What to consider before saying that a patient has a psychiatric diagnosis? Part II

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Abstract

Patients report their symptoms in a wide variety of expressions such as "I am tired", "my joints hurt", "my whole body itches", "my mouth is dry", among others. Faced with these symptoms, the physician automatically thinks of a limited number of pathologies that are familiar to him/her, but there are many other causes of these symptoms that are not taken into account. The physician's lack of knowledge causes the patient to feel dissatisfied with the lack of a correct diagnosis and adequate treatment, which leads to multiple consultations and the physician may even ask himself, "Does this patient have a psychiatric diagnosis? This article lists the frequent causes of these symptoms mentioned, describes causes that are rarely suspected and the clinical keys for the physician to make an effective diagnosis. The present article is the second part of the raised problem whose part I was published in 2019. Specifically, the following symptoms will be developed: food intolerance, xerostomia, syncope, dysphagia and manifestations in patients with bariatric surgery.

Key words: diagnosis; dyspepsia; irritable bowel syndrome; xerostomia; bariatric surgery; syncope; deglutition disorders.

Resumen

Los pacientes refieren sus síntomas en una gran variedad de expresiones como “estoy cansado”, “me duelen las articulaciones”, “me pica todo el cuerpo”, “tengo la boca seca”, entre otras. Ante estos síntomas, el médico piensa de manera automática en un número limitado de patologías que le son familiares, pero existen muchas otras causas de estos síntomas que no se tienen en cuenta. El desconocimiento del médico hace que en el paciente se genere inconformidad al no tener un diagnóstico correcto y un tratamiento adecuado, esto lleva a múltiples consultas y que el médico llegue a preguntarse a sí mismo “¿Será que este paciente tiene un diagnóstico psiquiátrico?”. En este artículo se enumeran las causas frecuentes de estos síntomas mencionados, se describen causas que son pocas veces sospechadas y las claves clínicas para que el médico pueda hacer el diagnóstico efectivo. El presente artículo es la segunda parte de la problemática planteada cuya parte I fue publicada en 2019. En específico, se desarrollarán los siguientes síntomas: intolerancia a los alimentos, xerostomía, síncope, disfagia y manifestaciones en pacientes con cirugía bariátrica.

Palabras claves: diagnóstico; dispepsia; síndrome de colon irritable; xerostomía; cirugía bariátrica; síncope; trastornos de deglución.

Introduction

Although syphilis was long considered the great simulator, it is now recognized that other diseases such as HIV/AIDS, systemic lupus erythematosus (SLE), lymphoma, tuberculosis and hepatitis C can have a host of systemic and nonspecific symptoms.

Many times, physicians encounter symptoms reported by their patients that are difficult to interpret. The question “Does this patient have a psychiatric diagnosis?” is formulated in the physician’s mind when reflecting on the patient’s symptoms.

There are several symptoms that cause uncertainty when not finding a diagnostic possibility within the common framework of diseases known by the physician, some of them are referred by the patient as “I am tired”, “everything makes me sick”, “I feel pecked or burning” and “my mouth is dry”. These frequent symptoms in the consultation cause discomfort in the physician and the patient because of the little improvement with the treatments due to the difficulty in the diagnosis.

This review article seeks to inform the physician of other diagnostic options that are not routinely considered in the office. In the first part, pu-

blished in 2019 (1), the causes of fatigue, paresthesia, pruritus, arthralgias, anxiety and behavioral changes were developed while in this second part we seek to describe the symptoms of food intolerance, xerostomia, syncope, dysphagia and manifestations in patients with bariatric surgery.

The patient who refers "everything I eat makes me sick".

Dyspepsia is the sensation of episodic or persistent pain or discomfort that is usually referred to in the upper gastrointestinal tract as epigastralgia and early satiety, affects 20% of the population and is associated with foods containing gluten, fats, processed foods and foods high in fermented carbohydrates [2]. There are also manifestations of the lower digestive tract such as abdominal distension, flatulence, constipation, diarrhea, among others. Irritable bowel syndrome is frequently diagnosed, but there are other possibilities that should be thought of before arriving at this diagnosis [3].

Some causes of food intolerance are:

Gastroesophageal reflux (due to scleroderma, pregnancy, transient lower esophageal sphincter relaxation, excessive food intake, aerophagia and obesity).

