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Oral Squamous Cell Carcinoma in a Patient with Myelodysplastic Syndrome: Report of a Case and Literature Review

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A B S T R A C T

Myelodysplastic syndrome (MDS) is a bone marrow clonal stem cell disorder characterized by the inability of immature blood cells to mature. Oral squamous cell carcinoma (OSCC) has not been previously reported in MDS patients without underlying diseases. We present a case of poorly differentiated OSCC in a 27-year-old patient with MDS. A literature review revealed 11 case reports about solid tumors in different organs of MDS patients. Among these, 5 articles reported head and neck carcinoma but none of them reported oral cancer in MDS patients. MDS predisposes patients to hematopoietic and non-hematopoietic malignancies. The oral cavity is one of the critical sites that needs to be examined periodically and regularly in MDS patients to detect OSCC in its early stages.

Keywords: Myelodysplastic Syndromes; Squamous Cell Carcinoma of Head and Neck; Primary Immunodeficiency Diseases

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INTRODUCTION

Myelodysplastic syndrome (MDS) is a bone marrow clonal stem cell disorder characterized by the inability of immature blood cells to mature. The characteristic feature of this syndrome is ineffective hemopoiesis, which results in variable blood cytopenias and acute myeloid leukemia in one-third of patients [1]. MDS is generally more common in older individuals with a mean age of 65-70 years, and less than 10% of MDS cases have been reported in patients under 50 years. A male predominance has been reported with the exception of the form with isolated 5q chromosomal deletion [2]. MDS is traditionally classified as primary and secondary. Primary MDS is an inherited defect in DNA repair or hematopoiesis that predisposes the patients to acute myeloid leukemia (AML)/MDS. Secondary MDS can be a late consequence of exposure to benzene or its derivatives, smoking, radiation therapy, or treatment with alkylating agents and purine analogs. Sustained complex cytogenic findings after chemotherapy generally result in a poor prognosis of secondary MDS [3].

Management, from symptomatic treatment to allogeneic stem-cell transplantation with different outcomes, is challenging [2]. The risk of death in MDS arises from direct related complications (AML, infection, bleeding) or indirect related complications, including cardiac failure and solid tumors [4]. Few studies have reported solid tumors in MDS patients, mostly squamous cell carcinoma (SCC) and adenocarcinoma of the lungs, prostate, gastrointestinal system, kidneys, or pharynx [5-7]. Underling genetic disorders in MDS patients probably influence the type of solid tumor. Gastrointestinal carcinoma and osteogenic sarcoma are common in Diamond-Blackfan anemia [8]. The head and neck squamous cell carcinoma (HNSCC) has a 400 to 500 times higher prevalence in patients with Fanconi anemia [9].

HNSCC can derive from the oropharyngeal and laryngeal epithelium. HNSCC is the sixth most prevalent cancer worldwide, and its incidence is on the rise. Although over the past three decades, the survival rate of HNSCC has increased, its 5-year survival reached 66% from 2002 to 2006 [10]. Oral squamous cell carcinoma (OSCC) has not been previously reported in MDS patients without any other underlying genetic disease. This study reported a case of MDS who simultaneously developed OSCC on the floor of the mouth.

