently, he was transferred to a new unit where he had even more difficulty adjusting and adapting.

A thorough collaborative history, examination and observation revealed episodes of hypomania. He also reported anxiety symptoms a few years before his first contact with a psychiatrist in which he copes with cigarette smoking. His diagnosis was revised to BD in 2019, and he was started on a mood stabilizer. He has no family history of psychiatric illness and no history of illicit substance use. Despite optimizing pharmacological treatment, he continuously displayed poor recovery. His superior could not tolerate his low performance and recommended that he is to be discharged from service.

<u>Case 2</u>

ZAR, is a 56 years old, married, and a senior army officer. He was first seen by a Ministry of Health (MOH) psychiatrist in 2013 with long-standing anxiety symptoms and panic attacks for almost 15 years. He was diagnosed with PD and started on medication. He was subsequently referred to a military psychiatrist for a continuation of care. However, he decided not to come forward due to concern about his career. He presented to our centre in February 2018 with worsening panic attacks and anxiety symptoms, poor sleep and irritability. He reported episodes of depression in the past. He was started on the tablet Sertraline, an antidepressant to which he minimally responded.

His early military career was excellent; he was an accomplished student and leader until the onset of symptoms, everything then spiralled. He struggled to control his irritability. He was verbally and physically abusive toward his subordinates, wherein he regretted and felt guilty later. The anxiety symptoms were terrifying and depressive episodes even worsen. He smoked heavily and took frequent time off as a way to cope.

He also had a frequent visit to the Armed Forces Sick Quarters (*RSAT – Rumah Sakit Angkatan Tentera*) for multiple non-specific somatic symptoms such as headache, backache, joint pain and tiredness. As a senior officer, he was still able to manage his working schedule on his own.

During his subsequent follow-up, he presented with a hypomanic episode. His diagnosis was revised to BD in 2019. He responded to the initiation of a mood stabilizer but is still not achieve remission yet. He opted for early retirement from the military service

Case 3

RA, is a 37 years old, married, ranked corporal (a junior non-commissioned officer), and an army administrative clerk. His first contact with psychiatric service was at MOH in 2013 when he presented with a six-month history of panic attacks. He also developed anticipatory anxiety and avoided crowded places. He was diagnosed with PD and started on tablet Sertraline once daily. However, after one year, he developed depressive episodes. He was then referred to a military psychiatrist.

He was first seen at our centre in July 2014. He was recruited into the military at the age of 18. He has been described as a hardworking, responsible and obedient personnel.

During subsequent follow up he had developed an episode of hypomania. He was started on a mood stabilizer. He is a smoker. There was no history of illicit substance use. His diagnosis was revised to BD in 2016. He has been in remission for the past 4 years. He showed a good response and was able to perform his duties efficiently. His commander was satisfied with his progress and performance. His PES (PULHEEMS Employment Status) was downgraded to BE (Base Everywhere).

| | Case 1 | Case 2 | Case 3 |
|---|----------------------|---|------------------|
| Military rank | NCO | Officer | NCO |
| Service | Navy | Army | Army |
| Age of onset (years) | 28 | 34 | 29 |
| First contact | Private psychiatrist | MOH psychiatrist | MOH psychiatrist |
| Duration of symptoms before first contact with psychiatrist | 2 months | 15 years | 6 months |
| Duration PD diagnosis and the diagnostic revision to BD (years) | 4.5 | 6 | 3 |
| Duration of illness before contact with military psychiatrist (years) | 4 | 5 | 1 |
| Occupational outcome | Poor functioning | Poor functioning | Good functioning |
| PULHEEMS Employment Status (PES) | UNFIT | BE (Opted for early retirement from military service) | BE |

Table 1: The patient Characteristic, Onset of Symptoms and Outcome

PULLHEEMS - Military medical classification system;

UNFIT - Medically unfit for military service

MOH : Ministry of Health

Onset of symptoms, diagnosis delay and outcome

In this case series, we describe 3 cases of male military personnel, with an initial diagnosis of PD revised to BD after 3-6 years. The anxiety symptoms were found to have responded to the initiation of a mood stabilizer. There is a significant delay in seeking treatment as well as diagnosis of BD in all 3 cases. The delay was 3-6 years after first contact and 4-11 years from the onset of symptoms. The longer the delay, the poorer outcome. Only case 3 remain in the service with good functioning. All the personnel seek help from psychiatric service outside the military. The longer the time taken to be seen by a military psychiatrist, the more upended the psychosocial and occupational challenges. The detail is shown in Table 1. We hypothesize that presentations of PD in these cases may be prodromal symptoms of BD, as cited in the literature.