Gastric or duodenal ulcers, Crohn's disease, Zollinger-Ellison syndrome, pancreatic insufficiency and biliary colic.

Helicobacter pylori infection.

- Medications.
- Reaction to food additives and lactose intolerance.
- Atopy.
- Neoplasms.
- Smoking, alcohol or coffee consumption.
- Esophagitis due to pills.
- Thyroid disease.
- Chronic intoxications.
- Functional dyspepsia.

Other causes to consider are:

1. Celiac disease

It affects 1% of the population and up to 1 in 6 patients with Down syndrome [4,5]. Its main manifestation is chronic steatorrhea; other manifestations are associated with micronutrient deficiency (iron and copper), anemia, osteoporosis, aphthous stomatitis, short stature, infertility, chronic fatigue, meteorism, flatulence, dermatitis herpetiformis and irritability [6,7]. The age of onset can be from childhood to adulthood, in children it

is confused with lactose intolerance [4]. Twenty percent of these patients may present different neurological and psychiatric manifestations, including initial manifestation. These include headache, cerebellar ataxia, peripheral neuropathy, myelopathy, myopathy and encephalopathy. Psychiatric manifestations may include depression, autism, schizophrenia, anxiety disorders, and attention deficit hyperactivity disorder [8,9].

2. Gastroparesis

It has a prevalence in men and women of 9.7 and 37.8 cases per 100 000 inhabitants, respectively [9]. It manifests with nausea, postprandial vomiting, early satiety, hyporexia, and abdominal distension in the absence of obstructive pathology [11]. The main cause of gastroparesis is diabetic neuropathy. Other causes include medications such as clonidine, opioids, tricyclic antidepressants, calcium antagonists, dopamine agonists, GLP-1 agonists, and cyclosporine [12,13]. Previous gastric surgery, neurological diseases (multiple sclerosis, brain stem CVD, Parkinson's disease), rheumatologic and paraneoplastic syndrome should also be considered [12]. In cases where no etiology is found (idiopathic), Norwalkvirus and Rotavirus infection is suspected to be the cause in patients with acute manifestations [14]. Post-viral gastroparesis may last up to one year. Cytomegalovirus, Epstein-Barr virus and Varicella-zoster virus infections can lead to severe dysautonomia [15].

3. Non-coeliac gluten sensitivity

Some individuals have gluten sensitivity in the absence of serologic markers or histologic findings suggestive of celiac disease and respond clinically to the gluten-free diet [16]. The prevalence of non-celiac gluten sensitivity is unknown, although it is thought to be higher than celiac disease [17]. The clinical manifestations are indistinguishable between the two entities; it is very common to find this disease in patients with misdiagnosis of irritable bowel syndrome [18,19]. Extra-intestinal symptoms have been described as generalized myo-arthralgias, fatigue, depression, anemia, dermatitis and "foggy brain" sensation given by the appearance of slowed thinking, memory problems and decreased level of consciousness [16,17].

4. Ovarian cancer

In Colombia there are about one thousand cases of ovarian cancer per year. Ninety-three percent of women with this pathology have presented at least one symptom during the course of their disease. Gastrointestinal symptoms, which can be high or low, are described in about 70% of pa-

tients, among which are: fullness or early satiety, constipation, diarrhea, nausea and abdominal pressure [20]. These symptoms may precede the diagnosis by six to twelve months [21]. It is easily confused with irritable bowel syndrome [22,23].

5. Eosinophilic esophagitis

Ten percent of patients with gastroesophageal reflux disease (GERD) refractory to proton pump inhibitors meet criteria for eosinophilic esophagitis [24]. It has a prevalence of 55 cases per 100,000 people. It occurs more in men between the ages of 20 and 40 years. The predominant symptoms are dysphagia, nonspecific chest pain, GERD-like symptoms and upper abdominal pain [25]. Seventy-seven percent of patients have associated symptoms of asthma, allergic rhinitis, urticaria, atopic dermatitis, and food allergy [26].

6. *H. pylori* eradication

This infection has been associated as a protective factor for GERD due to the presence of atrophic pangastritis and low gastric acidity [27]. After eradication of ***H. pylori*** in patients with peptic ulcer disease, symptoms of GERD may appear, mainly in the first year [28,29], which is why the presence of GERD alone is not an indication of ***H. pylori*** eradication [30].

