

The prevalence of prolonged grief disorder in late-life depression and its clinical features in Japan

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Abstract

Background : Prolonged grief disorder (PGD) , a new category related to bereavement, is a prolongation of grief and is distinct from depression, although its symptoms such as depressive state and a strong desire to die resemble those of depression. Until the concept of PGD was raised, many clinicians did not recognize PGD and regarded it as a form of depression. Here we examined the prevalence of PGD among older inpatients with and without PGD following their bereavement, and we analyzed the patients' clinical features.

Methods : We examined all depressive patients >50 years old who were admitted to the psychiatric ward of Jichi Medical University Hospital between January 2009 and December 2014. The concomitant depression with PGD was assessed based on the proposed diagnosis of persistent complex grief disorder in DSM-5 and the Brief Grief Questionnaire.

Results : Twenty-eight individuals (75.7%) consented to participate. The prevalence of PGD with depression was 57.1%. All individuals had lost a close relative. Suicide death, sudden death and death from chronic disease among the deceased relatives were more frequent in the PGD group than the non-PGD group. The rate of females, somatic symptoms in a limited body area, the use of tricyclic antidepressants or tetracyclic antidepressants, and lower number of educational years were more prevalent in the PGD group compared to the non-PGD group. The mean Global Assessment of Functioning (GAF-F) score at discharge was significantly lower in the PGD group.

Conclusions : PGD was prevalent in the patients with late-life depression following the death of a close relative. The development of PGD appears to be affected by both the death of a close relative and the cause of that relative's death. Clinicians should be aware of the possibility of concomitant PGD with depression, especially among older patients who respond poorly to antidepressant treatments.

(Key words : aged society, bereavement, depression, grief, prolonged grief disorder)

Introduction

The loss of close relatives has been regarded as one of the most stressful life events for humans. A considerable number of people suffer from depression after the separation from a loved one by death. Especially in later life, bereavement has been reported to be a main cause of depression¹. In the elderly, bereavement frequently leads to psychological sequelae such as grief, i.e., a transient normal reaction including guilt, suicidality, worthlessness, psychomotor retardation and depression. A 2008 report noted that 15%–30% of older adults develop clinically

significant depression within the year following their loved one's death², indicating that it would be pivotal for mental health in late-life to consider the potential experience of bereavement.

Pathological grief has been the subject of increasing attention in the mental health field, and the concept of pathological grief as a new diagnostic proposal is included in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). Prolonged grief disorder (PGD) will be added to the International Classification of Diseases, 11th edition (ICD-11) as a new diagnosis category in 2018. The

main characteristic of PGD is a persistent and pervasive grief response accompanied by intense emotional pain after the death of a partner, parent, child or other loved one. Individuals with PGD are liable to be depressed and to avoid many things that remind them of their loved one, and this avoidance causes serious problems in their later life. PGD is distinct from major depressive disorder (MDD), as the object of the subject's loss is clear. PGD is also distinct from post-traumatic stress disorder (PTSD), in which the fear experienced is threatening. Although essentially every academic discussion of grief mentions the depressive state³, unlike depression, PGD involves a persistent yearning for the deceased and a reluctance to undergo treatment for depression⁴. Recent studies showed that antidepressants' effect on PGD is only partial. Notably, complicated grief treatment, which focuses on grief and adaptation to loss, has been reported to be efficacious psychotherapy approach⁵.

PGD is most commonly associated with depression, and the rate of PGD among individuals with bereavement-related depression¹ has been reported to be approx. 55%⁶. There is thus a possibility that PGD exists "behind" or underlying the depression that commonly follows bereavement. In fact, in Japan prolonged grief had been treated as a type of depression until PGD's diagnosis was issued. The prevalence of PGD in a general population in Japan was estimated to be approx. 2.4%⁷.