DISCUSSION

Despite its prevalence, BD is often missed and delayed in diagnosis. The previous study found that there is often a delay in diagnosing BD during the initial presentation, which can approximately be between 5-7 years ⁶⁻⁷. The presentation can be non-specific until a history of mania or hypomania and the depressive episode is elicited ⁸. This is probably due to several reasons (Table 2).

Table 2 : Factors associated with delay in BD diagnosis.

| 1. The symptoms may not be recalled as illnesses | | |
|---|--|--|
| 2. Prodrome of bipolar disorder | | |
| 3. The onset of impairment may precede that of | | |
| recognizable manic episodes. | | |
| 4 .Highly comorbid with other psychiatric disorders | | |
| 5.Diverse spectrum of inter-episode BD | | |

1. The symptoms may not be recalled as illnesses

The patient or family members may not be able to recall the subsyndromal symptoms of manic/hypomanic or depression but usually more able to recall the consequence of the symptoms ⁹. However, this has been associated with lost workdays and productivity of the affected persons ¹⁰. Therefore, the patients should be asked about the consequences of interpersonal problems, impulsivity, or poor judgment, distorted interpersonal behaviour, or lack of respect for interpersonal boundaries that can accompany manic/hypomanic episodes ¹¹.

2. **Prodrome of bipolar disorder (BD)**

Prodrome of BD is defined as precursor symptoms, functional impairments, and other psychiatric diagnoses present in the months or years before developing the full-blown BD onset ³. It is comparatively less studied than the psychosis prodromes. However, recent reviews showed a wide spectrum of presentation suggestive of bipolar prodromes such as mood symptoms, anxiety symptoms, mood lability and mood swings, subthreshold manic and hypomanic symptoms, subsyndromal depression ¹², early-onset panic attacks, separation anxiety disorder, generalized anxiety disorder, conduct symptoms and disorder, ADHD, impulsivity ¹³ and chronic irritability ¹⁴.

3. The onset of impairment may precede long before recognizable manic episodes

The onset of impairment may precede that of recognizable manic episodes bring about contentious opinion about the illness. The person may be labelled as weak, an attention seeker, cowardice, lazy, irresponsible, disobedient and even manipulative. In a military setting, it is commonly misinterpreted as a behavioural problem and temperamental. The illness usually starts with depression rather than mania, so even when mania is detected accurately, the onset of bipolar disorder may be missed ^{5,15}

4. Highly comorbid with other psychiatric disorders

Highly comorbid with other psychiatric disorders such as anxiety disorders ¹⁶⁻¹⁸, substance use disorders ^{19,20}, personality disorders ²¹ and familial pattern ^{22,23}.

5. Diverse spectrum of inter-episode BD

A diverse spectrum of inter-episode BD was seen to have significant impairment ²⁴. Studies also showed that even without residual mood symptoms, the patient manifested executive functional impairment, poor focus and slower reaction time ²⁵⁻²⁶. Impulsivity and novelty-seeking behaviour during inter-episode BD have also been reported, perhaps increasing their susceptibility for substance abuse ²⁷⁻²⁸, which commonly misinterpreted as temperamental.

Stress, anxiety and BD

Stress has been associated with precipitating factors for BD. To explain this, let use the diabetes condition as an analogue. Diabetes is characterized by dysregulation of blood glucose, and impaired glucose tolerance is the prodromal phase. In this phase, the patient's blood high glucose level is still reversible. As the disease develops further, the patient is diagnosed with diabetes, indicating a more persistent pathology. As the disease continues to worsen, renal failure or other complications occur, and the patient enters the irreversible decompensation period. Similarly, BD might also follow the rules mentioned above, and the fluctuation of emotion, which is analogous in this case to blood glucose in diabetes, might follow the pattern of disease evolution, leading to more severe impairment and poorer response to the treatment.

