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DISTÚRBIOS NEUROLÓGICOS PARANEOPLÁSICOS: UMA REVISÃO DE LITERATURA

PARANEOPLASTIC NEUROLOGICAL DISORDERS: A LITERATURE REVIEW

TRASTORNOS NEUROLÓGICOS PARANEOPLÁSICOS: UNA REVISIÓN DE LA LITERATURA

https://doi.org/10.56238/sevened2025.026-020

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RESUMO

Introdução: As síndromes paraneoplásicas são um conjunto de sinais e sintomas associados ao processo cancerígeno que não se relacionam aos efeitos físicos do tumor, isto é, efeitos locais e metastáticos. Estima-se que acometimentos neurológicos paraneoplásicos estejam presentes em 1% dos pacientes com tumores em todo o mundo, abrangendo tanto o sistema nervoso central quanto o periférico. **Objetivo:** Elencar as principais síndromes neurológicas paraneoplásicas, abordando as suas manifestações clínicas e aspectos fisiopatológicos das mesmas. **Método:** Revisão integrativa realizada entre maio e junho de 2024 em publicações de artigos científicos originais encontrados nas bases eletrônicas BVS, LILACS, GOOGLE ACADÊMICO, PUBMED e SciELO, nas línguas espanhola, inglesa e portuguesa, utilizando critérios de inclusão e exclusão. **Resultados:** Obteve-se um total de 133 artigos, dos quais 126 foram excluídos após a leitura do título, do resumo e do texto completo, restando 7 artigos para compor esta revisão. Os estudos mostraram que a degeneração cerebelar subaguda é a mais comum das paraneoplasias neurológicas, estando envolvidos nos seus mecanismos fisiopatológicos a produção de hormônios, peptídeos, citocinas ou reações imunológicas cruzadas entres os tecidos sadio e tumoral. **Conclusão:** As manifestações neurológicas na forma de síndromes paraneoplásicas, apesar de raras, assumem particular importância quando ocorrem como primeira manifestação de um tumor desconhecido, permitindo o diagnóstico de uma neoplasia em um estágio precoce.

Palavras-chave: Neoplasia. Sistema Nervoso. Sinais e sintomas. Síndrome Paraneoplásica. Revisão.

ABSTRACT

Introduction: Paraneoplastic syndromes are a set of signs and symptoms associated with the cancerous process that are not related to the physical effects of the tumor, that is, local and metastatic effects. It is estimated that paraneoplastic neurological disorders are present in 1% of patients with tumors worldwide, covering both the central and peripheral nervous systems. **Objective:** List the main paraneoplastic neurological syndromes, addressing their clinical manifestations and pathophysiological aspects. **Method:** Integrative review carried out between May and June 2024 on publications of original scientific articles found in the electronic databases BVS, LILACS, GOOGLE ACADÊMICO, PUBMED and SciELO, in Spanish, English and Portuguese, using inclusion and exclusion criteria. **Results:** A total of 133 articles were obtained, of which 126 were excluded after reading the title, abstract and full text, leaving 7 articles to compose this review. Studies have shown that subacute

cerebellar degeneration is the most common of neurological paraneoplasms, with the production of hormones, peptides, cytokines or cross-immunological reactions between healthy and tumor tissues being involved in its pathophysiological mechanisms. **Conclusion:** Neurological manifestations in the form of paraneoplastic syndromes, although rare, assume particular importance when they occur as the first manifestation of an unknown tumor, allowing the diagnosis of a neoplasm at an early stage.

Keywords: Neoplasm. Nervous system. Signs and symptoms. Paraneoplastic Syndrome. Review.

RESUMEN

Introducción: Los síndromes paraneoplásicos son un conjunto de signos y síntomas asociados al proceso canceroso que no se relacionan con los efectos físicos del tumor, es decir, efectos locales y metastásicos. Se estima que la afectación neurológica paraneoplásica está presente en el 1% de los pacientes con tumores a nivel mundial, abarcando tanto el sistema nervioso central como el periférico. **Objetivo:** Enumerar los principales síndromes neurológicos paraneoplásicos, abordando sus manifestaciones clínicas y aspectos fisiopatológicos. **Método:** Revisión integrativa realizada entre mayo y junio de 2024 en publicaciones de artículos científicos originales encontrados en las bases de datos electrónicas BVS, LILACS, GOOGLE ACADEMICO, PUBMED y SciELO, en español, inglés y portugués, utilizando criterios de inclusión y exclusión. **Resultados:** Se obtuvieron 133 artículos, de los cuales 126 fueron excluidos después de leer el título, el resumen y el texto completo, dejando 7 artículos para componer esta revisión. Estudios han demostrado que la degeneración cerebelosa subaguda es la paraneoplasia neurológica más común, y sus mecanismos fisiopatológicos involucran la producción de hormonas, péptidos, citocinas o reacciones inmunológicas cruzadas entre tejidos sanos y tumorales. **Conclusión:** Las manifestaciones neurológicas en forma de síndromes paraneoplásicos, aunque poco frecuentes, son particularmente importantes cuando se presentan como la primera manifestación de un tumor desconocido, lo que permite el diagnóstico de una neoplasia en una etapa temprana.