CASE PRESENTATION

A 27-year-old female was admitted in July 2022, complaining of a sublingual ulcer. The progressive ulcer was first appeared 5 months earlier and then became painful recently. She was suffering from dysphagia. Her MDS had been diagnosed by an oncologist back in 2018, and the patient underwent chemotherapy. Bone marrow biopsy was performed showing bone trabeculae and marrow spaces with interstitial hemorrhage and significant artificial cell loss and about 10-15% cellularity in best-preserved areas composed of a polymorphic population of hematopoietic elements with interstitial hemorrhage. Megakaryocytes had been seen as well. CD34 marker was positive in 2-3% of all nucleated marrow cells, and the TdT marker was negative, suggesting markedly hypocellular marrow. Bone marrow aspiration and touch imprint with semidiluted smear revealed the differential count as: blasts 2%, promyelocytes 7%, myelocytes 8%, metamyelocytes 4%, band cells 3%, segmented neutrophils 8%, lymphocytes 10%, erythroid precursors 51%, eosinophilic precursors 2%, and plasma cells 5%. Megaloblastic changes, orderly myeloid maturation, and megakaryocytes with normal count and morphology were seen. Peripheral blood smear of good quality showed the following differential count: segmented neutrophils 19%, band cells 2%, monocytes 5%, lymphocytes 72%, eosinophils 1%, and basophils 1%. Red blood cell (RBC) morphology revealed mild anisopoikilocytosis and hypochromia. Platelets were adequate. The patient underwent chemotherapy. In June 2022, she was on the waiting list for bone marrow transplantation. No other disease was diagnosed. Her hematology profile revealed the following results: white blood cells=1.5/1000/mm^3, hemoglobin=10.8gr/dL, RBC=3.51mil/mm^3, hematocrit= 33.8%, mean corpuscular volume= 96.3fl, mean corpuscular hemoglobin=30.8pg, mean corpuscular hemoglobin concentration=32g/dL, RBC distribution width-coefficient of variation=17.2%, platelets=249 /1000/mm^3, slight anisocytosis, slight macrocyte, positive (++) poikilocyte, and Rouleaux formation. She had no history of familial disease. Cytogenetic examination of her bone marrow specimen reported 47, XX,+8, del(11)(q23), der(12)t(1;12)(q21;p13)[16]/47, sl, add(10)(q26)[2]. Twenty metaphase cells displayed abnormalities in three related clones. The first clone (16 cells) revealed a gain of chromosome 8, deletion of the long arm of chromosome 11, and a derivative of chromosome 12 with a translocation between the long arm of chromosome 1 and the short arm of chromosome 12. The second clone (2 cells) showed the same abnormalities of the stemline except for the loss of chromosome 8 but with a gain of one marker chromosome. The third clone (2 cells) showed the same abnormalities of the stemline plus an addition

to the long arm of chromosome 10. The result was consistent with disease persistence. Complex karyotype (>3 abnormalities) indicated tumor progression and poor prognosis in AML and MDS patients.

Clinical examination revealed a crater-like large ulcer with rolled borders in the floor of the mouth from the distal of the left first molar to the left central incisor and across the midline to the right side of the floor. Also, the free gingiva of the first molar and premolars was involved. The ulcer was indurated on palpation. The texture of the ulcer was non-homogenous with granular and nodular appearance, and was covered with a fibrinoleukocytic membrane in some parts (Fig. 1).

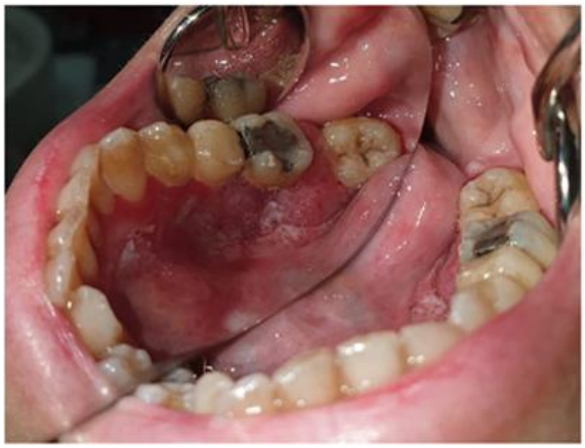

Fig 1. Clinical view. The ulcer with a granular and nodular appearance on the floor of the mouth.

The necrotic bone around the lower left first molar and exposed root were evident, and the tooth was mobile. All the teeth of the left lower quadrant of the jaw were sensitive to percussion. The left side of the tongue had an erosive and atrophic red plaque with irregular, diffuse borders. Generalized gingival edema had a linear erythematous appearance. The submandibular lymph nodes were enlarged, fixed, hard, and non-tender on palpation. Radiographic evaluation showed a unilocular radiolucent lesion without defined borders from the mesial of the third molar to the mesial of the second premolar of the lower left side. The intraosseous lesion involved the alveolar crest and extended to apical third of the root of second premolar and first molar. Lamina dura was not entirely present. The inferior alveolar nerve canal was intact. No root resorption was evident (Fig. 2). A soft tissue incisional biopsy was performed on the anterior border of the lesion.

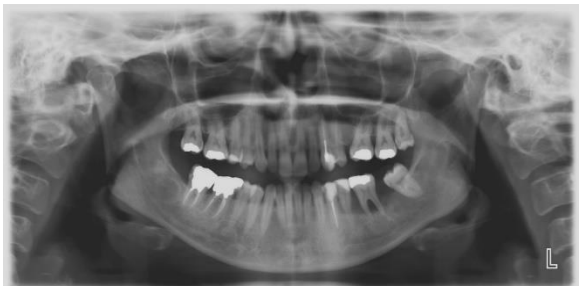

Fig 2. Panoramic view of the patient with radiolucent lesions

Microscopic examination (Fig. 3) showed a malignant epithelial neoplasm composed of dysplastic epithelial cells in the form of sheets, islands, small nests, and single cells invading the underlying connective tissue.