As hypothesized by Du et al. (2017), when the personnel experience stress, the common emotion of anxiety occurs. With the continuation of stress, this emotion gradually evolves into pathological anxiety, which indicates the beginning of the prodromal period of BD, although it is still manifested as anxiety disorder and lacks the typical symptoms of BD ²⁹. If the stress persists, it may result in the recession of anxiety and the emergence of more severe symptoms of BD as experienced by case 2 and 3. In such cases, the emotional dysregulation becomes pathological, a conversion that is difficult to reverse. If the stress continues, it may result in behaviour disinhibition, which manifests as BD's hypomanic/manic symptoms. For case 3, he was already under regular follow up. Thus, his stress was intervened earlier as compared to the other 2 cases.

PD and BD

Out of several prodromal symptoms, anxiety symptoms have emerged as a priority due to the high correlation between both. Patients with prominent anxiety and who showed poor efficacy with anxiolytic treatment, ultimately develop BD with the duration of prodromal symptoms in BD might be 1.8 to 7.3 years ²⁹. PD was reported to higher in BD ^{30,31} and up to 22.34% of the PD patients had BD ³². A meta-analysis showed that the early onset of PD to be a risk factor for the onset of BD ³³. Prospective studies also supported the association between anxiety disorder and BD ³⁴.

Lessons from our case series

1. Military personnel seeking mental health care outside of the military health services.

This is similar to another study that found that military personnel are making extensive use of outside mental health services, suggesting that military health and mental health services do not meet the needs of active duty service members ³⁶. Unique intricacies and challenges of the military environment may not be addressed by civilian psychiatric service. Diagnoses, medication choices, and treatment planning can also impact a service member's career in the military that civilian providers may not be aware of. The concepts such as confidentiality and consent have a slightly different meaning in the military that affects care in the civilian realm. Prolonged medical leave may do more harm to the personnel.

2. Stigma delays the treatment and intervention

In addition to the delay in diagnosing, the stigma leads to further delay in treatment initiation. Military personnel believe that seeking mental health service would be discrediting or embarrassing, causes harm to career progression, or causes peers or superiors to have decreased confidence in the member's ability to perform assigned duties. Seeking mental health treatment should be destigmatized and dealt with the same way our culture deals with physical illness.

3. Early referral to the military psychiatrist

All personnel with mental health issues should be referred to a military psychiatrist as soon as possible. Early referral to a military psychiatrist allows early psychosocial and occupational intervention to restore occupational functioning and preserve employability. This will also enhance the unit's commander's support, as reported by a local study by Siti Nordiana & Khairuddin (2015), which found that psychoeducation to the unit commanders resulted in more supportive behaviour toward their subordinates with mental health issues ³⁷.

CONCLUSIONS

Clinicians must be aware of PD in military personnel may suggest an early presentation of BD. Regimental Medical Officer (RMO) should be more vigilant in detecting and referring the personnel to a military psychiatrist. All military personnel with panic attack symptoms should be followed closely, and default tracing should be activated for any loss during follow-up. We hypothesize that presentations of PD in these cases may be a prodromal symptom of BD, as cited in the literature. A future study to further investigate PD and BD in the military population is needed to expand our ability to better care and improve their outcome with timely intervention.