To the best of our knowledge, the prevalence of PGD among hospitalized patients in a psychiatric ward has not been studied. Previous studies recruited subjects from a general population or bereaved individuals in a specific death situation. Investigations focusing on depressive patients with severely deteriorated social functions are warranted. In addition, individual responses to bereavement are known to be diverse and to vary among cultures and social backgrounds⁸. A 1986 study described cultural differences in bereavement reactions between individuals in western countries and those in China, suggesting that the forms of grief are strongly culture-bound⁹.

We conducted the present study to investigate the details of the clinical features of PGD in Japan and to obtain new insights into the psychopathology of PGD, which may be helpful for the prevention and treatment of PGD. We first examined the prevalence of PGD in Japanese inpatients experiencing late-life depression following their loved one's death. We then evaluated the characteristics of PGD in the depressive individuals, including their relationship to the deceased and the circumstances of the deaths. We also clarified the differences in the severity, period of hospitalization, and treatment between depression with PGD and depression without PGD.

Methods

Patients

We enrolled 225 Japanese patients aged >50 years with late-life depression¹⁰ who were admitted to the psychiatric ward of Jichi Medical University Hospital between January 2009 and December 2014. All patients were diagnosed with MDD on the basis of the criteria of the DSM-IV-TR at admission, by well-trained psychiatrists. To avoid the duplication of data, the latest episode was examined in the patients with multiple depressive episodes/hospitalizations during the observational period. Thirty-seven of the 225 patients (16.4%) were considered to be experiencing depression following their loved one's death, based on the interview of the patient conducted at admission or discharge from hospital. To screen for evidence of organic mental disorders, neurocognitive assessments and/or neuroimaging examinations (CT/MRI) were conducted.

The prevalence of PGD

For the determination of whether each patient had PGD, semi-structural interviews were conducted by a psychiatrist (the first author) who had received training in a prolonged grief disorder treatment program¹¹. The interview was based on the proposal criteria of persistent complex grief disorder (PCBD) in DSM-5 and the Brief Grief Questionnaire (BGQ) score >4 points^{12,13}.

Demographic data

The demographic data including age at admission, sex, and years of education were obtained from the patient and their close family member (s) at the admission interview. The family history of the patient's parents and siblings was surveyed.

Clinical characteristics of depression with and without PGD

The clinical characteristics of the patients were investigated by a semi-structured psychiatric interview based on the structured clinical interview for DSM-IV-TR (SCID) and a chart review. We also obtained information regarding the patients' relationship to the deceased and the cause of death. The causes of death were classified as follows : unnatural or violent death such as an accident, homicide and suicide¹⁴ ; sudden death, i.e., unexpected death within 24 hr. by disease : chronic disease, i.e., persisting for ≥3 months such as cancer, stroke and dementia. These causes are as defined by the U.S. National Center for Health Statistics¹⁵.

For our assessment of the clinical features of the patients, the following additional information was obtained : the duration of hospitalization, the Global Assessment of Functioning (GAF-F) numeric scale at admission and discharge, the treatment received (classes of medications and somatic antidepressant treatments), and social background. Somatic symptoms were referred

to the comments of bodily sensations or basic physical dysfunctions that an individual describes as worrisome or unpleasant, e.g., pain¹⁶ and excluded general symptoms, e.g., loss of appetite, fatigue and sleep disturbance. Psychotic symptoms include hallucinations, persecutory delusions, and depressive delusions such as delusions of guilt or poverty, and hypochondriac delusions¹⁷. The use of psychotropic medications or somatic antidepressant treatments, e.g., electroconvulsive therapy was recorded from the chart review.

Psychotropic medications were categorized as follows : tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin re-uptake inhibitors (SSRIs), serotonin-norepinephrine re-uptake inhibitors (SNRIs), noradrenergic and specific serotonergic antidepressants (NaSSAs), first-generation antipsychotics (FGAs), second-generation antipsychotics (SGAs) and mood stabilizers. The newer antidepressant drugs including SSRIs, SNRIs and NaSSAs were used as first-line treatments. If a patient did not respond to the first-line medication, TCAs and/or TeCAs were considered. Antipsychotics were used for the patients who suffered from psychotic symptoms, in accord with the guidelines of Japanese Society of Mood Disorders¹⁸.