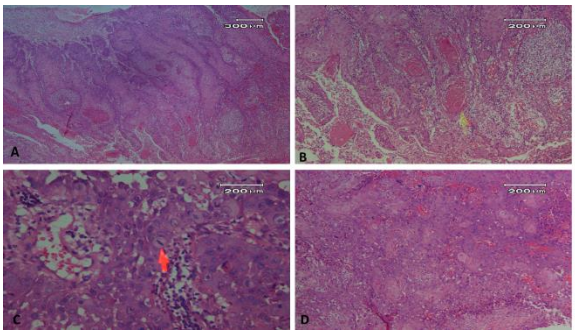

Fig 3. Microscopic view. (A) Sheets of dysplastic epithelial cells invading the underlying connective tissue (x40 magnification). (B) Keratin pearl formation in tumoral cells, yellow arrow (x100 magnification). (C) Nuclear pleomorphism and hyperchromatism in tumoral cells, red arrow (x400 magnification). (D) Sheets of epithelial cells with focal areas of dyskeratosis (x100 magnification) (H &E staining)

The tumoral cells demonstrated nuclear pleomorphism, hyperchromatic nuclei, increased nuclear/cytoplasmic ratio, atypical mitotic figures, and few keratin pearl formations. Severe mixed inflammatory cell infiltration was noted in the stroma. Extensive areas of hemorrhage were also evident. Lymphovascular or perineural invasion was not present in the specimen. The

definitive diagnosis was poorly differentiated SCC. The lesion was graded using the WHO grading system, which grades SCCs into three categories based on the degree of cell differentiation: well, moderately, and poorly differentiated tumors [11]. The patient was referred to a maxillofacial surgeon for a more extensive surgery. A positron emission tomography scan was performed, detecting no metastasis outside of the head and neck region. Tumor resection and neck dissection were performed in July 2022. Expected severe dysphagia led to a peg tube insertion before surgery. Unfortunately, despite all the extensive care, the patient expired about one week after surgery due to severe pancytopenia and peg tube infection that spread to the abdominal space.

Written informed consent was obtained from the family of the deceased patient for publication of her medical information.

DISCUSSION

The present study reported a young woman with MDS who simultaneously had OSCC on her floor of the mouth. Absence of other underlying genetic diseases and environmental predisposing factors such as radiotherapy or exposure to benzene, and age and sex of the affected person made this case of great interest. Although some studies have reported carcinoma of the oropharynx, esophagus, kidneys, lungs, and prostate in patients with MDS (Table 1), to the best of our current knowledge, it appears that to date, there has been no report of the occurrence of SCC in the oral cavity of a patient with MDS without an underlying disease, especially Fanconi anemia. This report shows the importance of considering life-threatening complications in MDS patients. SCC is a multifactorial cancer, and environmental and genetic factors play a role in its development. Smokeless and smoking tobacco, alcohol, and X-rays are among the known environmental risk factors for development of SCC [12]. The higher incidence of various neoplasms in patients with primary and even secondary immunodeficiency confirms the concept of immune surveillance, supporting the role of immunodeficiency in the occurrence of malignancy [13]. A higher frequency of lip and skin SCC has been reported in sun-exposed immunocompromised patients [14]. The most prominent immunologic change associated with head and neck cancer is a defect in cell-mediated immune responses that are not a feature in other carcinomas. Since immunodeficiency remains even after surgical treatment of the head and neck tumors, this is probably the primary cause, and factors such as alcohol, smoking, radiotherapy, chemotherapy, and malnutrition may also aggravate immunodeficiency [13]. Marked immunodeficiency is one of the hallmarks of MDS, which can affect the co-occurrence of solid tumors, including OSCC, with an unusual (unconventional) epidemiological pattern [15], as in the present case, OSCC occurred in a young woman with no history of smoking or alcohol consumption. In addition to immunodeficiency, prevalent chromosomal breakpoints could explain the co-occurrence of MDS and OSCC. HNSCC shows complex chromosomal rearrangements.

