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CASE REPORT

Muir-Torre syndrome: case report

Síndrome de Muir-Torre: um relato de caso

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Abstract

Muir-Torre syndrome (MTS) is characterized by the association of at least one, but often multiple, sebaceous skin neoplasms, and at least one visceral neoplasm, usually colorectal. MTS should be suspected in the presence of multiple sebaceous tumors, particularly if they appear at an early age and are in extraocular areas. We report the case of a 52-year-old man with a personal history of sigmoid colon adenocarcinoma, referred to the Dermatology department, 8 years later, due to multiple facial sebaceous tumors. Considering the clinical presentation, as well as the personal and family history, MTS was suspected and later confirmed by genetic testing. Although rare, hereditary cancer predisposition syndromes remind us of the importance of patient's global approach, especially those with cancer, allowing the early detection of potential carriers and promoting the health of their relatives.

Keywords: Muir-Torre syndrome. Lynch syndrome. Sebaceous adenoma. Colorectal carcinoma.

Resumo

A síndrome de Muir-Torre (SMT) caracteriza-se pela associação de, pelo menos, uma neoplasia sebácea e de, pelo menos, uma neoplasia visceral, sendo a colorretal a mais comum. Assim, deve suspeitar-se de SMT na presença de vários tumores sebáceos, particularmente, se estes surgirem em idade precoce e se estiverem localizados em zonas extraoculares. Relata-se o caso de um homem de 52 anos, com história de adenocarcinoma da sigmoide, referenciado a consulta de Dermatologia, 8 anos depois, por múltiplos tumores sebáceos faciais. Tendo em conta o quadro clínico, bem como os antecedentes pessoais e familiares, colocou-se a hipótese diagnóstica de SMT, que se confirmou após estudo genético. Apesar de raras, as síndromes de predisposição hereditária para cancro relembram-nos a importância do enquadramento global dos doentes, principalmente os oncológicos, detetando precocemente potenciais portadores e promovendo a saúde dos seus familiares.

Palavras-chave: Síndrome de Muir-Torre. Síndrome de lynch. Adenoma sebáceo. Carcinoma colorretal.

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Introduction

Muir-Torre syndrome (MTS) is a rare syndrome, initially described by Muir in 1967 and subsequently by Torre in 1968. It is typically characterized by the synchronous or metachronous occurrence of at least one sebaceous skin neoplasm, typically an adenoma or carcinoma, and at least one visceral malignancy, most commonly colorectal. MTS is considered an autosomal-dominant phenotypic variant of Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome), caused by mutations in DNA mismatch repair genes and leading to microsatellite instability. The most frequently mutated genes in MTS include *MLH1*, *MSH2*, *MSH6*, and *PMS2*. However, some cases of MTS have been described without microsatellite instability but with biallelic inactivation of the *MUTYH* gene (mutY homolog), causing defects in base excision repair. This subtype of MTS is called MTS type 2, has an autosomal-recessive inheritance pattern, and accounts for approximately one-third of cases. Most reported cases are related to Caucasians, probably due to a lack of epidemiologic data from Asia and Africa. MTS is more common in males, with a male/female ratio of 3:2, and the mean age at diagnosis of the first cutaneous neoplasm is 53 years[1-3].

The authors intend, with this case report, to demonstrate the importance of early diagnosis and maintenance of a high level of suspicion in the presence of multiple skin tumors, associated or not with visceral neoplasia.

Case report

We present the case of a 52-year-old male, born in Brazil, married, with three healthy children. His medical history included asthma and poorly differentiated adenocarcinoma of the sigmoid colon (stage IIIB, T3N2M0) diagnosed in 2015. For that, he underwent segmental resection of the sigmoid colon and lymphadenectomy followed by adjuvant chemotherapy. He denied taking any regular medications and had no known drug allergies. Family history is notable for a maternal grandmother and aunt with colorectal cancer diagnosed before the age of 50. Additionally, the patient's mother had liver and skin neoplasms diagnosed at the age of 68, although the specific types are unknown.