7. Chronic Giardiasis

It is diagnosed in up to 10% of patients with irritable bowel syndrome [31]. Chronic diarrhea is the most frequent symptom (76%) [32]. Other reported symptoms are chronic fatigue, steatorrhea, weight loss, depression, abdominal colic, flatulence, pruritus, urticaria, and uveitis [32,33]. These symptoms may be intermittent over months, persist after treatment, lead to malnutrition and vitamin deficiencies (cyanocobalamin and folic acid) [33]. About 40% of patients become lactose intolerant [34]. Enzyme recovery may take a few weeks after parasite eradication.

8. Systemic and gastrointestinal amyloidosis

Both AA and AL amyloidosis commonly affect the gastrointestinal system, leading to symptoms of gastroparesis, diarrhea, abdominal pain, steatorrhea, constipation, bacterial overgrowth, malabsorption, intestinal pseudo-obstruction, and gastrointestinal bleeding [35-37]. Hepatic involvement is frequent, with jaundice, portal hypertension, splenomegaly and ascites [36,37]. In a series of patients with amyloidosis, 3% had gastrointestinal symptoms, of which 80% were due to systemic amyloidosis and 20% limited to the intestine [38].

9. Abdominal migraine

Abdominal migraine has a prevalence of 4% in the pediatric population but rarely continues into adulthood. It is characterized by severe abdominal pain and vasomotor symptoms, nausea and vomiting that may occur in the absence of headache or precede it. Triggers are similar to those of migraine (stress, fatigue, and travel) [39].

The patient who refers "I can't swallow".

Frequent episodes of dysphagia have been reported in 3% to 4% of the general population [40,41]. Patients refer to dysphagia with terms such as "I have a choking" and "I can't pass food". Neuromuscular dysphagia is initially characterized by difficulty swallowing liquids or solids from the onset of symptomatology, while structural dysphagia is characterized by difficulty swallowing solids.

Causes of dysphagia include:

- CVD, Parkinson's disease, brain stem tumor, Guillain-Barre syndrome and multiple sclerosis.
- Head and neck surgery or radiation therapy.
- Achalasia and diffuse esophageal spasm.
- Zenker's diverticulum, cricopharyngeal membrane, neoplasms, osteophytes and corrosive injury.
- Schatzki's ring and hiatal hernia.
- Pill esophagitis, infectious esophagitis, sclerotherapy.
- Behçet's syndrome.

Other causes to consider are:

1. Myasthenia Gravis

The prevalence is between 150 to 200 cases per million population [42]. Dysphagia presents progressively and occurs in 15% to 40% of patients with the generalized form. Dysphagia may be the only presentation and as the initial symptom is described in 6% of patients [43]. Conventional electromyography, edrophonium test and antibodies may be normal [44]. Other symptoms include weakness of the lips, tongue, jaw, and chewing fatigue, with high risk of aspiration and pneumonia [45].

2. Inflammatory myopathies

Dysphagia occurs in 10 to 73% of patients due to weakness of the oropharyngeal, laryngeal, or esophageal musculature [46,47]. Thirty-eight to 84% of cases of inclusion body myositis and 12 to 54% of cases of dermatopolymyositis manifest with this symptom [48]. Dermatomyositis is

suspected by dermatologic findings, this does not occur in polymyositis in which high suspicion is needed. It manifests with nasal voice, hoarseness, regurgitation, dysphonia, nutritional deficits, dyspnea and aspiration pneumonia [49]. Dermatomyositis is associated with occult malignancy in 20-30% of cases, and a higher incidence of dysphagia has been reported in these patients [46]. It has also been described in congenital and hereditary myopathies, but with less frequency.

3. Eosinophilic esophagitis

Dysphagia occurs in 90% of adults with this condition. Other symptoms such as repeated choking on food, gastroesophageal reflux, and vomiting may occur. Lack of response to proton pump inhibitors is usual [49]. Seventy-seven percent of patients have associated symptoms of asthma, allergic rhinitis, urticaria, atopic dermatitis, and food allergy [26].

