An atypical finding of Muir-Torre syndrome: A case report

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ABSTRACT

Background: Muir-Torre syndrome (MTS) is an infrequent autosomal-dominant genodermatosis characterized by the presence of sebaceous tumors and visceral malignancies. These tumors typically manifest as sebaceous adenomas, epitheliomas, or carcinomas. Colorectal cancer is the most prevalent internal malignancy linked with MTS. The syndrome stems from germline mutations in the DNA mismatch repair (MMR) genes hMSH2 and hMLH1, aligning it with Lynch syndrome, also recognized as hereditary nonpolyposis colorectal cancer. Lynch syndrome involves inherited deficiencies in DNA MMR genes, resulting in microsatellite instability.

Case Presentation: We describe the case of a 54-year-old man diagnosed with sebaceous adenomas. Given his family's history of colorectal cancer, genetic screening for Hmsh2 genes was recommended. Molecular gene sequencing revealed two heterozygous deletion mutations in exon 7 and 9 of the Hmsh2 gene in the patient.

Conclusion: This case underscores the significance of a multidisciplinary care approach, comprehensive medical history assessment, and timely identification of high-risk individuals. Such measures facilitate appropriate screening and surveillance, thereby mitigating the morbidity and mortality associated with this syndrome.

Keywords: Muir-Torre, gastroenterology, lynch syndrome, sebaceous adenomas.

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Background

Muir-Torre syndrome (MTS) is an infrequent disease that is clinically defined by the co-occurrence of sebaceous glands and internal malignancies. The disease has a propensity to affect more males than females with an estimated ratio of 3:2. The median age of onset of the disease is 53 [1]. It is an autosomal dominant disease that is considered to be a phenotypic variant of Lynch syndrome also known as hereditary nonpolyposis colorectal cancer (HNPCC) due to their similar pathogenic mechanisms. MTS is seen in less than 10% of patients with HNPCC [1]. The mechanism behind these diseases is characterized by inherited defects in DNA mismatch repair (MMR) genes that result in microsatellite instability (MSI) and consequently lead to the accumulation of errors in the genome and the development of cancer [2]. The set of MMR genes encompasses MSH1, MLH1, hMSH2, PMS2, and MSH6. These genes are responsible for preserving genomic integrity and rectifying base mismatches throughout DNA replication. Of these genes, hMSH2 is the most involved in MTS [3].

The cutaneous neoplasms reported in MTS include the presence of sebaceous adenomas, sebaceous epitheliomas, sebaceous carcinomas, and keratoacanthomas. Sebaceous adenomas are the most common among these tumors [1]. Early recognition of sebaceous adenomas is clinically important, as these rare tumors often serve as the first visible indicator of an underlying hereditary cancer syndrome. Prompt identification can lead to earlier cancer surveillance and intervention, significantly reducing the risk of advanced malignancy. Colorectal carcinomas are the most common internal malignancies found in MTS. Patients with even a single sebaceous malignancy should be prompted for a thorough history of cancer and undergo genetic testing [4]. Patients with MTS require a multidisciplinary care approach and timely identification for appropriate screening and surveillance for the reduction of morbidity and mortality of this disease.

Case Presentation

We present a case of a 54-year-old male who was referred to the oncology clinic from the dermatologist's office a few weeks after a biopsy confirmed the diagnosis of a

sebaceous adenoma in the patient's right shoulder. The patient's past medical history is significant for hypertension, hypercholesterolemia, and pre-diabetes all controlled with medication. Social history is significant for smoking.

A review of the patient's family history revealed that his father died of colorectal cancer at the age of 42, placing the patient in a high-risk category for colorectal malignancies. In the context of a rare sebaceous adenoma, which is often the first and sometimes only external indication of an underlying MMR defect and a suggestive family history, the clinical suspicion for MTS was high, warranting further investigation into the condition. As a result, the patient was referred for genetic evaluation, with specific testing of the hMSH2 gene, the most commonly implicated gene in MTS. Molecular genetic sequencing revealed two heterozygous deletion mutations in exons 7 and 9 of the hMSH2 gene (Table 1), confirming the diagnosis of MTS.

The patient was referred for genetic counseling. He was informed about his condition and his increased risk of developing cancer. His sibling was also referred for genetic testing and was found to be a carrier of the same mutation; however, the sibling does not currently present with any cutaneous or visceral findings. A surveillance plan was discussed. The plan includes series of colonoscopies every 5 years for the patient and yearly skin exams. As for the patient's sibling only routine, colonoscopies every 5 years were suggested due to her carrier state and the absence of any pathologic findings.