The patient presented to his primary care physician with multiple yellowish papules, spread across the face (Fig. 1), which had been evolving for several years. In Brazil, he periodically received surgical treatment or CO_2 laser therapy for these lesions. In this context, after referral to a Dermatology hospital consultation, four of these lesions were biopsied, as they were ulcerated or becoming large, concluding that they were adenomas and sebaceous hyperplasia. A nodule, mainly subcutaneous, with a violet surface and hard consistency, was also detected in the left lumbar region (Fig. 2), which, after excision and histopathological examination, revealed a keratoacanthoma. Based on the histological findings and the patient's personal history of colorectal cancer, a diagnosis of MTS was suspected. This diagnosis was subsequently confirmed by genetic testing, which revealed a large heterozygous deletion involving exons 17-19 of the *MLH1* gene.

Despite being aware of the high number of cases of neoplasia in the family, for the first time, the patient was referred to a hospital consultation for family risk of cancer, also to study this syndrome and to screen his relatives for cancer.

Discussion

Sebaceous adenomas are the most common cutaneous tumors found in MTS and are considered the most specific marker of the disease, occurring in approximately 68% of cases. They typically present as multiple yellowish or skin-colored papules, less than 0.5 cm in diameter, scattered on the trunk, face, and scalp. Other sebaceous tumors include sebaceous epithelioma, sebaceous carcinoma, and keratoacanthoma. These tumors tend to occur at a younger age than their sporadic counterparts and may precede, occur simultaneously or follow the diagnosis of visceral malignancy[2,4]. Other muco-cutaneous findings sometimes also present in MTS are Fordyce spots (ectopic sebaceous glands) on the vestibular oral mucosa[5].

Colorectal adenocarcinoma represents more than half of all cases of visceral neoplasms associated with MTS and tends to occur proximally, unlike sporadic neoplasms. Other reported neoplasm includes urogenital neoplasia (present in approximately 25% of cases), endometrial, ovarian, urothelial, and kidney. Other cancers that are linked to MTS include those of prostate, pancreas, breast, brain, lung, gastric, small intestine, and hematological cancers[2,6,7].

Therefore, the diagnosis of MTS should be suspected in the presence of multiple sebaceous tumors, particularly if they appear at an early age and are located outside the head and neck area, especially the trunk[2,3,8]. A detailed clinical history, particularly oncologic, must be collected. As a support tool, there is the Mayo risk score, which includes the following