4. Chagas disease

The predilection for the digestive or cardiovascular system depends on the strain. In half of the cases there is only cardiovascular involvement, 8% cardiodigestive and 32% only digestive [50]. It affects the esophagus in 7 to 10% of cases [51], causing from esophageal motility disorders to megaesophagus. Digestive manifestations include dysphagia and constipation. Dysphagia is an early or late manifestation; the intensity of the symptom varies with the degree of esophageal involvement and can go as far as the inability to swallow liquids and solids. Other manifestations are odynophagia, gastroesophageal reflux, weight loss, aspiration cough, and regurgitation [52].

5. Esophageal candidiasis in HIV/AIDS patient

In these patients, esophageal symptoms are the second most common manifestation of gastrointestinal disease. Forty to 50% of HIV-infected patients will have symptoms of esophageal disease during the course of their illness [53]. Thirty-four percent of patients with HIV have CD4 less than 200/microL at diagnosis [53], and esophageal candidiasis is present in 9 to 30% of these cases. The main symptom is odynophagia with localized retrosternal pain; dysphagia and retrosternal pain without odynophagia may also occur [55].

6. Multiple systemic atrophy

Dysphagia is the most important disability, as it leads to silent aspiration and secondary pneumonia which are the main cause of death in these patients. It occurs in about 73% of cases and is severe in 33%. It may

be accompanied by sialorrhea, sensory changes in the oral cavity, difficulty chewing, swallowing sound and dry mouth [56]. Other symptoms may include recurrent falls, dysphonia and dysarthria [57].

7. Thyroid nodules

Palpable thyroid nodules are present in 4-7% of adults and this frequency increases with age [58,59]. Nodules as small as 1.5 cm can generate compressive symptoms such as dysphagia (up to 80%), hoarseness, cough, coughing, coughing, dyspnea or tickling in the throat, but the average size described for the occurrence of dysphagia is 3.8 cm [60].

8. Plummer Vinson Syndrome

Also called sideropenic dysphagia, it consists of a triad of dysphagia, iron deficiency anemia and esophageal membranes. Dysphagia is painless, intermittent, progressive, for solids and liquids. It is associated with glossitis, cheilitis and koilonychia. Low hemoglobin levels are not necessary for the development of dysphagia associated with iron deficiency. The syndrome may be secondary to gastrointestinal or gynecologic blood loss [61].

9. Amyotrophic Lateral Sclerosis

One third of patients may present dysphagia in the early stages, which is almost always accompanied by dysarthria. Dysphagia in the bulbar form occurs in 95% of cases. Other clinical manifestations of the bulbar presentation are increased jaw reflex, facial diplegia, palmomental reflex, poor palatal elevation, slow tongue movement, difficulty in keeping the jaw closed, and sialorrhea [62,63].

10. Systemic sclerosis sine scleroderma

It represents 9% of cases of systemic sclerosis. Esophageal involvement is the most frequent (80%) [63]. It should be suspected in the presence of Raynaud's phenomenon, arterial hypertension, impaired renal function, dysphagia, gastroesophageal reflux, and pulmonary hypertension. Cutaneous findings may appear late [65].

11. Medications

Antipsychotics such as haloperidol, olanzapine, risperidone, clozapine and quetiapine and antidepressants are associated with dysphagia. They typically do not respond to anticholinergic management and their treatment is discontinuation of the medication [66,67].

The patient who says: "I have a dry mouth".

Xerostomia is the subjective sensation of dryness in the mouth, with a prevalence between 8 and 42% [68].

Causes of xerostomia are:

- Anticholinergics, beta and alpha blockers, calcium antagonists and diuretics.
- Sjögren's syndrome.
- Chronic parotitis and salivary duct obstruction.
- Diabetes mellitus, hyperthyroidism, hypothyroidism and Addison's disease.
- Radiation therapy.
- Systemic sclerosis and mixed connective tissue disease.
- Inflammatory bowel disease.
- Autoimmune liver disease.
- Central nervous system trauma, Bell's palsy, cerebral palsy, Parkinson's disease and Alzheimer's dementia.

Other causes to consider are:

1. IgG4-related disease

It has a prevalence of 0.8 cases per 100,000 population and is responsible for 6% of chronic pancreatitis [68]. It is more frequent in men, in the age range of 42 to 79 years, clinically mimics Sjögren's syndrome as patients present with dry eye and mouth. It should be suspected in the presence of bilateral and symmetric enlargement of the parotid glands and retroperitoneal adenopathy, which is uncommon in Sjögren's syndrome. Xerostomia is present in 27 to 53% of patients [70,71.

