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Fatigue and Cancer
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Depression and Cancer

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Introduction

The problem of depression in cancer patients needs to be re-examined in light of the therapeutic progress made in the field of oncology, which has transformed the prognosis of this disease. Cancer is now a potentially curable, somatic disease with a chronic course. Cancers and the therapeutic strategies adopted to treat them constitute repeated stress for the patient and the family, but also for health care professionals. In addition to dealing with the patient's physical pain, the dimension of mental distress therefore becomes a major challenge that concerns all partners of the health care process. However, the concepts and methods designed to investigate the issue of psychological distress in oncology remain poorly defined and the diagnosis of depression in oncology and the modalities of its management are still controversial. The quality of the relational approach and the communication between the patient and the health care professionals will be decisive in terms of the quality of management and the satisfaction of the patient and his/her family.

Distress and depression

The most recent studies propose a pragmatic approach based on the concept of "psychological distress". Jimmie Holland [1] defines this concept as follows: "Distress is an unpleasant experience of an emotional, psychological, social, or spiritual nature that interferes with the ability to cope with cancer treatment. It extends along a continuum, from common, normal feelings of vulnerability, sadness and fear, to problems that are disabling, such as true depression, anxiety, panic, and the feeling of isolation or spiritual crisis".

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The term was chosen because it is less stigmatising than others having a psychopathological connotation, and is more acceptable and easier to use for health care professionals who question the patient about his or her emotional state.

It should be noted that this approach is based on the one already applied to pain management and, like this method, can be used to demonstrate and quantify the patient's needs. It can define the various dimensions of the concept of psychological distress without stratifying its various aspects. This approach assumes the existence of a continuum of mental states ranging from "normal" to "pathological", but nevertheless does not minimise the difficulties observed.

The psychopathological point of view tends to emphasise the concept of rupture: in situations in which the patient's mental functioning appears to represent an obvious rupture with his or her previous ways of functioning, the presence of authentic psychiatric disorders can be considered.

How can we establish a distinction between identification of symptoms, demonstration of true depression, and suggestion of the possibility of depression – in the sense of depressive illness – particularly in a context of chronicity?

From adjustment disorders ... to depression?

The patient's efforts of adjustment are the expression of a psychological process designed to preserve mental and bodily integrity, to recover whatever is reversible and to compensate for whatever is irreversible, but also and most importantly to attenuate the dimension of mental suffering and physical pain. This corresponds to the concept of "coping".

The emotional, cognitive, and behavioural reactions triggered by these efforts of adaptation can be described as "normal", inasmuch as they help to achieve the lowest possible level of distress. However, the failure of these efforts could also lead patients to experience difficulties, or even express disorders, described as "adjustment disorders", considered to be transient, situational, and fluctuating disorders of variable intensity, often described as being moderate. They are nevertheless a source of distress and can have major implications on the patient's family and social life.

The patient is considered to display depressive disorders when the permanent presence of the symptoms lowers the probability of their spontaneous resolution, and seriously interferes with the patient's ability to deal with more concrete problems which he or she must cope with in the context of his or her cancer [2,3].

Diagnosis of depression

The observed prevalence of depressive symptoms varies considerably, ranging from 4.5% (6% according to Derogatis [4]) to 58%, and this reflects the difficulty

of defining diagnostic criteria of depression in oncology: the more precise the definition of depression, the lower the observed prevalence rate.

Greater emphasis should always be placed on psychological rather than somatic symptoms [5]: depressed mood, feelings of helplessness and hopelessness, loss of self-esteem, feelings of uselessness and guilt, anhedonia, ideas of "death wish" or even suicide, and, in terms of behaviour, irritability and aggressiveness.

The recommendations proposed by the French medical evaluation agency ANAES [6] for the follow-up of patients with non-metastatic breast cancer, which were designed to identify depressive disorders, advocate the use of a structured interview looking for the nine symptoms corresponding to the DSM-IV definition of Major Depressive Episodes: depressed mood, markedly diminished interest or pleasure, significant weight loss or weight gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, diminished ability to think or concentrate, and recurrent thoughts of death or suicidal ideation.

In practice, as evaluation of the depressive dimension is intimately related to the organic context, it is often difficult to differentiate symptoms of depression from those possibly related to the course of the cancer and to adverse effects of treatment. Endicott therefore proposed replacement criteria, replacing somatic items by more specific "psychological" items: items such as "significant weight loss or weight gain", "insomnia or hypersomnia", "fatigue or loss of energy" are replaced by items evaluating social withdrawal, anxious rumination and pessimism, inability to regain courage, etc. Particular attention should be paid to feelings of helplessness and hopelessness, often described in the context of the psychological distress observed in cancer patients.

The clinical approach is essential, and in practice is based on simple questions. There is a risk of failure to recognise the diagnosis in the hospital setting due to the short duration of hospital stay, the patients' reluctance to express their distress, and the health care professionals' fear of hearing the patient express this distress, as the general level of conversation is often deliberately positive and combative.

Screening tools may therefore be necessary. The two tools most widely used in oncology are two self-assessment scales:

- HADS (Hospital Anxiety and Depression Rating Scale), composed of 14 items, designed to detect anxiety and depressive disorders;
- GHQ (General Health Questionnaire) for which an abridged 12-item form is available. These two tools do not comprise somatic items.

Suicide

Cancer patients have a twofold higher relative risk of suicide than that observed in the general population [7]. The following risk factors have been identified: advanced disease and poor prognosis; uncontrolled pain; delirium; de-

pression and especially feelings of hopelessness; psychiatric history (particularly previous suicide attempts); social isolation. Male sex and advanced age also accentuate this risk. Some cancer sites are associated with a higher risk of depression [8] and suicide (pancreas, head and neck, lung).