We also examined the social background related to the current depressive episode for each patient. Information regarding whether the patient lived alone, the presence of social conflicts with friends, immediate family, and/or relatives^{19,20}, the presence of other stressful life events that influenced the current depressive episode²¹⁻²³, and the need for social support or intervention was obtained. As outcomes of treatment in hospitalization, the comparison of the GAF-F scores at admission and discharge and the duration of hospitalization were examined.

Statistical analysis

The prevalence of PGD in the patients with depression following bereavement and the differences between the clinical features of the PGD group and those of the non-PGD group were analyzed. Differences in the relationship of the deceased to the patient and the cause of death were analyzed. Differences in demographic data, clinical characteristics of depression, medications, and social background were examined using Fisher's exact test and the Mann-Whitney U-test. Statistical analyses were performed using SPSS Statistics 22 software (IBM, Chicago, IL). The significance level $p < 0.05$ was used.

Ethical approval was granted by the ethics committee at Jichi Medical University. All participants provided written informed consent for their data to be analyzed and published.

Results

Demographic data

Among the 37 enrolled patients >50 years old with late-life depression, 28 patients (75.7%) consented to our research. Nine of the 37 patients were excluded for the following reasons : losing contact with the hospital (n=3), refusal by the participant (n=2), suicide death (n=2), suffering from severe depression (n=1), and progressing dementia (n=1). The demographic data of the remaining 28 patients including age, sex, years of education, past history of mental illness and family history of mental illness are summarized in Table 1.

Table 1. Demographic data of 28 patients following the death of their loved ones

Items	Mean (\pm SD) or Number(%)
Age, Years (\pm SD)	64.5 (8.2)
Gender	
Male, Number (%)	12 (42.9)
Female, Number (%)	16 (57.1)
Years of education, Years (\pm SD)	12.3 (3.0)
Past history of mental illnesses	11 (39.3)
Family history of mental illnesses	11 (39.3)

The prevalence of PGD

Among the 28 participants, 16 patients (57.1%) were diagnosed as having depression with PGD (the PGD group). The other 12 patients (42.9%) were diagnosed as having depression without PGD (the non-PGD group).

Each patient's relationship to the deceased

As summarized in Table 2, in the PGD group, the relationships of the patients to the deceased were as follows : husband's death (n=5, 31.3%), wife's death (n=1, 6.3%), father's death (n=3, 18.8%), mother's death (n=2, 12.5%), sibling's death (n=3, 18.8%), sister's death (n=1, 6.3%) and brother's death (n=1, 6.3%). In contrast, in the non-PGD group the relationships of the patients to the deceased were as follows : husband's death (n=3, 25.0%), wife's death (n=5, 41.7%), father's death (n=2, 16.7%) and mother's death (n=2, 16.7%). Notably, spousal death and parental death were common and notable in both of groups, but child's death and brother's/sister's death were seen only in the group of patients with PGD.

Table 2. Relationship with the deceased

Relationship with the deceased	PGD n=16 (%)	Non-PGD n=12 (%)
Spouse	6 (37.5)	7 (58.3)
Husband	5 (31.3)	3 (25.0)
Wife	1 (6.3)	5 (41.7)
Parent	5 (31.3)	5 (41.7)
Father	3 (18.8)	2 (16.7)
Mother	2 (12.5)	2 (16.7)

Child	3 (18.8)	0 (0.0)
Brothers and sisters	2 (12.5)	0 (0.0)
Brother	1 (6.3)	
Sister	1 (6.3)	
Others	0 (0.0)	0 (0.0)