2. Sarcoidosis

It is more frequent in black patients. In about 3% to 6% of patients there is involvement of the lacrimal or salivary glands [72]. Other manifestations of sarcoidosis include uveitis, cutaneous sarcoidosis, erythema nodosum, peripheral lymphadenopathy and pulmonary involvement [73].

3. HIV

Xerostomia is one of the oral manifestations in patients with HIV/AIDS, with a prevalence ranging from 1.2% to 63%. The occurrence of xerostomia is independent of the time of disease progression and age [74,75].

4. C Hepatitis

80% of patients have histologic findings of salivary and lacrimal gland involvement. In patients diagnosed with Sjögren's syndrome, 14% have he-

patitis C. Approximately 15% of patients present with xerophthalmia or xerostomia [76,77].

5. Granulomatosis with polyangiitis

This systemic vasculitis has a prevalence of approximately 23 to 156 cases per million population, mainly involving the kidneys, upper and lower respiratory tract. It can also affect major salivary glands, although this is unusual, and in some cases may be the first manifestation of the disease. Symptoms include xerostomia and enlarge parotid or submaxillary glands unilaterally or bilaterally [78]**.**

6. Tuberculosis

Of the presentations of extrapulmonary tuberculosis, 10% affect the head and neck, including the salivary glands. Salivary gland tuberculosis can be primary or secondary, most commonly secondary due to mycobacterial extension from regional lymph nodes. It involves the parotid gland, producing chronic infectious granulomatous sialadenitis that manifests as a chronic tumor lesion [79].

7. Chronic graft-versus-host disease

It is a late complication of allogeneic hematopoietic cell transplantation, occurring in 18 to 70% of recipients. It involves oral tissues and salivary glands in 80% of cases. The main symptoms are pain, xerostomia and dysgeusia and the severity of the oral manifestations may be associated with the severity of the disease [80].

8. Sialosis

It is a non-inflammatory, non-neoplastic disease of the parotid gland. It consists of diffuse, bilateral, chronic and non-painful enlargement of the parotid gland. It has been associated with multiple systemic diseases, mainly diabetes. Other causes include alcoholism, obesity, starvation and anorexia nervosa. This condition typically improves when the underlying cause is treated, except when there is already fatty replacement of the glandular tissue [81,82].

Symptoms in bariatric surgery patients.

Colombia is the second Latin American country where most bariatric surgeries are performed; it is estimated that 12 thousand surgeries of this type are performed annually [83]. The following are frequent symptoms after bariatric surgery:

1. Dizziness and postprandial confusion

1.1 Dumping syndrome

It may occur in 76% of bypass patients [84]. The early variety is characterized by chills, sweating, hypotension, palpitations, dizziness, diarrhea, and flushing in the first 30 minutes postprandial, without alteration of consciousness [85].

1.2 Nesidioblastosis

Also called post-gastrectomy hyperinsulinemic hypoglycemia, with a prevalence in post-surgical patients of 0.4%. It remits the symptoms of dumping, except that it is accompanied by neuroglycopenic symptoms that can be severe, with disorders of consciousness following carbohydrate ingestion [86].

2. Gait instability

2.1 Vitamin B12 deficiency

All patients undergoing total gastrectomy and 16% of those undergoing subtotal gastrectomy have vitamin B12 deficiency within 4 years [87]. Some patients, despite multiple warnings from the surgeon, stop taking vitamin B12. About 20% of patients present vitamin B12 deficiency with normal blood counts [88].

2.2 Copper deficiency

Ingested copper is stabilized by gastric acid and absorbed in the stomach and duodenum [89]. In addition to its low absorption secondary to bypass surgery, it is important to note that high zinc intake (multivitamins, dental fixatives) decreases intraluminal copper absorption, leading to increased deficiency [90]. It should be suspected when a patient has gait instability and does not improve with vitamin B12 administration [91].

2.3 Vitamin E deficiency

Five percent of patients present deficiency of this vitamin at 28 months post-procedure [84]. Neurological symptoms vary, the most frequent being ataxia, weakness, hyporeflexia and ophthalmoplegia [85]. It should be suspected when a patient has gait instability that does not improve with the administration of vitamin B12 and copper [85].

3. Fatigue:

3.1 Iron deficiency:

Already mentioned in the first part of this review.

