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Gastrointestinal Manifestation and Bipolar Disorder: About a Clinical Case

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Abstract **Case Report**

Introduction: The frequency of gastrointestinal manifestations in patients suffering with mood disorders, particularly bipolar disorders, pose specific physiopathological, etiological and therapeutic questions. We propose to address this issue through this clinical case. ***Clinical Case***: We report here the case of a female patient 29-year-old, followed in psychiatry since 2014 for bipolar disorder type I and presenting an irritable colon syndrome, a biliary cyst, gastric diverticula and a chronic constipation. ***Discussion:*** Several hypotheses on the links between affectivity and gastrointestinal functioning are discussed in the light of the literature, explaining the role of the brain-gut axis as well as the involvement of the receptological profile of neuroleptics and also the role of the iatrogenicity of psychotropic drugs. *Conclusion:* There are definite links between affectivity and gastrointestinal manifestations. A better understanding of these links could enlighten us on the etiopathogeny of mood disorders, especially bipolar disorders, in order to guarantee a better management of psychiatric pathology as well as gastrointestinal manifestations.

Keywords: Gastrointestinal manifestations, bipolar disorders, psychotropic drugs, digestive side effects.

INTRODUCTION

Mood disorders such as depression and anxiety are common in people with functional gastrointestinal disorders [1]. Studies about the relationship between anxiety, depression and gastrointestinal symptoms might be biased by higher primary care utilization in patients with psychiatric comorbidity [2, 3]. It is difficult to study the timing between the onset of intestinal symptoms and the onset of mood disorders due to the insidious onset and fluctuating course of mostly functional gastrointestinal disorders [3, 4]. Most studies that aim to explore the relationship between intestinal disorders and mood disorders are performed on patients hospitalized in gastroenterology units. These patients often present persistent and disabling intestinal symptoms with negative impact on their quality of life.

In a large group of patients with unipolar depression, we previously described that gastrointestinal symptoms were common and related to symptoms of anxiety and depression [6]. Patients with unipolar depression have more pain, including abdominal pain, which in part correlates with depression severity, and these patients show greater primary care utilization for symptoms not labeled "psychiatric" [5-9].

Bipolar disorder, including different subtypes such as bipolar 1 and 2, is a common condition with a reported lifetime prevalence in the population estimated at 2.4% [10]. In addition, over the past decade, bipolar disorder is being described more as a chronic, progressive disorder with significant residual symptoms between episodes of depression, mania, and hypomania rather than as a classic cyclical illness [11]. It is estimated that patients with bipolar disorder suffer from affective symptoms 50% of the time, even with appropriate treatment and mood-stabilizing medications.

The total health care costs for these patients are estimated to be two to four times higher than for controls [12]. Unlike patients with unipolar depression, there is little published data regarding functional gastrointestinal symptoms in patients with bipolar disorder.

Through a clinical case, we will review the gastrointestinal manifestations accompanying bipolar disorders and the role of iatrogenic pharmacological treatment in these manifestations, while insisting on adequate management that must be multidisciplinary, in order to prevent a negative impact on the psychiatric

pathology as well as on all areas of life of these patients.

Clinical Case: Patient and Observation

It is about Mrs. A.K aged 29 years, single, without profession, without particular ATCD, who was following a psychiatric treatment since 2014. The onset of her disorders seems to date back to the age of 23 years following an emotional shock (death of the father) where the patient became, for more than a month, excited, logorrheic, insomniac and refusing to eat, adopting potomania behaviors, Drinking more than 5 liters of water per day, with verbalization of delusions of grandeur, and mystico-religious, which required a psychiatric consultation with the psychiatric emergency service of the ARRAZI hospital, from which her first hospitalization. The diagnosis of a bipolar disorder type I was retained according to the DSM 5 criteria (5), a pre-therapeutic assessment was requested including a NFS showed a microcytic hypochromic anemia corrected by a sufficient iron intake. A normal ionogram, liver, syphilitic and HIV serology came back negative. No abdominal radiological exploration was requested because the patient did not present any intestinal symptomatology.

The evolution was marked by a very good clinical improvement, a Young's scale [43] was used for the evaluation of the manic symptomatology (figure 1) passing from 47 to 5 for a duration of 45 days.

Then the patient presented a stabilization of her psychiatric symptomatology with a good therapeutic compliance and a regular follow-up of the post treatment appointments

After 2 years, she developed a digestive symptomatology made of nausea, vomiting, transit disorder sometimes diarrhea sometimes constipation, which required a consultation with a gastroenterologist. A radiological assessment was requested showing a multi lithiasic gallbladder, a segment 1 biliary cyst and a suspicion of gastric diverticulum. The patient was then cholecystectomized and put on a medical treatment based on PPI, activated charcoal and a diet rich in fiber. The evolution is marked by a stabilization of the symptomatology, but the patient still complains of dyspepsia, chronic constipation and gastrointestinal discomfort, not improved by the usual symptomatic treatment. An endoscopic exploration (fibroscopy and colonoscopy) was requested but did not show any particularity, and thus a diagnosis of functional dyspepsia with irritable intestine syndrome was retained. This persistent and disabling gastrointestinal symptomatology had a negative impact on the patient's quality of life. She became irritable, very complaining, and reported that the treatment of her psychiatric illness and especially carbamazepine were responsible for her gastrointestinal symptomatology.