Palabras clave: Neoplasia. Sistema nervioso. Signos y síntomas. Síndrome paraneoplásico. Revisión.

INTRODUCTION

Paraneoplastic syndromes are a group of clinical events associated with malignant tumors, not directly related to a physical effect of the primary tumor or metastatic lesions, infections, ischemia, metabolic or nutritional deficit, surgery, or other forms of treatment. It is estimated that the occurrence of paraneoplastic syndromes is up to 8% of cancer patients, although these numbers have been growing with the increase in the incidence of cancer in the population[1]. Neurological paraneoplastic syndromes can involve any level of the nervous system, whether central or peripheral, and can be classified according to the location of the predominant manifestation. Their incidence is about 1% in patients with systemic cancer and they are associated with small cell lung carcinoma in about 50% of cases. Other tumors associated with these syndromes are those that express neuroendocrine proteins or organs that perform immunoregulatory functions[2].

Consequently, these syndromes are associated with a wide variety of symptoms, which, in most cases, have a subacute onset, evolving over weeks or months. Once symptoms have started, the cancer may be too small to be detected and may go unnoticed for years. In typical cases, there is a predominance of clinical manifestations such as cerebellar ataxia, dysphagia, autonomic dysfunctions, sensory neuropathies, and even progressive changes in personality and mood. Such exuberance of signs and symptoms makes the differential diagnosis of neurological paraneoplastic syndromes extremely complex, requiring a high level of suspicion on the part of the health professional[3].

At the same time, among the most common presentations of neurological paraneoplastic syndromes is subacute cerebellar degeneration, which can manifest more frequently in tumors such as small cell lung carcinoma, gynecological tumors including breast, and Hodgkin's lymphoma. Symptoms are almost always preceded by prodomes such as dizziness, nausea, and vomiting, later evolving with gait changes, dyslalia, diplopia, nystagmus, among other less common[ones 1,4]. In addition, paraneoplastic cerebellar degeneration is associated with several antineuronal antibodies, such as anti-Yo (also known as PCA-1), anti-Tr (PCA-Tr), and anti-mGluR1 (metabotropic glutamate receptor 1), which attack proteins expressed by cerebellar Purkinge cells[1,5].

In addition, another important neurological paraneoplasm is encephalitis/myelitis, which can compromise areas such as the limbic system (progressing with limbic encephalitis), brainstem (causing bulbar symptoms) and spinal cord. When more than one area is affected in the presence of a probable malignant neoplasm, the condition will be known as paraneoplastic encephalomyelitis[3]. As clinical manifestations of limbic encephalitis, delirium and dementia with severe memory deficit are expected, easily

confused with psychiatric disorders, in addition to occasional epileptic seizures. Concomitantly, brainstem encephalitis most frequently progresses with cranial nerve dysfunctions, causing oculomotor disorders (nystagmus, supranuclear vertical gaze paralysis), respiratory abnormalities, among other symptoms. The antibodies most involved in the development of the pathology in question are anti-Hu, anti-CV2/CRPm5 (antibody of the colapsin-response mediator protein) and antiamphiphysin[6].

Additionally, to complement the scope of the most rarely occurring neurological paraneoplastic syndromes, there are sensory neuronopathies, which cause progressive loss of all sensory modalities as a consequence of inflammatory or autoimmune destruction of the dorsal root ganglia. The first symptom to appear is usually painful neuropathy, which may be accompanied by severe sensory ataxia, in addition to a possible involvement of the cranial nerves, and these involvements are asymmetric in most cases. The most frequently associated antibody is anti-Hu. Anti-CRMP5/CV2 antibody can also be found. In these patients, however, the clinical picture is more associated with cerebellar ataxia[3,7].