PGD : Prolonged grief disorder

The cause of death for the deceased

In the PGD group, the cause of death for the deceased included sudden deaths due to acute diseases such as strokes and myocardial infarction (n=5, 31.3%), death from chronic diseases such as strokes requiring a long duration of caregiving (n=4, 25.0%), cancers (n=3, 18.9), suicide deaths (n=2, 12.5%), and death by accident (n=1, 6.3%). As for the non-PGD group, death by cancer (n=6, 50.0%) was frequent, followed by sudden death by stroke and hematemesi (n=3, 25.0%), senility (n=2, 16.7%) and death by neither chronic nor acute disease (n=1, 8.3%) (Table 3). The duration of caregiving for chronic strokes ranged 8 years to 20 years. Violent deaths including suicide deaths and death by accident were seen only in the group of patients with PGD.

Table 3. Cause of death

Cause of death	PGD n=16 (%)	Non-PGD n=12(%)
Violent death (suicide)	2 (12.5)	0 (0.0)
Violent death (accident)	1 (6.3)	0 (0.0)
Sudden death by disease	5 (31.3)	3 (12.0)
Chronic disease (cancer)	3 (18.9)	6 (50.0)
Chronic disease (stroke)	4 (25.0)	0 (0.0)
Chronic disease (dementia)	1 (6.3)	0 (0.0)
Disease other than sudden or chronic ones	0 (0.0)	1 (8.3)
Senility	0 (0.0)	2 (16.7)

PGD : Prolonged grief disorder

Clinical features of the PGD and non-PGD patients

Our comparison of the clinical features of the PGD versus non-PGD groups revealed that the rate of females in the PGD group (n=12, 75.0%) was significantly higher than that in the non-PGD group (n=4, 33.3%) (p=0.019) (Table 4). The number of years of education was significantly lower in the PGD group compared to the non-PGD (p=0.008). In addition, the rate of having one or more somatic symptoms was significantly higher in the PGD patients compared to the non-PGD patients (p<0.001). Among the individuals in the PGD group, the use of TCAs/TeCAs was significantly more frequent than that in the non-PGD group (p=0.039), as seen in Table 4.

The GAF-F scores

There was no significant difference in the GAF-F scores between the PGD and non-PGD groups at admission

(p=0.543), but at discharge, the scores in the non-PGD group (mean 77.5) were significantly higher (p=0.023) than those in the PGD group (mean 66.9) (Table 5). Higher GAF-F scores indicate greater levels of functioning.

Duration of hospitalization

The duration of hospitalization was slightly longer in the PGD group (mean 102.9 days) compared to the non-PGD group (mean 95.5 days), but the difference was not significant (p=0.265) (Table 5).

Discussion

The prevalence of PGD associated with depression among late-life patients

In this study, PGD was identified in more than half of the late-life patients with severe depression who needed to be hospitalized after the loss of a close relative. In general populations in the Netherlands and Japan, the prevalence of PGD was reported to be 4.8% and 2.4%, respectively^{7,24}. The reported prevalence of PGD among people who were experiencing grief is much higher at 10%–25%^{24,25}, suggesting that PGD may be a common disorder. The comorbidity rate of PGD with depression in the present study is in line with that of a previous study although the subjects in that study were outpatients⁶. In fact, major depression is the most common mental complication among individuals with PGD^{6,26} and vice versa : a high rate of PGD was seen in a group of psychiatric outpatients with chronic major depression²⁷.

Symptoms due to PGD such as depressive state and suicidal ideation are sometimes difficult to distinguish from symptoms of depression. It is thus quite possible that a significant number of patients with PGD remain undiagnosed and are thought to simply have depression.

The patients' relationship to the deceased and the cause of death

In regard to the patients' relationship to the deceased, the death of a spouse and the death of a parent were remarkable in both the PGD and non-PGD groups. The loss of a child or of a brother or sister was observed only in the PGD group. Loss of a child has been reported to be the most notable predictor of PGD²⁴. In addition, the context of the relationship being close¹², supportive, confiding and dependent with the deceased⁴, and their unexpected situations have been shown to relate strongly to PGD.

