MUIR-TORRE SYNDROME: A CASE REPORT

SÍNDROME DE MUIR-TORRE: UM RELATO DE CASO

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ABSTRACT

Muir-Torre Syndrome is characterized by the association of sebaceous gland neoplasms and multiple visceral neoplasms. There are several types of visceral neoplasms that can be associated with the syndrome, especially adenocarcinomas of the colon, stomach, duodenum, breast, laryngeal, bladder tumors, hematologic neoplasms, retroperitoneum sarcomas, among others. The general objective of the work is to study aspects of Muir-Torre Syndrome. Therefore, a literature review was carried out, seeking authors who spoke about the proposed theme. The objective is also to report the case of a patient at the Hospital Escola de Valença (HEV), located in the city of Valença - RJ, who presented a year ago in a cyst back filled with bloody purulent secretion, who upon receiving the biopsy result, after exeresis of the cyst, with diagnosis of sebaceous carcinoma, was referred to Hospital Hinja, located in the city of Volta Redonda – RJ. The patient has a history of malignant neoplasms in first-degree relatives. The mother died of uterine cancer, the sister died of bowel cancer and the maternal grandmother of bowel cancer. The discussion is based on the correlation between sebaceous carcinoma and Muir-Torre Syndrome, as according to literature data, the factors that predispose the appearance of sebaceous carcinoma are unknown, however, some cases are associated with Muir-Torre Syndrome. The study verifies that the presence of multiple sebaceous gland tumors is the most constant dermatological manifestation that most characterizes Muir-Torre Syndrome.

KEYWORDS: Sebaceous carcinoma; sebaceous gland; Muir-Tower Syndrome

RESUMO

A Síndrome de Muir-Torre se caracteriza pela associação de neoplasias de glândulas sebáceas e neoplasias viscerais múltiplas. São diversos os tipos de neoplasias viscerais que podem estar associados à síndrome, destacando-se os adenocarcinomas de cólon, estômago, duodeno, tumores de mama, laringe, bexiga, neoplasias hematológicas, sarcomas de retroperitônio entre outros. O objetivo geral do trabalho é estudar aspectos da Síndrome de Muir-Torre. Para tanto foi realizada uma revisão de literatura onde se buscou autores que discorram sobre o tema proposto. Objetiva-se também relatar o caso de um paciente do Hospital Escola de Valença (HEV), situado na cidade de Valença – RJ, que apresentou há um ano em região de dorso cisto preenchido de secreção purulenta sanguinolenta, que ao receber o resultado da biópsia, após exérese do cisto, com diagnóstico de carcinoma sebáceo foi encaminhado para o Hospital Hinja, situado na cidade de Volta Redonda – RJ. O paciente apresenta história de neoplasias malignas em familiares de primeiro grau. A mãe faleceu de câncer no útero, a irmã faleceu de câncer no intestino e a avó materna de câncer no intestino. A discussão está baseada na correlação entre carcinoma sebáceo com a Síndrome de Muir-Torre, pois conforme dados da literatura os fatores que predispõem o surgimento do carcinoma sebáceo são desconhecidos, no entanto, alguns casos estão associados à Síndrome de Muir-Torre. O estudo verifica que a presença de múltiplos tumores das glândulas sebáceas é a manifestação dermatológica mais constante e que mais caracteriza a Síndrome de Muir-Torre.

PALAVRAS-CHAVE: Carcinoma sebáceo; Glândula sebácea; Síndrome de Muir-Torre.

1. INTRODUCTION

Muir-Torre Syndrome is characterized by the association of sebaceous gland tumors, called keratoacanthomas and visceral neoplasms. It is a rare condition, which was described for the first time in two cases reported by Muir et al., in 1967, and Torre in 1968, when they found the association of several skin lesions of the sebaceous lineage and visceral malignancy. In 1982, Fahmy and collaborators proposed the ending that gave this pathology its name[1,2].

Sebaceous adenomas are the most frequent skin lesions. Muir-Tower Syndrome patients may have mutations in one of the hMLH1 and hMSH2 genes, which are responsible for DNA repair, and their sebaceous tumors may show microsatellite instability[3,4].

Studies[5] also argue that in its hereditary form mutations occur in DNA repair genes, implying the absence of crucial enzymes for the process of replication of the genetic material. The patient described in the study developed by these authors had a sebaceous adenoma and colorectal cancer, thus meeting the clinical criteria for Muir-Torre Syndrome.