Discussion

MTS is a rare condition related to HNPCC, that is associated with mutations in the DNA MMR genes, particularly hMSH2 which leads to MSI. MTS is characterized by the presence of at least one sebaceous malignancy (e.g., sebaceous adenoma, sebaceous carcinoma, keratoacanthoma, and/or epithelioma) with at least one visceral malignancy (e.g., colorectal, genitourinary, lung, ovarian, endometrial, parotid, gastric, breast, small intestinal, and hematological) that occur early in life [5]. When patients present with sebaceous tumors, genetic testing for MMR proteins and MSI is recommended. Reported incidences indicate a higher prevalence in males than in females, with an average age of malignancy onset at 53 years [6]. Of the skin lesions in MTS, greater than 50% occur after the diagnosis of visceral malignancy, about 6% occur synchronously, and around 20% of skin tumors occur as the first lesion. The cutaneous lesions may occur more than 20 years before or after the visceral malignancy; multiple visceral malignancies can occur at the same time as well [3].

The group of MMR genes includes MSH1, MLH1, MSH2, PMS2, and MSH6, which have the task of maintaining genomic integrity and repairing base mismatches during the process of DNA replication [3]. Alteration in said genes leads to a buildup of replication errors, specifically in microsatellite regions, which are short repetitive segments of DNA bases that are prone to mismatch errors. Pathogenesis of MTS is directed towards germline mutations in MMR genes, where the MSH2 gene is most affected, as was in this patient, and leads to MSI. MTS is related to HNPCC Syndrome due to the similar pathogenesis of MMR genes and MSI [3,7]. In addition, MTS is inherited in 59% of the cases and may remain latent for a long period, potentially being triggered by immune suppression, radiotherapy, and/or ultraviolet radiation [8,9].

The most seen skin malignancies in MTS are sebaceous adenomas, which were the presenting lesions in this patient, and keratoacanthomas [5,9]. The area that is most involved is the trunk, but lesions may also appear on the face, involving the orbital area. As sebaceous adenomas are characteristic of MTS, a person with a score of >2 in the MTS scoring system (Table 2) requires genetic testing to confirm the diagnosis [11]. Also seen in MTS are ectopic sebaceous glands that can manifest as yellowish macular/papular lesions on the buccal mucosa, which are called Fordyce granules [3]. Regarding visceral malignancies, the most commonly seen is colorectal cancer (most commonly in the proximal colon), followed by genitourinary malignancies such as gynecological and urological cancers. MTS may also cause upper gastrointestinal tract and breast malignancies.

Close follow-up for cancer screening and genetic counseling for risk identification is very important in these cases, as it is widely reported to affect multiple family members [7,12]. Screening must include

Table 1. *Gene sequence/analysis results showing heterozygous deletion mutation in exons 7 and 9.*

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
MSH2	Deletion (Exon 7)	Heterozygous	Pathogenic
MSH2	Deletion (Exon 9)	Heterozygous	Pathogenic
EGFR	c.2996G>A (p.Arg999His)	Heterozygous	Uncertain significance

Table 2. *Mayo MTS risk score.*

CRITERIA	SCORE
Age <60 at first presentation of sebaceous tumors	1
Two or more sebaceous tumors	2
Personal history of any Lynch-related cancers	1
Family history of any Lynch-related cancers	1

routine endoscopy/colonoscopy, breast and pelvic examinations, urinalysis with cytology, routine laboratory testing, ultrasonography, and dermatological consultation beginning between 20 and 25 years of age [10]. Treatment is tailored based on the underlying defects and associated malignancies. A function-sparing strategy improves quality of life and supports long-term follow-up. Regarding the sebaceous/cutaneous lesions, wide local excision with 5–6 mm margins remains the mainstay of treatment; with fine-needle aspiration performed for any suspicious lymph nodes, followed by regional lymphadenectomy for confirmed nodal metastases. The role of radiotherapy in the treatment of sebaceous carcinoma is mainly palliative and should be reserved for metastatic disease [13,14].

Limitations

This case report is limited by its focus on a single patient, which restricts the generalizability of its findings. As with all case reports, there is an inherent risk of selection and reporting bias, and broader conclusions regarding screening, management, or prognosis should be interpreted with caution. Further studies involving larger cohorts are necessary to validate these observations.