As for ophthalmologic manifestations, opsoclonus-myoclonus can be mentioned, characterized by chaotic eye movements (arrhythmic, irregular in direction and with associated myotonic muscle movements). It is important to emphasize that opsoclonus-myoclonus is rarely caused by a paraneoplastic process, and it is necessary to investigate other etiologies. Other forms of visual impairment are cancer-associated retinopathy, the most common etiology of which is an antibody directed against recoverin (a photoreceptor protein that binds to calcium) and optic neuropathy, which causes subacute, painless, and bilateral visual loss[1,8].

Finally, neuromuscular disorders can be mentioned, such as myasthenia gravis, proven to be associated with thymoma, in addition to its variant, Lambert-Eaton Myasthenic Syndrome (SMLE), associated with small cell lung carcinoma. This is caused by antibodies directed against the voltage-regulated calcium channel (VGCC), and the anti-Sox1 antibody is also a marker of paraneoplastic SMLE. In addition, about 20% of patients with dermatomyositis started after 40 years of age have some associated tumor, and current studies also indicate paraneoplasia as a possible etiology for Guillain-Barré Syndrome[7,9].

MATERIALS AND METHODS

The work in question is a literature review, presenting as guiding questions: What are the main paraneoplastic neurological syndromes? What are the epidemiological data regarding these diseases? What are its main clinical manifestations? What are its main pathophysiological aspects?

It was developed through research in the following electronic databases: Virtual Health Library (VHL), Latin American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), Público/Editora Medline (PUBMED) and GOOGLE SCHOLAR. The descriptors for the research were obtained through a previous consultation in the Health Sciences Descriptors (DeCS) Finder, namely: "Paraneoplastic syndromes", "Paraneoplastic syndromes of the nervous system" and "signs and symptoms".

To this end, the inclusion criteria adopted were publications of the types of scientific articles containing full texts available in English, Portuguese and Spanish and that contemplated the objectives of the present review. Nevertheless, the exclusion criteria adopted were incomplete texts, publications that did not meet the guiding questions of the research, as well as studies that did not meet the inclusion criteria. The results obtained were arranged in order of publication in Table 1.

Table 1 – Studies included in the review and their background information

Publication title	YEAR	Database	Author
Paraneoplastic subacute cerebellar degeneration	2000	GOOGLE SCHOLAR	Bardy et al., 2000
Progressive encephalomyelitis with rigidity	2004	SCIELO	Spitz et al., 2004
Ataxia and chorea as manifestations of paraneoplastic syndrome	2014	GOOGLE SCHOLAR	Oliveira et al., 2014
Guillain-Barré syndrome: Paraneoplastic?	2019	LILACS	Santori et al., 2019
Transverse myelitis as a paraneoplastic syndrome in lung cancer	2020	GOOGLE SCHOLAR	Martins et al., 2020
Opsoclonus-Myoclonus-Ataxia Syndrome secondary to Paraneoplastic Syndrome	2022	GOOGLE SCHOLAR	Passaglia et al., 2022
Autoimmune encephalitis and paraneoplastic syndrome due to mature ovarian teratoma	2023	LILACS	Trejo et al., 2023

Source: Elaborated by the author (2024)

RESULTS

After applying the inclusion criteria and using the databases cited during the study methodology, 133 articles were obtained, of which 7 were selected because they met the

requirements proposed for the elaboration of the work in question, and 126 were discarded because they touched the desired objectives.

Bardy et al., in their study, reported that about 50% of patients with systemic neoplasms present neurological complications during the course of the disease. According to the study, neoplasms originating outside the nervous system can affect its central and peripheral portions in two ways, namely: direct mechanisms (direct invasion or metastases) and indirect mechanisms (vascular obstruction, nutritional or metabolic deficit, toxic effects of treatment, paraneoplastic syndromes). Paraneoplasms can affect any level of the nervous system and their manifestations often precede tumor detection. Its correct diagnosis depends on a high degree of suspicion on the part of the physician and, because it precedes the diagnosis of the neoplasm, it is of great importance for identifying and treating the tumor early, which is often small and escapes detection even after repeated investigations[10].

Still on the panorama evidenced by Bardy et al., it is possible to establish the relationship between ovarian adenocarcinoma and subacute paraneoplastic cerebellar degeneration (PCD). PCCD is characterized by the presence of symptoms of cerebellar dysfunction such as visual changes, dysarthria, and ataxia, with subacute onset and rapidly progressive course, resulting in disability of the patient due to a pancerebellar syndrome. The neoplasms most commonly associated with PCCD are ovarian carcinoma, breast carcinoma, lung carcinoma (small cell type), and lymphoma. Histopathologically, there is almost complete destruction of Purkinje cells and astrogliosis, and there may also be demyelinating changes in the posterior columns of the spinal cord. In order to rule out alternative diagnoses, it is necessary to detect "specific" antibodies such as anti-Hu, anti-Yo, anti-Ri, anti-RT, and anti-NM in serum and/or cerebrospinal fluid, as well as other imaging tests[10].