DISCUSSION

Many studies have demonstrated the relationship between affectivity and gastrointestinal symptoms.

But they also demonstrate that the group of patients with low scores on the affectivity domain do not present gastrointestinal symptoms, or present the same symptoms as the control subjects, despite the use of medications with gastrointestinal side effects (thymoregulators, antipsychotics, SSRIs). Therefore, unexplained gastrointestinal symptoms in these patients should be seriously considered as an atypical symptomatology of depression and require adequate treatment that may reduce the number of unnecessary somatic examinations.

A study made (6) showing that patients with recurrent depressive disorder have high scores on gastrointestinal symptoms, but when in remission, they do not differ from controls [6]. We thus believe that affectivity has a definite effect on the functioning of the gastrointestinal tract

The brain-gut axis ; It is not known how the cerebrointestinal axis is involved in the physiopathology of anxiety/depression. But many neurobiological studies show that the areas that process visceral afferents and the areas involved in fear and anxiety are closely linked. For example, functional imaging studies on patients with Irritable Colon Syndrome have shown that balloon distention of the recto-sigmoid colon increases activity in certain brain areas involved in the regulation of affective and sensory processes such as the amygdala, insula, cingulate and prefrontal cortex [23-26].

There are also studies that explain that intestinal symptoms and visceral hypersensitivity treated with antidepressants, hypnosis and cognitive-behavioral therapy [27-29]. A possible mechanism for these therapies could be an increase in prefrontal inhibition of the amygdala and anterior cingulate cortex [30].

Another factor that links affectivity to the gut is corticotropin (CRH); the receptors for this hormone are abundant in the amygdala as well as in the intestine and the increase in its blood concentration is significantly related to anxiety, depression and stress [31]. For example, CRH injection leads to increased visceral hypersensitivity, exaggerated colonic motility and inhibition of upper intestinal motility as well as mood changes [34 - 37]. CRH also regulates the hypothalamic-pituitary-adrenal axis leading to hypercortisolaemia and activates the locus caeruleus [31] leading to activation of the autonomic nervous system and the sympathetic system with possible complex effects on intestinal function (including

motility, sensitivity, secretion and the intestinal immune system) [30, 38, 39].

Microbiota plays a very important role in the brain-gut axis so any subtle inflammation in the gut may play a role in mood regulation [40].

Iatrogenicity ; in order not to forget the side effects of thmoregulators and psychotropic drugs providing mood regulating activity here is this table which summarizes the main side effects all with emphasis on the gastrointestinal side effects.

Implication of the recptological profile of neuroleptics ; the anticholinergic activity ; acetylcholine is a neurotransmitter that can bind to nicotinic receptors and more predominantly muscarinic receptors.

Muscarinic receptors are divided into five classes (from M1 to M5). These are the M1, M3 and M5 receptors known as excitatory, inducing a muscle contraction.

Acetylcholine is therefore the excitatory neurotransmitter of the intestine on the smooth muscles and stimulates the Cajals cells, cells which are at the origin of the automatism of the smooth fibers of the digestive tract.

All neuroleptics have an anticholinergic activity, more or less marked depending on the molecule, which can be the cause of an atropinic syndrome.

The clinical picture of the atropine syndrome associates mydriasis, blurred vision, dry mouth, nausea, difficulty in urinating, tachycardia and constipation. In the digestive system, this effect is responsible for a decrease in digestive secretions and a decrease in peristalsis, which may lead to colonic distension due to sectoral stasis [24, 25]. The combination of several drugs with atropinic properties leads to an addition of atropinic effects, which is referred to as an atropinic load.

Involvement of antiserotoninergic activity; antagonistic activity on 5-HT3 receptors has been shown to decrease visceral sensitivities and peristalsis, and increase colonic compliance and intestinal absorption resulting in decreased transit [31-33].

Implication of anti-dopaminergic activity ; dopamine blockade in addition to being the main cause responsible for the activity of neuroleptics also plays a role in the decrease of peristalsis. Indeed, dopamine improves mesenteric perfusion because at low doses it has a vasodilatory effect via DA1 receptors [36]. Inhibition of mesenteric vasodilation may thus play an additional role in digestive ischemia

Involvement of antihistamine activity ; some neuroleptics have antihistaminic activity, which could accentuate GI hypomotility by inducing sedation and sedentary living with decreased physical activity. Clozapine is the neuroleptic with the highest affinity for H1 receptors followed by olanzapine and quetiapine [37].

CONCLUSION

Early somatic excess mortality in patients with bipolar disorder compared with the general population (odds ratio of 2.1 in women and 1.9 in men) (11). This increase is attributable, on the one hand, to an increase in the rate of suicide and the occurrence of accidents, but also to the major risk of developing serious somatic comorbidities. While cardiovascular, metabolic and neurological disorders induced by psychotropic drugs are well identified, digestive disorders are often underestimated and trivialized.

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