Table 1. Characteristics of reviewed studies that reported solid tumors in MDS patients

Author, year	Location of solid tumor	Age (Sex)	Type of tumor	Survival	Management	Associated medical history
Iwahara, 1993 [20]	1. Left auditory meatus 2. Sigmoid colon 3. Tonsil	33 (M)	1. Well-differentiated SCC 2. Moderately differentiated adeno-carcinoma 3. Poorly differentiated SCC	5 years	1. Radiation therapy 2. Resection 3. Palliative with morphine sulfate	Bloom's Syndrome

Table 1 Cont'd

Arai, 1999 [21]	Lung	59 (M)	Non-small-cell lung cancer	4 years	Surgery	Four years after the surgical removal of lung cancer, developed MDS
Otsuka, 2005 [5]	1. Esophagus 2. Lung	50 (M)	1. Moderately differentiated SCC 2. Small cell lung cancer	8 months	1. Surgery + chemotherapy 2. Chemo-radiation	Secondary MDS to chemo-radiotherapy
Mukherjee, 2014 [6]	Prostate	31 P 79 (64–99) (M)	Prostate adeno-carcinoma	10-year survival rate: 78.9%	Prostatectomy+ radiotherapy	Secondary MDS to radiotherapy
Kamihara, 2015 [22]	Esophageal and oro-pharyngeal	80 (M)	Esophageal and oropharyngeal carcinoma	8 months	Chemo-radiotherapy	secondary MDS to chemo-radiotherapy
Vlachos, 2016 [8]	Gastro-intestinal track	23 solid tumors, 8 MDS	Gastro-intestinal carcinomas	23% had died	HSCT	Diamond Blackfan anemia
Wang, 2016 [23]	Prostate	122 (M)	Prostate cancer	-	Surgery and radiotherapy for prostate cancer	Secondary MDS to Radiotherapy
Shenoy, 2018 [24]	Kidney	37 P (37-86) (M/F: 4.4/1)	Renal cell carcinoma	78% (29P) Dead 22% (8P) SUP	Nephrectomy	-
Liu, 2020 [25]	Esophagus	51 (M)	Esophageal SCC	20 days	therapeutic intervention was refused	Primary (coincides)
Feng, 2021 [26]	Lung / Bone	66 (M)	Non-small cell lung cancer (adeno-carcinoma) and bone metastases	The progression-free survival was 4 months.	Chemotherapy	Secondary to occupational exposures
Imamura, 2021 [27]	Esophagus	68 (M)	Esophageal SCC	SUP	Esophagostomy	Primary (coincidence)

SCC: Squamous cell carcinoma, M: Male, F: Female, MDS: Myelodysplastic syndrome, P: Patients, HSCT: Hematopoietic stem cell transplantation, SUP: Survived until publication.

The molecular mechanisms of HNSCC are still unknown. Prevalent chromosomal changes in OSCC are, for example, deletions, translocations, and isochromosomes. It appears that genomic instability following chromosomal breakage events in HNSCC is not random, and involves specific chromosomes more than others [15, 16].

The karyotype of our patient showed gain on chromosome 8, deletion on chromosome 11, a translocation between chromosomes 1 and 12, loss of chromosome 8, a gain of a marker chromosome, and insertion on chromosome 10, similar to chromosomal changes in HNSCC. Genetic abnormality in the long or short arms of chromosome 8 has been implicated in the

development and poorer prognosis of HNSCC and OSCC [12, 17]. In a cohort study of 104 HNSCC patients, a genetic aberration in chromosomes 12, 8, and 11 was found in most of the patients. Also, the highest number of breakpoints was detected in chromosome 8 after chromosomes 6 and 14. OSCC patients with a genetic change in 11q had a poorer prognosis in a previous study [17]. Gawas et al, [18] in an in vivo and in vitro animal study proved the occurrence of t (1;12) in one of the OSCC lines from the buccal mucosa of a 70-year-old woman. In addition, genetic aberrations in chromosome 10 seem to play a substantial role in OSCC oncogenesis [15, 19]. Finally, we can say that neglecting and postponing periodic and regular oral examinations in MDS patients can lead to a late diagnosis of OSCC. Due to the low health level, immune disorder, and general weakness of MDS patients, they will have a poorer prognosis. In addition, the karyotyping and gene sequencing techniques can provide more information about the etiopathogenesis of concomitant diseases with similar genetic aberration and more effective diagnosis and treatment.