3.2 Folic acid deficiency

Up to 65% of patients with a history of by-pass may have folic acid deficiency despite the recommendation to take multivitamins [92].

3.3 Vitamin C deficiency

Up to 14% of men and 10% of women in the general population have vitamin C deficiency. Frequent symptoms are orthostatic hypotension, bruising, gingivorrhagia with tooth loss, and fatigue [89]. The presence of perifollicular purpura and corkscrew hairs are characteristic [93]. It should be suspected in patients with slow progressive fatigue who respond rapidly to vitamin supplementation [89].

4. Heart failure:

4.1 Selenium deficiency

HIV and bariatric surgery are frequent causes of selenium deficiency; up to 15% of patients with gastric bypass present this deficiency [94]. It should be suspected in the presence of heart failure of unknown origin [95].

5. Neurological disorders

5.1 Thiamine deficiency

Thiamine reserves last three to six weeks. Internuclear ophthalmoplegia occurs in 70% of patients. It should be suspected in the presence of cardiac failure or neurological disorder with conjugate gaze disturbance [96,97].

Other deficiencies reported are vitamin A, D, K, B10, and Zinc.

The patient who refers: "I feel lightheaded".

The annual incidence of syncope is 6.2 per 1000 persons, which is higher in the elderly [97]. It is defined as the transient loss of consciousness and postural tone, with spontaneous and complete recovery without neurological sequelae. In presyncope, loss of consciousness is felt to be imminent but does not occur because the patient prevents it by muscle tension or lying down [98,99].

The causes of syncope are:

- Vasovagal syncope (provoked fear, pain, anxiety, visualization of blood, unpleasant images and odors and orthostatic pressure).
- Situational syncope (coughing, Valsalva maneuvers, after urination, glossopharyngeal neuralgia, esophageal stimulation, defecation, carotid sinus tenderness and ocular compression).
- Parkinson's disease and dementia with Lewy bodies.
- Diabetes, hereditary and acquired autonomic neuropathies, Sjögren's syndrome and HIV neuropathy.

- Medications (diuretics, clonidine, beta-blockers, calcium antagonists, iECAS and prazosin).
- Arrhythmias, valvular heart disease, acute coronary syndrome, obstructive cardiomyopathy and atrial myxoma.

Other causes to consider are:

1. Postprandial hypotension

It is a common entity in the elderly. Criteria for postprandial hypotension are found in up to 73% of patients older than 65 years who consult cardiology services, and this has been associated with syncope, falls, coronary events, cerebrovascular events and all-cause mortality in long-term follow-up [100, 101]. Avoidance of large or high-carbohydrate meals, drinking water during meals, avoiding alcohol consumption, and drinking coffee have been associated with symptom reduction [102, 103].

2. Pulmonary embolism

Between 30% and 35% of patients with high-risk pulmonary thromboembolism initially manifest as syncope. Attempts have been made to attribute the presence of this symptom to the following three mechanisms: thrombosis of more than 50% of the pulmonary circulation, activation of the vasovagal reflex, and rhythm disturbances and cardiac conduction blockade [104,105].

3. Amyloidosis

Syncope in this pathology can be explained by myocardial involvement leading to arrhythmias or heart block, angina or infarction due to coronary artery infiltration [105] and in addition to peripheral nerve involvement with the development of dysautonomia and orthostatic hypotension, the latter being mainly associated with AL and hereditary (transthyretin) variants [107]. Cardiac amyloidosis should be suspected on ECG when there are low QRS voltages and pseudo-infarct patterns [108].

4. Pheochromocytoma

Adrenomedullin-producing tumors can lead to symptomatic severe hypotension and hemodynamic instability which may alternate with classic episodes of hypertensive crisis [109]. The most sensitive diagnostic tests are 24-hour urine fractionated catecholamines and metanephrines (97%) or serum fractionated metanephrines (99%) [110].

5. Diabetes insipidus

Most patients with diabetes insipidus of central origin have autonomic nervous system involvement. Despite correction of water-electrolyte dis-

turbances and management with desmopressin, these patients persist with symptoms of orthostatic hypotension and syncope [111].