According to Spitz et al., progressive encephalomyelitis with rigidity and myoclonus (PEWR) is a rare disease characterized by muscle rigidity, painful spasms, myoclonus, and evidence of brainstem and spinal cord involvement, whose etiology is still unknown, but current studies corroborate its possible paraneoplastic origin, mainly associated with small cell lung carcinomas and Hodgkin lymphoma. The poor prognosis of the pathology in question is highlighted, causing the death of the affected patient in a few weeks or years. As pathophysiological aspects, the high prevalence of anti-GAD (glutamic acid decarboxylase) antibodies is evidenced, in addition to intense perivascular lymphocytic infiltration, increased microglial activity, astrogliosis and neuronal loss, affecting both the brain and the spinal cord, especially the cervical region. It is postulated that PEWR is a serious disease

whose differential diagnosis should be raised in all patients who present acute encephalomyelitis associated with muscle spasms and myoclonus, making screening for small cell lung carcinoma essential [11,12].

From the point of view of Oliveira et al., it is estimated that neurological involvement related to paraneoplasms is present in approximately 1% of patients with tumors, with the exception of Eaton-Lambert myasthenic syndrome, which is present in 3% of small cell lung cancer, and myasthenic syndrome, which is present in 15% of thymomas. In addition, the pathophysiological basis of the manifestations is the production of hormones, peptides, cytokines or immunological cross-reactions between healthy and tumor tissues. The main neoplasms related to neurological conditions are: pulmonary (small cells), thymoma, gynecological system (breast and ovary) and hematological (lymphoma). Regarding their prognosis, it is postulated to be slightly better compared to patients who do not have this symptomatology, since it allows for an earlier diagnosis of the neoplasm[13].

According to the authors, ataxia is the movement disorder most commonly related to paraneoplastic syndromes, making up the scope of clinical manifestations of PCCD. However, the presentation of chorea is uncommon and, when associated with subacute-onset ataxia, should be considered in the differential diagnosis of neoplasms. Chorea is associated with antibodies such as CV2/CRMP5, which are present in small cell lung neoplasms and thymoma. The differential diagnosis of sporadic ataxias is extensive and covers a series of diseases such as alcoholic cerebellar degeneration, vitamin B1 and E deficiency, medications (valproate, phenytoin, amiodarone, etc.), Miller-Fisher syndrome, ataxia associated with GAD (glutamic acid decarboxylase), celiac disease, and paraneoplastic syndromes, with history, physical examination, and complementary tests being fundamental in guiding the etiological diagnosis[13].

Santori et al. highlight a possible pathogenic association between cancer and Guillain-Barré Syndrome (GBS), mainly associated with lymphomas. GBS is an acute inflammatory polyradiculoneuropathy, characterized by motor paralysis, minimal sensory and autonomic symptoms, associated with cranial nerve involvement. In the vast majority of cases, it is preceded by some respiratory or digestive infection in about 1 to 4 weeks, both viral (cytomegalovirus, E.Barr, among others) and bacterial (Campylobacterjejuni, Mycoplasmaplasmapneumoniae, among others). The symptoms are possibly caused by inflammatory demyelination, axonal degeneration, or both, in addition to the action of anti-Hu antibodies, which can cause a direct immune-mediated injury to the neuronal body, explaining the possible etiological nature of paraneoplastic GBS, since such antibodies are commonly found in patients with small cell carcinoma of the lung, breast, and prostate.

Therefore, the authors also emphasize the importance of initiating a broad investigation in order to detect some type of occult neoplasm in patients with atypical GBS, especially when associated with hyperproteinorrhachia (increased levels of protein concentration in the CSF)[9,14].