In the present study's depressed patients with PGD, unexpected deaths (such as suicide death and sudden death) were more prevalent compared to the depressed patients without PGD, as indicated in a previous study²⁸. We also observed that a relative's death after suffering from a chronic illness that needed long-term caregiving (such as stroke) was also prominent in the PGD group.

Table 4. Comparison of clinical features between PGD and Non-PGD

Clinical features	PGD n=16 (\pm SD/%)	Non-PGD n=12(\pm SD/%)	P-value
Age	63.4 (8.6)	65.8 (7.9)	0.456
† Female	12 (75.0)	4 (33.3)	0.019*
Past history of mental illnesses	4 (25.0)	7 (58.3)	0.121
Family history of mental illnesses	6 (37.5)	5 (41.7)	1
† Years of education	11.1 (2.4)	14.0 (3.0)	0.008**
† GAF-F at admission	32.6 (19.2)	29.3 (13.5)	0.543
First episode	11 (68.8)	6 (50.0)	0.441
Somatic symptom	14 (87.5)	2 (16.7)	<0.001**
Suicide ideation	14 (87.5)	9 (75.0)	0.624
Suicide attempt	7 (43.8)	3 (25.0)	0.434
Psychotic features	7 (43.8)	4 (33.3)	0.705
Treatment			
SSRIs/SNRIs/NaSSAs	7 (43.8)	6 (50.0)	1
TCAs/TeCAs	8 (50.0)	1 (8.3)	0.039*
Mood stabilizer	6 (37.5)	7 (58.3)	0.445
Antipsychotics	6 (37.5)	7 (58.3)	0.445
ECT	5 (31.3)	3 (25.0)	1
Social background			
Overlap of life event	11 (68.8)	8 (66.7)	1
Living alone	3 (18.8)	7 (58.3)	0.05
Conflict with family	7 (43.8)	3 (25.0)	0.434
Need for social support	4 (25.0)	4 (33.3)	0.691

† Man-Whitney U test, *p<0.05, ** p<0.01

PGD : Prolonged grief disorder,SSRIs/SNRIs/NaSSAs Selective Serotonin Reuptake Inhibitors/Serotonin and Norepinephrine Reuptake Inhibitors/Noradrenergic and Specific Serotonergic Antidepressant, TCAs Tricyclic Antidepressants, TeCAs Tetracyclic Antidepressants,ECT electroconvulsive therapy

Table 5. Duration of hospitalization and GAF-F scores at discharge

Outcomes	PGD n=16 (\pm SD/%)	Non-PGD n=12(\pm SD/%)	P-value
† Duration of hospitalization	102.9 (47.8)	95.5 (90.0)	0.265
† GAF-F at discharge	66.9 (12.0)	77.5 (6.9)	0.023*

† Man-Whitney U test, *p<0.05, ** p<0.01

PGD : Prolonged grief disorder, GAF-F : Global Assessment Functioning

The prevalence of PGD after at-home caregiving for a family member with Alzheimer's disease was reported to be approx. 20%²⁹, which is higher than the prevalence in individuals undergoing general bereavement. A role as spouse caregiver and depression before death have been indicated as risk factors associated with PGD after caregiving^{29,30}.

We observed that the cause of death highly influenced the occurrence of PGD. On the other hand, depression without PGD may be more common among the bereaved confronted with natural losses such as senility and also death due to cancer¹⁴.

Demographics and clinical features of the PGD and non-PGD

groups

Our analysis of the patients' clinical features revealed that female gender, less years of education, and the presence of somatic symptoms in a limited body area were significant in the PGD group. Female gender was previously described as a risk factor for PGD²⁴, and the prevalence of pathological grief was highest among elderly females²⁰. Lower number of educational years was also reported to be associated with PGD¹⁴. Our present findings indicated that female gender and fewer educational years were associated with the occurrence of PGD. However, we should note that of the nine individuals who were excluded from this study, those who refused to participate and those who attempted suicide were all male. It has been reported that the suicide rate was

higher in males than in females during the year following their spouses' deaths³¹.