6. Multiple systemic atrophy

It affects about 8 people per 100,000 population after the age of 40 years. Initial symptoms of sexual dysfunction, prostatic symptoms, REM sleep disturbances and orthostatic hypotension are described with subsequent progression to symptoms of parkinsonism, cerebellar ataxia, cognitive deficits, prostration and death over the course of 6 to 9 years [57].

7. Adrenal insufficiency

Most patients present with orthostatic hypotension (70%). Other symptoms include fatigue, polyuria, nausea, vomiting, weight loss, fever, abdominal pain, hyperpigmentation, hyponatremia, hyperkalemia, and hypoglycemia [112].

8. Tumarkin crisis

They are described as abrupt falls to the ground, of short duration, without prodrome and without loss of consciousness. They occur in patients with a history of decreased hearing acuity, full ear and tinnitus, and may even be the first clinical manifestation of Ménière's disease [113].

The multisymptomatic patient

Few patients cause as much uncertainty for the physician as the multisymptomatic patient. Causes of multiple symptoms in otherwise healthy patients are:

1. Medicated hypotension

It particularly affects the elderly; the prevalence is 5 to 33%. The associated drugs are diuretics, calcium antagonists, beta-blockers, ACE inhibitors, nitrates and antiparkinsonian drugs. Dizziness, occipital headache, chest pain, arm pain, nausea, blurred vision, phosphenes, palpitations, coldness, diaphoresis, fainting and lateropulsion are frequent symptoms in a single patient. Symptoms predominate in the morning and when the patient is standing [114].

2. Dysautonomia

Causes of dysautonomia are prediabetes and diabetes, vitamin deficiencies (cyanocobalamin, thiamine, niacin, vitamin E and pyridoxine), celiac disease, chronic inflammatory demyelinating polyneuropathy, paraneoplastic syndrome, sarcoidosis, toxicity (arsenic, cadmium, mercury and thallium) and Sjögren's syndrome [115,116].

Symptoms are similar to those of orthostatic hypotension but should be

suspected in patients not receiving antihypertensive drugs and when pupillary abnormalities (slow response to light or Argyll-Robertson pupil) coexist [117].

3. Amyloidosis

Up to 4% of the population over 70 years of age has the transthyretin gene. It should be suspected in heart failure with preserved ejection fraction in patients older than 70 years. Other findings include alopecia, ecchymosis with minor trauma, skin fragility, onychodystrophy, macroglossia, gastrointestinal bleeding, and low QRS complex voltage on the electrocardiogram [118][119].

Autonomic involvement generates fainting, dizziness and other symptoms of orthostatic hypotension, mainly associated with AL and hereditary (transthyretin) variants [120][119].

4. Multiple systemic atrophy

Urinary symptoms, erectile dysfunction, orthostatic hypotension, REM sleep disorders that may precede by months to years the onset of motor disorders such as cerebellar syndromes, pyramidal and extrapyramidal signs that mimic Parkinson's disease [57].

5. Menopause

It should be considered in women around 45 years of age who present with nonspecific symptoms such as irritability, sleep disturbances, arthralgias, loss of libido, vaginal dryness and itching, dysuria, dyspareunia, eczema, hot flashes, depression, sleep disturbances and cognitive changes [121,122].

6. Hypogonadism

It begins around the age of 40 years. Manifestations are loss of energy, cognitive decline, decreased memory and spatial orientation, fatigue, depression, emotional changes, irritability, muscle weakness, decreased libido, loss of morning erections, anorgasmia, decreased body hair, and osteoarticular pain [123].

7. Postural orthostatic tachycardia syndrome

It is an autonomic disorder that affects patients between 12 and 50 years of age, predominantly in women. It is common after stressful situations such as sepsis, pregnancy, fever, surgery or trauma. It has two forms of presentation, a primary one present in adolescents and a secondary one that can accompany disorders such as diabetes mellitus, amyloidosis, Sjögren's syndrome and paraneoplastic syndrome. It is characterized by a spectrum

of symptoms related to orthostatic intolerance such as headache, fatigue, sleep disturbances, weakness, hyperventilation, dyspnea, sweating, palpitations, dizziness, syncope that improve when the patient lies down. Most of the patients are diagnosed with panic disorder [124,125].

Conclusions

Many symptoms can be difficult to interpret clinically, it is necessary to recognize unusual causes when more frequent pathologies have been ruled out, when the patient has consulted multiple times or when a clear diagnosis has not been achieved.

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