REFERENCES

- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication [published correction appears in Arch Gen Psychiatry. 2005;62(7):709. Merikangas, Kathleen R [added]]. Arch Gen Psychiatry. 2005;62(6):617-627. doi:10.1001/archpsyc.62.6.617
- Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*. 1997;349(9063):1436-1442. doi:10.1016/ S0140-6736(96)07495-8
- Conroy S, Francis M, Hulvershorn LA. Identifying and treating the prodromal phases of bipolar disorder and schizophrenia. *Curr Treat Options Psychiatry*. 2018;5(1):113-128. doi:10.1007/s40501-018-0138-0
- 4. Janardhan Reddy YC. Prodromal symptoms of recurrences of mood episodes in bipolar disorder. *Indian J Med Res.* 2012;135(2):154-156.
- Lish JD, Dime-Meenan S, Whybrow PC, Price RA, Hirschfeld RM. The National Depressive and Manic-depressive Association (DMDA) survey of bipolar members. J Affect Disord. 1994;31(4):281-294. doi:10.1016/0165-0327(94)90104-x
- Morselli PL, Elgie R; GAMIAN-Europe. GAMIAN-Europe/ BEAM survey I--global analysis of a patient questionnaire circulated to 3450 members of 12 European advocacy groups operating in the field of mood disorders. *Bipolar Disord*. 2003;5(4):265-278. doi:10.1034/j.1399-5618.2003.00037.x
- Ghaemi SN, Sachs GS, Chiou AM, Pandurangi AK, Goodwin K. Is bipolar disorder still underdiagnosed? Are antidepressants overutilized?. *J Affect Disord*. 1999;52(1-3):135-144. doi:10.1016/s0165-0327(98)00076-7
- Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: how far have we really come? Results of the national depressive and manic-depressive association 2000 survey of individuals with bipolar disorder. *J Clin Psychiatry*. 2003;64(2):161-174.
- Dunner DL, Tay LK. Diagnostic reliability of the history of hypomania in bipolar II patients and patients with major depression. *Compr Psychiatry*. 1993;34(5):303-307. doi:10.1016/0010-440x(93)90015-v

- Matza, L., De Lissovoy, G., Sasané, R., Pesa, J., & Mauskopf, J. (2004). The impact of bipolar disorder on work loss. *Drug Benefit Trends*, 16(9), 476-481.
- Janowsky DS, Leff M, Epstein RS. Playing the manic game. Interpersonal maneuvers of the acutely manic patient. *Arch Gen Psychiatry*. 1970;22(3):252-261. doi:10.1001/arch-psyc.1970.01740270060008
- Faedda GL, Serra G, Marangoni C, et al. Clinical risk factors for bipolar disorders: a systematic review of prospective studies. J Affect Disord. 2014;168:314-321. doi:10.1016/j. jad.2014.07.013
- Faedda GL, Marangoni C, Serra G, et al. Precursors of bipolar disorders: a systematic literature review of prospective studies. *J Clin Psychiatry*. 2015;76(5):614-624. doi:10.4088/JCP.13r08900
- Sparks GM, Axelson DA, Yu H, et al. Disruptive mood dysregulation disorder and chronic irritability in youth at familial risk for bipolar disorder. *J Am Acad Child Adolesc Psychiatry*. 2014;53(4):408-416. doi:10.1016/j. jaac.2013.12.026
- Perugi G, Micheli C, Akiskal HS, et al. Polarity of the first episode, clinical characteristics, and course of manic depressive illness: a systematic retrospective investigation of 320 bipolar I patients. *Compr Psychiatry*. 2000;41(1):13-18. doi:10.1016/s0010-440x(00)90125-1
- Chen YW, Dilsaver SC. Comorbidity for obsessive-compulsive disorder in bipolar and unipolar disorders. *Psychiatry Res.* 1995;59(1-2):57-64. doi:10.1016/0165-1781(95)02752-1
- 17. Hantouche EG, Kochman F, Demonfaucon C, et al. TOC bipolaire: confirmation des résultats de l'enquête "ABC-TOC" dans deux populations de patients adhérents versus non adhérents à une association [Bipolar obsessive-compulsive disorder: confirmation of results of the "ABC-OCD" survey in 2 populations of patient members versus non-members of an association]. *Encephale*. 2002;28(1):21-28.
- DelBello MP, Geller B. Review of studies of child and adolescent offspring of bipolar parents. *Bipolar Disord*. 2001;3(6):325-334. doi:10.1034/j.1399-5618.2001.30607.x
- Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19):2511-2518.
- Borchardt CM, Bernstein GA. Comorbid disorders in hospitalized bipolar adolescents compared with unipolar depressed adolescents. *Child Psychiatry Hum Dev*. 1995;26(1):11-18. doi:10.1007/BF02353226
- 21. Dunayevich E, Strakowski SM, Sax KW, et al. Personality disorders in first and multiple episode mania. *Psychiatry Res*.1996;64(1):69-75. doi:10.1016/0165-1781(96)02925-3
- Gershon ES, Hamovit J, Guroff JJ, et al. A family study of schizoaffective, bipolar I, bipolar II, unipolar, and normal control probands. *Arch Gen Psychiatry*. 1982;39(10):1157-1167. doi:10.1001/archpsyc.1982.04290100031006
- Rice J, Reich T, Andreasen NC, et al. The familial transmission of bipolar illness. *Arch Gen Psychiatry*. 1987;44(5):441-447. doi:10.1001/archpsyc.1987.01800170063009