At the same time, Martins et al. state that, for the diagnosis of paraneoplastic syndromes, it is essential to prove that the symptoms do not come from direct effects of the tumor, such as metastases, infections, or even from drug or radiotherapy therapy. According to them, there is a wide variety of neurological paraneoplastic syndromes, such as limbic encephalitis, cerebellar degeneration, sensory and motor neuropathies, axonal neuropathies, demyelinating neuropathies and necrotizing myelopathy, among others. The authors emphasize that, among all these presentations, transverse myelitis is an uncommon process, usually progressing with flaccid paraparesis and sphincter disorders or spinal cord involvement. In most cases, the involvement is progressive and ascending, and the prognosis is reserved. In order to facilitate the diagnosis of the pathology in question, antibody measurement can be performed, with the anti-Hu antibody (nuclear antineuronal) being the most frequently detected. However, not all patients have a paraneoplastic antibody, so negative results for antibodies do not exclude the diagnosis. Other complementary tests, such as MRI and cerebrospinal fluid cellularity, can contribute to the differential diagnosis, but in most cases, they reveal only nonspecific alterations, such as edema and involvement of white and gray matter structures, in addition to hyperproteinorrhachia[15].

In their article, Passaglia et al., report that Opsoclonus-Myoclonus-Ataxia Syndrome (SOMA), also called Kinsbourne syndrome, can also present as a manifestation of neurological paraneoplasia. It is a rare disease that progresses with opsoclonus (rapid, involuntary and multidirectional eye movements), myoclonus (sudden contraction of limb and trunk muscle groups) and ataxia, in addition to behavioral changes and sleep disorders. SOMA in adults covers a range of etiologies, being in 61% of cases related to infectious, metabolic, or toxic causes and 39% associated with paraneoplastic causes, mainly related to lung, breast, and gonad cancers. Other entities with which SOMA may be associated are neuroblastomas and ganglioneuromas, which can be preceded by different viral infections, such as Coxsackie B3 virus, Epstein Barr virus, and aseptic meningitis, as well as pharmacological intoxication, demyelinating diseases, and traumatic brain injury. Regarding differential diagnoses, other syndromes that may present with similar clinical manifestations are Guillain Barré Syndrome and its variant, Miller Fisher Syndrome, which

should be differentiated by cerebrospinal fluid collection, excluding cytological protein dissociation[16].

Also according to Passaglia et al., the exact pathophysiological mechanism of SOMA has not been fully clarified, but it is postulated that it is caused by immunological mechanisms (humoral and cellular), as well as the presence of autoantibodies associated with paraneoplastic SOMA. The evidence of the autoimmune process is due to the presence of B-cell activating factor (BAFF) in serum and cerebrospinal fluid. Regarding treatment, it is based on immunotherapy and, mainly, tumor resection. Treatment with immunosuppressants aims to reduce the formation of antibodies, possibly involved in the pathophysiology, reducing lymphocyte and phagocytic responses, and the production of interleukins. In refractory cases, plamapheresis can also be used as a therapeutic option[16].

Trejo et al., in their studies, reported that about 25-40% of the cases of encephalitis due to antibodies against the N-methyl-D-aspartate receptor (NMDAr) are of paraneoplastic etiology, and 90% of the cases are associated with ovarian teratoma. The main etiologies of the encephalitis in question are post-viral episodes and autoimmune encephalitis. Regarding the clinical manifestations, patients may have psychiatric symptoms very similar to schizophrenia, namely: auditory and visual hallucinations, delusions of persecution, disorganized thinking, cognitive dysfunction, abulia, anhedonia, among others. In addition to these, conditions such as seizure, memory alterations, autonomic instability, and central hypoventilation may also be present. The pathophysiological aspects consist of the generation of antibodies whose target is the N1 glutamate subunit of the NMDA receptor, reducing its surface expression, mainly affecting the hippocampal regions and the prefrontal cortex. The definitive diagnosis consists of the detection of IgG against the GluN1 subunit of NMDAr in both blood and CSF, with cerebrospinal fluid samples being more sensitive. Compared with other autoimmune encephalitis, anti-NMDAr encephalitis has a better prognosis. Treatment includes, in addition to tumor resection, immunotherapy (steroids, intravenous immunoglobulin, plasmapheresis)[17].

DISCUSSION

The term neurological paraneoplastic syndrome (PNS) can be applied to any neurological dysfunction in patients with neoplasms, as long as these dysfunctions are not caused by direct effects of the primary tumor, metastases, secondary effects of radiotherapy and/or chemotherapy, or as a result of infections or deficiencies. Of these, subacute cerebellar degeneration, sensory neuronopathy, dermatomyositis/polymyositis, Eaton-Lambert myasthenic syndrome, subacute motor neuronopathy, and autoimmune

encephalitis make an exhaustive investigation in search of a primary tumor mandatory, given its strong correlation with occult neoplasia, anticipating and favoring the prognosis of such patients[2].