Conclusion

This case highlights the importance of recognizing sebaceous adenomas as potential cutaneous markers of MTS, particularly in individuals with a family history of Lynch-associated cancers. It adds to the existing literature by demonstrating that even a single, isolated sebaceous adenoma can serve as a critical clue prompting genetic evaluation for MTS, even in the absence of visceral malignancies. Furthermore, the identification of pathogenic *MSH2* mutations in both the patient and an asymptomatic first-degree relative underscores the broader familial implications and the importance of cascade testing. A multidisciplinary approach and lifelong surveillance are essential to reducing the morbidity and mortality associated with this hereditary cancer syndrome.

What is new?

Muir-Torre is a rare subtype of Lynch syndrome that presents as a combination of dermatologic manifestations and colon cancer. The patient in this report was diagnosed based on his skin lesions alone. He had no other symptoms and past colonoscopy was negative for any sign of malignancy. The authors aim to present a case of an unusual condition and how it may manifest as simple skin findings, also aim to emphasize the importance of multidisciplinary care among various specialties in the field of medicine.

List of Abbreviations

HNPCC	hereditary nonpolyposis colorectal cancer
MSI	microsatellite instability
MMR	mismatch repair
MTS	Muir-Torre syndrome

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Written informed consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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References

1. Gay JT, Troxell T, Gross GP. Muir-Torre syndrome. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [Updated 2023 Jul 3].
2. Abbas O, Mahalingam M. Cutaneous sebaceous neoplasms as markers of Muir-Torre syndrome: a diagnostic algorithm. J Cutan Pathol. 2009;36(6):613–9. https://doi.org/10.1111/j.1600-0560.2009.01248.x
3. Pancholi A, Collins D, Lindley R, Gandhi P. Muir-Torre syndrome: a case report and screening recommendations. Ann R Coll Surg Engl. 2008;90(8):W9–10. https://doi.org/10.1308/147870808X360387
4. Boennelycke M, Thomsen BM, Holck S. Sebaceous neoplasms and the immunoprofile of mismatch-repair proteins as a screening target for syndromic cases. Pathol Res Pract. 2015;211(1):78–82. https://doi.org/10.1016/j.prp.2014.10.002
5. Sheth R, Menon P, Malik D. A case of Muir-Torre syndrome. Cureus. 2021;13(4):e14582. https://doi.org/10.7759/cureus.14582
6. Bhaijee F, Brown AS. Muir-Torre syndrome. Arch Pathol Lab Med. 2014;138(12):1685–9. https://doi.org/10.5858/arpa.2013-0301-RS
7. Kientz C, Joly MO, Faivre L, Clemenson A, Dalac S, Lepage C, et al. A case report of Muir-Torre syndrome in a woman with breast cancer and MSI-Low skin squamous cell carcinoma. Hered Cancer Clin Pract. 2017;15(1):6. https://doi.org/10.1186/s13053-017-0066-9
8. Prieto VG. PhD. Muir-Torre syndrome: background, pathophysiology, etiology. Available from: https://emedicine.medscape.com/article/1093640-overview (Acccessed December 20, 2023).
9. Sugi T, Shimomura O, Hashimoto S, Takahashi K, Doi M, Miyazaki Y, et al. Well-concealed advanced duodenal carcinoma with Muir-Torre syndrome: a case report and review of literature. Surg Case Rep. 2023;9(1):24. https://doi.org/10.1186/s40792-023-01603-0

10. Babu J, Balakrishnan S. Muir-Torre syndrome - An Indian case report. Int J Mol Immuno Oncol. 2021;6(2):93–6.
11. Bagga E, Innes D, Leung E. Looking beyond the surface: Muir Torre syndrome. Arch Clin Cases. 2023;10(3):119–22. https://doi.org/10.22551/2023.40.1003.10255
12. Torre K, Ricketts J, Dadras SS. Muir-Torre syndrome: a case report in a woman without personal cancer history. Am J Dermatopathol. 2019;41(1):55–9. https://doi.org/10.1097/DAD.0000000000001210
13. Shaker N, Shaker N, Abid A, Shah S, Shakra RA, Sangueza OP. Muir-Torre syndrome and recent updates on screening guidelines: the link between colorectal tumors and sebaceous adenomas in unusual locations. J Surg Oncol. 2023;128(8):1380–4. https://doi.org/10.1002/jso.27440
14. Ávila LV, Saeb LM. Muir-Torre syndrome with loss of expression MSH2 and MSH6: a case report. Dermatol Cosmet Med Quir. 2021;19(1):24–7.

Summary of case

1	Patient (gender, age)	54 years old, Male
2	Final diagnosis	Muir-Torre syndrome
3	Symptoms	Sebaceous adenomas
4	Medications	None
5	Clinical procedure	Genetic testing
6	Specialty	Gastroenterology