A relationship between somatic symptoms and depression had been indicated in Eastern countries⁹, but the association between somatic symptoms and grief has not been clarified. Several studies conducted so far indicated that somatic symptoms can express grief itself which includes a traumatic aspect, as in cases in which persistent pain may be associated with traumatic experiences³²⁻³⁴.

The PGD and non-PGD groups' clinical outcomes

We observed some differences in clinical outcomes as well as clinical features between our patients with depression with and without PGD following the death of a close relative. In a prior study, longer hospitalization was found in bereavement-related depression³⁵, but in the present study there was no significant difference in the length of hospitalization based on the presence/absence of PGD. We should consider other resources such as the existence of social and/or family support in relation to the duration of hospitalization.

On the other hand, the GAF-F scores at discharge were lower in the present PGD group although the PGD and non-PGD patients had almost the same GAF-F scores at admission. This suggests that PGD tends to be insufficiently treated compared to depression alone. A greater use of TCAs or TeCAs may support this hypothesis, since these are second-line drugs and are used for refractory depression following the treatment failure of first-line antidepressants. A significant use of these medications may highlight the difficulties of treating grief itself. Complicated therapy that focuses on grief was recently described, and drug therapy has shown the same limitations for treating grief as those that have been described for treating depression⁵.

Study Limitations

The present study population was small, and a quantitative study as well as a further qualitative analysis are needed.

Conclusion

Our present findings revealed that PGD was prevalent among patients with depression following the death of a close relative. If antidepressant therapy is insufficient after bereavement, concomitant PGD should be considered.

Declarations

Disclosure Statement : The authors declare that they have no competing interests.

Competing interests

This work was free from any financial or other limitations that might have constituted a conflict of interest. In addition, none of the individual authors report any conflicts of interest.

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初老期うつ病における遷延性悲嘆障害合併率ならびに臨床的諸特徴に関する研究

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要 約

背景：遷延性悲嘆障害（Prolonged grief disorder：PGD）は、死別反応に関連した新たな疾患である。この疾患は、うつ病とは異なり、故人への悲嘆が遷延し日常生活が破綻する。しかしながら抑うつ状態や故人のもとへ向かう希死念慮の強さなど表面上はうつ病と区別が付き難く、実際、PGDの概念が登場するまで、多くの臨床家はPGDをうつ病の一種としてみなしてきた。そこで、本研究では、近親者との死別後に初老期うつ病で入院を要した患者を対象に、PGDの合併率ならびに臨床的諸特徴を検討した。

方法：自治医科大学附属病院精神科に2009年1月から2014年12月の間にうつ病の診断で入院となった50歳以上の男女を対象とした。PGD合併の有無については、近親者との死別を契機にうつ病を生じた患者のうち、DSM-5で新たに提案された持続性複雑死別障害の診断基準ならびに複雑性悲嘆質問票を用いた面談を行い、診断した。

結果：近親者との死別後にうつ病となった者37名のうち、28名（75.7%）から研究同意を得た。PGDの合併率は57.1%であった。28名の対象者のうち、全員が親密な家族との死別経験であった。死別状況としては、自死などの暴力的な死、突然死、脳血管性障害など介護を要する慢性疾患による死がPGDを合併する群で目立っていた。その他、女性、教育年数の低さ、身体症状の合併、三環系もしくは四環系抗うつ薬の使用がPGD合併群で有意に多かった。退院時の機能の全体の尺度では、PGD合併群の方が非合併群より有意に点数が低かった。

結論：PGDは、近親者との死別後に生じた初老期うつ病の中で約半数を占めていた。PGDは最愛の人との死別、そして衝撃の強い死別状況において罹患しやすい。精神科临床上、抗うつ薬に反応が乏しい初老期うつ病患者の中にはPGDが合併している可能性があり、注意が必要である。

（キーワード：高齢社会、死別反応、うつ病、悲嘆、遷延性悲嘆障害）