Depression and pain

The anxiety and depression dimension can only be rigorously evaluated after taking into account the possible presence of pain, especially as cancer patients tend to attribute a pejorative significance to pain. Pain management usually leads to the resolution of depressive symptoms if particular attention is paid to irritability, insomnia, aggressiveness and agitation, and non-compliance with treatment.

Depression and fatigue

Fatigue constitutes an extremely frequent complaint in oncology. Can it constitute a criterion of depression in patients suffering from a somatic disease? Is there a causal relationship between fatigue and depression? To what degree do these disorders influence quality of life? Fatigue and depression do not follow the same clinical course; the cause-and-effect relationship between these two dimensions has not been established; however, both of these disorders influence quality of life.

Depression and end of life

The prevalence of depression in the advanced stages of cancer is high and increases as the general condition of the patient worsens. The diagnosis can be difficult in often complex psycho-organic situations. It is vital to distinguish between symptomatic depression, which is responsive to psychotropic drugs (antidepressants and/or psychostimulants), thus allowing an improvement of the patient's quality of life, and a "request for euthanasia", often expressed by the patient or his or her family.

It is essential to take into account the ethical and medicolegal implications in the light of recent media interest in the problem of "medically-assisted suicide", which cannot be likened to suicidal behaviour subtended by undiagnosed depression.

Depression and organic factors

Depressive symptoms can be related to organic factors: the tumour site (primary

or secondary brain tumours, cancer of the pancreas, etc.), hormonal dysfunction (thyroid dysfunction, etc.), metabolic or water and electrolyte disorders, as well as iatrogenic factors: corticosteroids, interferon or interleukin, which are frequently used, but also certain anticancer drugs (vincristine, vinblastine, procarbazine, L-asparaginase, tamoxifen). Identification of the factor responsible for the depressive symptoms may enable it to be corrected or eliminated.

Treatment modalities

The management of depression in cancer patients raises two main questions: institution of psychotropic treatment and/or the justification for psychotherapy.

Psychotropic treatment

Psychopharmacological approaches are designed to resolve practical problems of prescribing modalities [9,10] by avoiding possible drug interactions and potentiations, in order to achieve the best benefit/risk compromise. Anxiolytics and hypnotics are widely used, in over half of the patients, to treat the frequently observed anxiety and sleep disorders. Antidepressants are prescribed when depressive symptoms have been demonstrated; there is currently a preference for more recent molecules (especially SSRIs) that appear to be better tolerated than tricyclic antidepressants. Practice guidelines have been proposed: start treatment at low doses and increase the dosage very gradually in view of the hypothesis of a therapeutic response at doses lower than those traditionally required, as well as increased sensitivity to adverse effects. However, few controlled studies are available, and these empirical prescribing modalities need to be assessed in randomised trials.

Psychostimulants (methylphenidate, dextroamphetamine) appear to provide real benefit in depressed patients suffering from pain and/or in the terminal phase of the disease. Although these molecules are widely used in English-speaking countries, their use is limited in France, where legislation prohibits their marketing due to the fear of secondary addiction.

Although a consensus has been reached that a major depressive episode in a cancer patient justifies treatment with antidepressants, no consensus has been reached concerning the management of adjustment disorders associated with depressive symptoms, giving rise to a more empirical prescription of antidepressants. This raises the question of the misuse of psychotropic drugs: Does a symptomatic approach lead to anxiolytic and hypnotic treatments being overused and, as a corollary, are antidepressants underused due to a defect of diagnostic identification?

Psychotherapeutic treatment

Various types of "psychotherapeutic" approaches have been proposed [11,12].

The psychosocial approach can have various dimensions: health education, information, advice, support, reassurance. Relaxation therapy may be indicated. Such approaches can be applied individually or in groups. They must be adapted to the context of malignant disease and must take somatic aspects into account. They often consist of short-term management, requiring the "therapist" to adopt a more active attitude than in non-cancer settings.

Some of these techniques have the advantage that they can be administered by various categories of health care professionals: psychiatrists and psychologists, but also attending physicians, and any other health care professionals trained in these techniques. The psychosocial approach must take into account the family context, but also the social support, including voluntary or patient associations.

The cognitive-behavioural approach in psychotherapy may represent a solution to the difficulties experienced by some patients to adjust to their disease and its consequences. This approach, characterised by the fact that it requires the person's motivation and cooperation, helps the patient to restore a form of control over his/her body and a feeling of mastery over the disease. Based on short-term treatment, it is designed to control particular symptoms considered to be disabling. In the context of depression, the work consists of what behavioural therapists call cognitive restructuring of "negative" thoughts.

It is very useful to combine various psychological or psychiatric approaches. Although many studies designed to evaluate the efficacy of such approaches have demonstrated improvement of depressive symptoms and quality of life, studies concerning the effects of these treatments on survival remain controversial and must be interpreted with caution.

Conclusion

The objective of psycho-oncology today is to deal with the global aspect of psychological distress and to refine its dimensions. The approach to depression in cancer patients therefore requires the definition of precise diagnostic criteria involving specific management modalities. The diagnostic and therapeutic approaches to often complex comorbid situations must take into account the multifactorial nature of the patient's complaint (depression and pain, depression and fatigue, etc.).

Many questions have yet to be resolved in the field of neuropsychoimmunology, and hypotheses concerning the psychogenesis of cancer must be interpreted very cautiously.

The diagnosis of depression in cancer patients therefore represents a priority for all health care professionals, as the management of depression can lead to a reduction of the patient's emotional distress, better adjustment to the stressful events of cancer and its implications, and improvement of quality of life.

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