About colorectal cancer, other authors[6] assess that Lynch syndrome is responsible for approximately 3%

of the incidence of colon cancer worldwide and can also manifest itself with cancer of the urogenital tract, stomach, small intestine, brain, and hepatobiliary tract. It is caused by germline mutations in mismatch repair system genes, mainly hMSH2 and hMLH1.

Molecularly, Lynch tumors are characterized by high microsatellite instability and absence of expression of one or more of the proteins that comprise the incompatibility repair system[6]. These same features are present in Muir-Torre syndrome, but this syndrome differs from Lynch syndrome due to the appearance of skin lesions, such as sebaceous adenomas and carcinomas, among others[7,8,9].

Tumors appear at an earlier age than usual, and colonic tumors are more repeatedly proximal and the occurrence of synchronous and metachronic damage is much greater than in occasional colorectal cancer. However, the survival of patients with these tumors is greater when compared to patients with colorectal cancer unrelated to the disease at an identical stage of the disease[10.]

It is observed, therefore, that Muir-Torre Syndrome is classified as a variant of hereditary colorectal cancer, not associated with hereditary non-polyposis colorectal cancer (HNPCC), having a more indolent neoplastic course and, therefore, a better prognosis[11].

Clinical diagnosis requires the presence of at least one sebaceous gland tumor (sebaceous adenoma, sebaceous epithelioma, sebaceous carcinoma, sebaceous hyperplasia and keratoacanthoma with sebaceous differentiation), associated with a primary visceral tumor[12].

According to the literature[13], the Syndrome can also be diagnosed if the patient has multiple keratoacanthomas with various internal neoplasms and a family history of Muir-Torre Syndrome.

Thus, the diagnosis of Muir-Torre syndrome is based mainly on clinical dermatological characteristics and the presence of visceral malignancies or family history. According to authors[14], Muir-Torre Syndrome may not be recognized if physicians do not know its characteristics.

The role of physicians in detection and treatment is fundamental, as the presence of skin lesions requires a search for visceral malignancies and an interest in family history, highlighting the importance of these clinical characteristics[15].

Authors[16] state that most cases occur between 50 and 60 years of age, mainly in males, in a 2:1 ratio. Sebaceous tumors usually appear before visceral tumors and may appear up to 20 years earlier.

As part of sebaceous carcinomas does not have a defined etiology and may in some cases be associated with Muir-Torre Syndrome, characterized by the presence of sebaceous tumors (benign or malignant) or keratoacanthoma associated with visceral malignancies, it is very important that patients who with a diagnosis of sebaceous carcinoma are investigated, clinically and laboratory, for detection and exclusion of systemic neoplasms[12.]

For this reason, a fast and accurate dermatological diagnosis is very relevant, as the prognosis of the disease is closely linked to the time of its evolution. It is also worth noting the necessary investigation to exclude systemic neoplasms, due to the association with Muir-Torre Syndrome, and the importance of referring these patients to cancer treatment, as they can often be aggressive and recurrent tumors[11.]

The general objective of the article is to study aspects of Muir-Torre Syndrome. The specific objective is to describe the clinical case of a patient seen at the outpatient clinic of the Hospital Escola de Valença (HEV), located in Valença - RJ, in 2020, who presented a cyst filled with purulent bloody secretion in the back region, diagnosed as carcinoma sebaceous.

2. CASE REPORT

The case to be reported is a 47-year-old male patient, treated at the outpatient clinic of the Hospital Escola de Valença (HEV), located in the city of Valença - RJ,Brazil in March 2020, being later transferred to the Hinja Hospital, in Volta Redonda.

In 2019, the patient presented a cyst filled with bloody purulent secretion in the dorsum region, which upon receiving the biopsy result, after exeresis of the cyst, was referred to the HEV oncology clinic. He underwent resection of the lesion and the anatomopathological examination revealed that it was a sebaceous carcinoma. The cutaneous cyst consisted of irregular sebaceous gland lobes, where basaloid cells and mature sebocytes were identified.

He had a history of malignant neoplasm in first-degree relatives. The mother died of uterine cancer, the sister died of bowel cancer and the maternal grandmother of bowel cancer.

Due to the results of the anatomopathological examination and family history, she underwent screening tests for the diagnosis of visceral neoplasms. Where chest X-ray, upper digestive endoscopy, indirect laryngoscopy was performed, which revealed no alterations.