- 24. Swann AC, Geller B, Post RM, et al. Practical Clues to Early Recognition of Bipolar Disorder: A Primary Care Approach. Prim Care Companion J Clin Psychiatry. 2005;7(1):15-21. doi:10.4088/pcc.v07n0103
- 25. Kirrane RM, Siever LJ. New perspectives on schizotypal personality disorder. *Curr Psychiatry Rep.* 2000;2(1):62-66. doi:10.1007/s11920-000-0044-0
- Wilder-Willis KE, Sax KW, Rosenberg HL, Fleck DE, Shear PK, Strakowski SM. Persistent attentional dysfunction in remitted bipolar disorder. *Bipolar Disord*. 2001;3(2):58-62. doi:10.1034/j.1399-5618.2001.030202.x
- Swann AC, Anderson JC, Dougherty DM, Moeller FG. Measurement of inter-episode impulsivity in bipolar disorder. *Psychiatry Res.* 2001;101(2):195-197. doi:10.1016/ s0165-1781(00)00249-3
- Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC. Psychiatric aspects of impulsivity. *Am J Psychiatry*. 2001;158(11):1783-1793. doi:10.1176/appi. ajp.158.11.1783
- 29. Du N, Zhou YL, Zhang X, Guo J, Sun XL. Do some anxiety disorders belong to the pro-drome of bipolar disorder? A clinical study combining retrospective and prospective methods to analyse the relationship between anxiety disorder and bipolar disorder from the perspective of biorhythms. BMC Psychiatry. 2017;17(1):351. Published 2017. doi:10.1186/s12888-017-1509-6
- Chen YW, Dilsaver SC. Comorbidity of panic disorder in bipolar illness: evidence from the Epidemiologic Catchment Area Survey. *Am J Psychiatry*. 1995;152(2):280-282. doi:10.1176/ajp.152.2.280
- Correll CU, Penzner JB, Frederickson AM, et al. Differentiation in the preonset phases of schizophrenia and mood disorders: evidence in support of a bipolar mania prodrome. *Schizophr Bull.* 2007;33(3):703-714. doi:10.1093/ schbul/sbm028
- Sugaya N, Yoshida E, Yasuda S, et al. Prevalence of bipolar disorder in panic disorder patients in the Japanese population. *J Affect Disord*. 2013;147(1-3):411-415. doi:10.1016/j. jad.2012.10.014
- 33. Van Meter AR, Burke C, Youngstrom EA, Faedda GL, Correll CU. The Bipolar Prodrome: Meta-Analysis of Symptom Prevalence Prior to Initial or Recurrent Mood Episodes. J Am Acad Child Adolesc Psychiatry. 2016;55(7):543-555. doi:10.1016/j.jaac.2016.04.017
- 34. Mesman E, Nolen WA, Reichart CG, Wals M, Hillegers MH. The Dutch bipolar offspring study: 12-year follow-up. Am J Psychiatry. 2013;170(5):542-549. doi:10.1176/appi. ajp.2012.12030401
- 35. Waitzkin H, Cruz M, Shuey B, Smithers D, Muncy L, Noble M. Military Personnel Who Seek Health and Mental Health Services Outside the Military. *Mil Med.* 2018;183(5-6):e232-e240. doi:10.1093/milmed/usx051
- Siti Nordiana D, Khairuddin H. Military Mental Health Care in East Malaysia – An Innovative Approach. Jurnal KKD. Vol 4 (1) 2017.

Correspondence: Captain (Dr) Sylas Sebastian, Medical Officer, Department of Psychiatry, Tuanku Mizan Armed Forces Hospital, Kuala Lumpur, Malaysia. Telephone: +603-41454200. Email: drsylassebastian@gmail.com