Paraneoplastic syndromes are extremely rare, affecting less than 0.1% of all patients with neoplasia. They are characterized by a wide range of signs and symptoms, which typically have a subacute onset, evolving over weeks to months, making the wide range of differential diagnoses even more difficult. At the same time, most patients have neurological symptoms even before the primary cancer is diagnosed, opening a window of opportunity for it to be detected early. However, it may be too small to be diagnosed, going unnoticed for months and, in some cases, being diagnosed only at necropsy[3].

Merrit et al. reaffirm that any cancer can be associated with a paraneoplastic syndrome, but some syndromes are associated with specific types of neoplasia, such as the close correlation of autoimmune encephalitis with antibodies against NMDAr and ovarian teratoma[3,17]. Small cell cancer (CCPP) is one of the tumors most commonly associated with paraneoplastic syndromes, and other common tumors are those that express neuroendocrine proteins, those that affect organs that perform immunoregulatory functions, or those that originate in immunoglobulin-producing cells[3].

Regarding the pathogenesis of paraneoplastic syndromes, although not fully elucidated, it is postulated that it is triggered by immune mechanisms. Neoplasms, in general, are thought to express proteins that are normally restricted to the nervous system, triggering an antigenic cross-reaction in which antibodies directed against neoplastic antigens attack nerve antigens. Therefore, the detection of some antibodies directed against such antigens, both in the blood and in the cerebrospinal fluid, has become an important diagnostic resource for NPS. However, the pathogenesis of these antibodies is not yet fully understood, and there are many patients with supposed neurological syndromes of paraneoplastic origin who do not have any laboratory-detected antibodies[13].

The immunopathological mechanisms currently proposed in order to understand the neurological damage caused are the expression of a neuronal protein (onconeul antigen) by a tumor not involving the nervous system that is recognized by the immune system as not its own. Subsequently, these antigens are phagocytosed by dendritic cells, which migrate to local lymphatic organs, activating antigen-specific CD4+, CD8+ and B T cells, resulting in a cross-immune response. Therefore, activated B cells differentiate into plasma cells that produce antibodies against onconeural antigens. Despite the fact that antibodies and cytotoxic T cells impair tumor growth, they can also cross the blood-brain barrier and

attack structures that express common tumor antigens, causing inflammation, neuronal damage, and cell death[18].

The diagnosis requires a high level of suspicion, since numerous pathologies can generate very similar symptoms, such as autoimmune disorders unrelated to neoplasms, cerebrovascular diseases, nervous system infections, toxic-metabolic alterations or hereditary diseases. In addition, cancer patients alone may present neurological involvement by a series of mechanisms complementary to paraneoplasia, such as brain metastases, lepto-meningeal disease, nerve or spinal cord compression, and adverse effects of treatments such as radiotherapy and chemotherapy (cisplatin, taxanes, among others).

At the same time, the diagnosis of PNS and primary neoplasm can be made through imaging methods, serological studies, electroencephalogram, and CSF analysis. It is necessary to perform complementary exams such as thoracic, abdominal and pelvic computed tomography (CT), as well as complementary magnetic resonance imaging (MRI). If these methods are not sufficient for diagnostic elucidation, further investigation can be carried out by performing PET-CT and tumor markers (CEA, CA 19-9, CA 125, among others). Regarding cerebrospinal fluid analysis, it most often presents nonspecific results suggestive of an inflammatory process, such as moderate lymphocytic pleocytosis, high protein concentration, oligoclonal bands, and intrathecal IgG synthesis.

Regarding the treatment of neurological paraneoplastic syndromes, this consists of tumor removal and immunotherapy in order to reduce the production of onconeural antibodies, reducing the lymphocyte and phagocytic response, and the production of interleukins, with the following options: corticosteroids, ACTH, immunoglobulins, Rituximab, cyclophosphamide, cyclosporine A, and azathioprine. If the symptoms are refractory to the proposed therapy, plasmapheresis can also be performed[16].

CONCLUSION

Paraneoplastic syndromes have a range of presentations, whose involvement of the central and peripheral nervous systems is justified by the mechanism of cross-antigenic recognition, with the production of autoantibodies as their pathophysiological basis. Neurological manifestations in the form of paraneoplastic syndromes, although rare, are particularly important when they occur as the first manifestation of an unknown tumor, allowing the diagnosis of a neoplasm at an early stage. Consequently, the ability of health professionals to recognize and treat them has a substantial effect on the prognosis, despite

the broad differential diagnosis that clinical manifestations and nonspecific complementary tests raise.

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