The biopsy showed the following result: Skin fragment labeled lesion on the back / Sebaceous gland neoplasm with differential diagnosis between well-differentiated sebaceous gland carcinoma (low grade) and sebaceoma/ Free margins: smaller lateral margin: 0.2mm / Circumscribed dermal nodule non-infiltrative consisting of more than 50% basaloid cells mixed with mature sebocytes. There are frequent typical mitosis and visible nucleolus in areas/ Mixed inflammatory infiltrate with abscess and foreign body type reaction.

After the exeresis of the skin lesion and the result of the biopsy, the patient had his care directed to the Hinja Hospital in Volta Redonda. Currently, he is submitted to biannual control at the Coloproctology outpatient clinic of the hospital, since sebaceous gland neoplasms, especially when located outside the head and neck, can be skin markers for Muir-Torre Syndrome. Complying with the ethical precepts of Resolution 196/96 for research with human beings, the project was submitted

and approved by the Ethics and Research Committee of the Faculty of Medicine of Valença with the CAAE: 43521221.3.0000.5246.

3. DISCUSSION

The sebaceous glands are microscopic glands that are formed by a varied number of lobes, composed of two types of epithelial cells. The reserve epithelial cells, located in the gland's periphery, constituted by two layers of cuboid cells and sebaceous cells, in a maturation phase with sebocytes located in the central region of the gland[3,16].

Sebaceous carcinomas are rare neoplasms, with aggressive behavior, with several clinical presentations that usually make the diagnosis difficult, causing the treatment to be delayed and worsening the prognosis. They can appear in any race or gender, with a higher incidence in patients over 60 years of age[15].

Histologically, sebaceous carcinoma is characterized by the presence of 33 multilobulated, irregular, circumscribed neoplastic masses, composed of islands of epithelial cells, which are generally larger in size than the basaloid reserve cells. Neoplastic cells have intracytoplasmic lipid vacuoles, with large nuclei and prominent nucleoli, with moderate pleomorphism, with a presence of variable mitosis figure[12.]

Sebaceous carcinomas can be classified into two types: sebocytes and epitheliomatous[17]. Sebaceous sebocyte carcinomas are predominantly composed of mature sebocytes. Epitheliomatous sebaceous carcinomas are reserve cells, like sebaceous epitheliomas, which are neoplasms differentiated by the large amount of basaloid reserve cells in the sebaceous glands[18].

According to the literature[19,] the factors that predispose to the appearance of sebaceous carcinoma are unknown. However, some cases are associated with Muir-Torre Syndrome. Other authors[15] describe that some authors argue that the use of certain medications, such as thiazide diuretics, may also be related to the onset of the disease, however, they warn that there are no consistent studies in the literature to confirm this hypothesis.

The sebaceous glands, despite being present throughout the body, are more concentrated in the phase and in the neck. Most cases of sebaceous carcinoma described occur in the eyelid region, mainly in the Meibomius glands[4.]

In the early stages, differential diagnosis is not easy. There are few reports of sebaceous carcinoma described in the world literature, of which approximately 30% occur in the extraocular form, reaching the most varied locations, such as the external auditory canal, oral mucosa, scalp, vulva, ovarian cysts, uterine cervix, parotid, breast, lung, pharynx, in addition to the appearance of sebaceous carcinoma in previous dermatological lesions[8].

As the predisposing factors to the appearance of sebaceous carcinoma are not well known, some authors[12] emphasize an association between sebaceous gland tumors and visceral neoplasms, characteristic of Muir-Torre Syndrome, considered a variant of colorectal cancer not associated with polyposis. For this reason, the patient in the case reported is undergoing an observation process at the Coloproctology outpatient clinic of the Hinja hospital, in Volta Redonda.

Among the visceral neoplasms of Muir-Torre Syndrome, those that originate in the digestive tract, mainly in the colon, stand out. Authors8 describe that skin tumors can be sebaceous neoplasms, keratoacanthomas, basal or squamous cell carcinomas, the first two being the most frequent.

Studies13 point out that sebaceous gland tumors are rare in the general population, and when diagnosed, they should suggest the diagnosis of Muir-Torre Syndrome. These tumors are classified according to the types presented in Table 1.

Table 1. Classification and characteristics of tumors linked to Muir-Torre Syndrome.