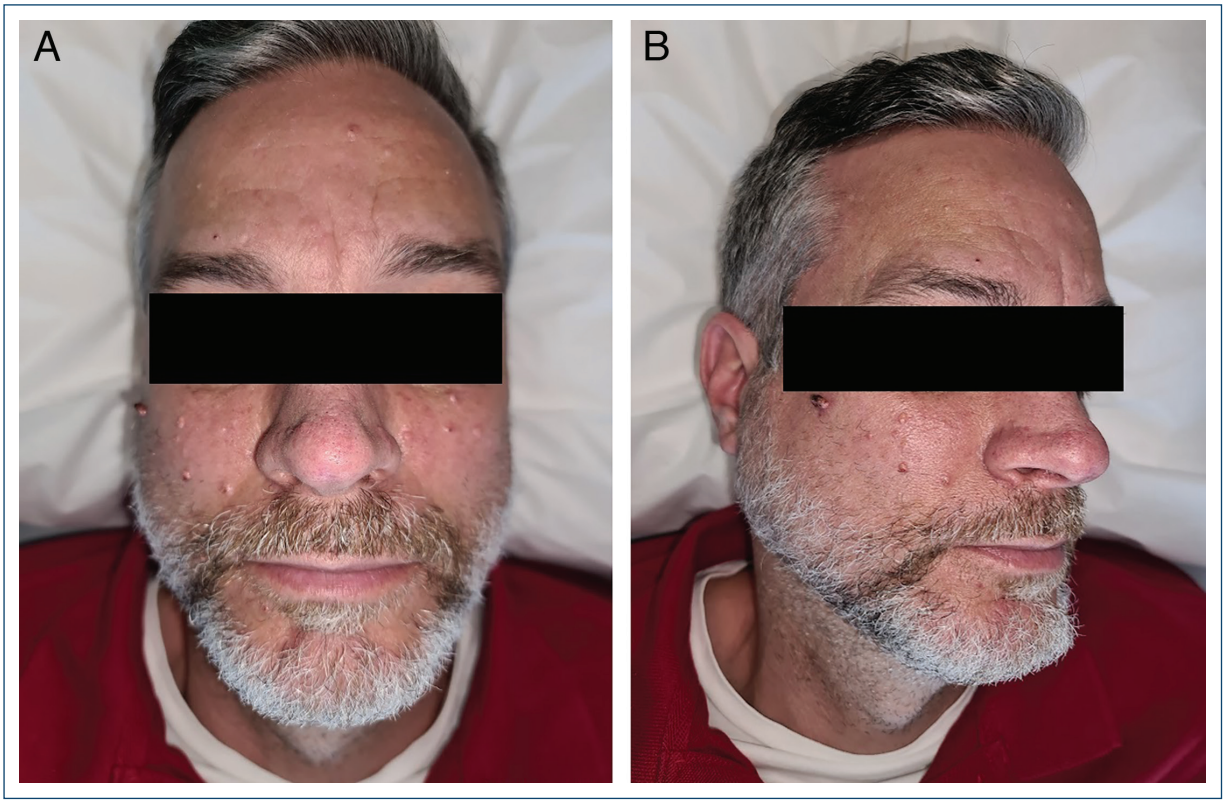

Figure 1. A-B: multiple yellowish papules spread across the face.

criteria: age less than 60 years (1 point), number of sebaceous tumors (2 points), personal history (1 point), and family history (1 point) of any Lynch-related cancers. Any patient with a total of two or more points has a high risk of having MTS and, therefore, should undergo genetic testing for germline variants screening of the *MLH1*, *MSH2*, *MSH6*, and *PMS2* genes[8,9].

This strategy was challenged by some experts due to the risk of not detecting patients with a single sebaceous neoplasm and unknown family history. Therefore, it is reasonable to consider that young patients, with only one extraocular sebaceous tumour and suspected MTS, who do not meet the Mayo risk criteria, also undergo immunohistochemical tests to detect mismatch proteins in sebaceous tumors[8,10].

Regarding cancer screening in people with MTS and their first-degree relatives, annual full-body skin examination, starting at late teens/early twenties, is recommended. Colonoscopy surveillance is recommended starting at age 25 years for *MLH1* and *MSH2*-mutation carriers, and at age 35 years for MSH6 and PMS2-mutation carriers; colonoscopy should be performed every 2–3 years, unless they have had colorectal cancer before, after which biennial colonoscopy is recommended. Upper gastrointestinal endoscopy should be considered in patients with a positive family history of gastric cancer, and Helicobacter pylori eradication is recommended in mutation carriers. Female patients should receive annual surveillance for breast, endometrial, and ovarian cancers. Therefore, annual mammography, pelvic examination, transvaginal ultrasounds, and endometrial biopsies are warranted, starting between the ages of 30 and 35. As for male patients, prostate and testicular cancer laboratory testing is also recommended. In addition, annual urinalysis and cytologic examination are recommended starting at age 30–35 years for testing for renal and genitourinary cancers. Prophylactic surgeries may be considered in high-risk individuals to reduce the cancer burden. Prophylactic colectomy should be considered in patients above 25 years with gene mutation, and prophylactic hysterectomy and bilateral salpingo-oophorectomy may be considered after childbearing is complete or at age 40[11–15].

Although rare, it is important to adopt a low threshold of suspicion for this syndrome to allow for early diagnosis and a multidisciplinary approach for appropriate treatment and follow-up, reducing patient morbidity and mortality.

Figure 2. Violet nodule with a hard consistency, in the left lumbar region, whose histopathologic examination revealed a keratoacanthoma.

Documenting cases of genetic familial cancer syndromes makes it possible to adapt the follow-up of index patients, while also having important consequences for their relatives. All doctors involved in the care of these patients and their relatives must be included.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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