Sebaceous adenoma – benign tumor most frequently associated with Muir-Torre Syndrome. It is characterized by the presence of sebaceous gland lobes, exhibiting basaloid cells in the periphery.
Sebaceous epithelioma – benign tumor characterized by the presence of small lobules of sebaceous glands surrounded by basaloid cells, presenting atypia.
Sebaceous carcinoma – malignant tumor characterized by the presence of irregular glandular lobules with several atypias and undifferentiated cells.
Sebaceous hyperplasia – benign tumors that, despite originating from the sebaceous glands, are not associated with an increased incidence of malignant visceral tumors or with other characteristics of Muir-Torre Syndrome.
Keratoacanthomas – are considered part of Muir-Torre Syndrome due to their high prevalence in these patients. The association of keratoacanthoma with sebaceous tumors can be explained by the fact that both are derived from pilosebaceous units.

Source: Adapted from Dasgupta; Wilson; Yu (2009)[13].

Thus, Muir-Torre Syndrome is characterized by the occurrence of at least one sebaceous neoplasm connected to the visceral neoplasm, without presenting predisposing factors. Sebaceous neoplasia can present itself before, during or after the diagnosis of colorectal cancer, and it can be considered as a subtype of hereditary non-polypoid colorectal cancer syndrome, which makes it important to evaluate family members[5].

Many types of visceral neoplasms can be associated with Muir-Torre Syndrome, however, as highlighted[9,11], they are neoplasms with a low degree of malignancy, with longer survival in these cases.

Muir-Tower Syndrome usually arises in families with a history of colorectal cancer, but not necessarily in a history of skin tumors. Therefore, a fundamental issue in diagnosing Muir-Torre syndrome is the correct identification of any family history of tumors[7]. For this reason, the patient in the case reported is under semiannual control at Hinja Hospital since his family has three cases of cancer history.

Authors[1] also describe that the most frequent internal neoplasm found in Muir-Torre Syndrome is

colorectal cancer, which, according to the authors, usually appears about 10 years earlier than in the general population. It is frequently followed by genitourinary neoplasms (20%), as well as hematological, head and neck or upper digestive tract neoplasms. They agree with other authors[9,11], when revealing that both internal and cutaneous neoplasms behave less aggressively when compared to those not associated with Muir-Torre Syndrome.

4. CONCLUSION

The present study verified, through a literature review, that the presence of multiple sebaceous gland tumors is the most frequent dermatological manifestation that most characterizes Muir-Torre Syndrome.

These are usually located in the head and neck and may precede, coexist, or appear after the diagnosis of internal neoplasia. Adenomas are the most common sebaceous tumors, however, hyperplasia, sebaceous cystic tumors, epitheliomas or carcinomas are also described. Keratoacanthomas grow rapidly and can be seen in approximately a quarter of patients with Muir-Torre Syndrome. The most common internal neoplasm found in Muir-Torre Syndrome is colorectal cancer.

In the case reported in this study, the patient had a sebaceous carcinoma on the back, and, as Muir-Torre Syndrome has not yet been diagnosed, he is being submitted to a control, with constant colonoscopies, to detect tumors and/or pre-malignant lesions (polyps) in early stages, for later removal, ensuring better survival.

This report is quite interesting due to its specificity, because when a sebaceous tumor is diagnosed, its association with Muir-Torre Syndrome should be sought. And doctors, in general, must have this knowledge.

The importance of the role of the dermatologist is also noteworthy, who, when encountering multiple or single tumor lesions, can develop studies that provide a diagnosis of a visceral neoplasm and risk associations, for the evaluation and treatment of patients who are in the early stages of the tumor.

It was found that although the clinical characteristics of these neoplasms are not very striking, which can lead to a diagnosis of little clinical relevance, it is essential that, when the lesion is removed, all parts are sent for a histopathological study for a diagnosis more accurate.

Thus, regular screening for neoplasms should be carried out in patients diagnosed with Muir-Torre Syndrome, as well as their first-degree relatives, emphasizing that everyone should receive genetic counseling.

Whenever possible, genetic analysis of visceral and skin tumors should be performed, as it will greatly facilitate the understanding of the disease. As seen throughout the article, the presence of sebaceous gland tumors alone justifies an investigation of visceral tumors, since, for example, in cases of adenomatous intestinal polyps, an early resection could prevent cancer in the future.

It is believed that new studies should be developed as this is a very current and interesting topic, with few cases reported in the world literature.

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