CONCLUSION

MDS predisposes patients to hematopoietic and non-hematopoietic malignancies. The oral cavity is one of the critical sites that needs to be examined periodically and regularly in MDS patients to detect OSCC in its early stages.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Tefferi A, Vardiman JW. Myelodysplastic syndromes. N Engl J Med. 2009 Nov 5;361(19):1872-85.
2. Steensma DP, Bennett JM. The myelodysplastic syndromes: diagnosis and treatment. Mayo Clin Proc. 2006 Jan;81(1):104-30.
3. Adès L, Itzykson R, Fenaux P. Myelodysplastic syndromes. Lancet. 2014 Jun 28;383(9936):2239-52.
4. Bersanelli M, Travaglino E, Meggendorfer M, Matteuzzi T, Sala C, Mosca E, et al. Classification and Personalized Prognostic Assessment on the Basis of Clinical and Genomic Features in Myelodysplastic Syndromes. J Clin Oncol. 2021 Apr 10;39(11):1223 .
5. Otsuka Y, Konishi T, Nara S, Furushima K, Nakajima K, Shimada H. Secondary myelodysplastic syndrome after small cell lung cancer and esophageal cancer. J Gastroenterol Hepatol. 2005 Sep;20(9):1318-21.
6. Mukherjee S, Reddy CA, Ciezki JP, Abdel-Wahab M, Tiu RV, Copelan E, et al. Risk for developing myelodysplastic syndromes in prostate cancer patients definitively treated with radiation. J Natl Cancer Inst. 2014 Mar;106(3):djt462.
7. Breslow NE, Lange JM, Friedman DL, Green DM, Hawkins MM, Murphy MF, et al. Secondary malignant neoplasms after Wilms tumor: an international collaborative study. Int J Cancer. 2010 Aug 1;127(3):657-66.
8. Vlachos A, Rosenberg PS, Kang J, Atsidaftos E, Alter BP, Lipton JM. Myelodysplastic syndrome and gastrointestinal carcinomas characterize the cancer risk in Diamond Blackfan anemia: a report from the Diamond Blackfan Anemia Registry. Blood 2016 Dec,128(22):333.
9. Beckham TH, Leeman J, Jillian Tsai C, Riaz N, Sherman E, Singh B, et al. Treatment modalities and outcomes of Fanconi anemia patients with head and neck squamous cell carcinoma: Series of 9 cases and review of the literature. Head Neck. 2019 May;41(5):1418-26.
10 .Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers. 2020 Nov;6(1):92 .
11. Lindenblatt Rde C, Martinez GL, Silva LE, Faria PS, Camisasca DR, Lourenço Sde Q. Oral squamous cell carcinoma grading systems--analysis of the best survival predictor. J Oral Pathol Med. 2012 Jan;41(1):34-9.
12. Shaikh MH, Barrett JW, Khan MI, Kim HAJ, Zeng PYF, Mymryk JS, et al. Chromosome 3p loss in the progression and prognosis of head and neck cancer. Oral Oncol. 2020 Aug 19;109:104944.
13. Mortaz E, Tabarsi P, Mansouri D, Khosravi A, Garssen J, Velayati A, et al. Cancers related to immunodeficiencies: Update and perspectives. Front Immunol. 2016 Sep;7:365.
14. Bota JP, Lyons AB, Carroll BT. Squamous cell carcinoma of the lip-A review of squamous cell carcinogenesis of the mucosal and cutaneous

junction. Dermatol Surg. 2017 Apr;43(4):494-506.
15. Jin C, Jin Y, Wennerberg J, Akervall J, Dictor M, Mertens F. Karyotypic heterogeneity and clonal evolution in squamous cell carcinomas of the head and neck. Cancer Genet Cytogenet. 2002 Jan;132(2):85-96.
16. Ribeiro IP, Carreira IM, Esteves L, Caramelo F, Liehr T, Melo JB. Chromosomal breakpoints in a cohort of head and neck squamous cell carcinoma patients. Genomics. 2020 Jan;112(1):297-303.
17. Ribeiro IP, Esteves L, Santos A, Barroso L, Marques F, Caramelo F, et al. A seven-gene signature to predict the prognosis of oral squamous cell carcinoma. Oncogene. 2021 Jun;40(22):3859-3869.
18. Gawas NP, Navarange SS, Chovatiya GL, Chaturvedi P, Waghmare SK. Establishment and characterization of novel human oral squamous cell carcinoma cell lines from advanced-stage tumors of buccal mucosa. Oncol Rep. 2019 Apr;41(4):2289-98 .
19. Yamashita Y, Miyakawa A, Mochida Y, Aisaki K, Yama M, Shiiba M, et al. Genetic aberration on chromosome 10 in human oral squamous cell carcinoma. Int J Oncol. 2002 Mar;20(3):595-8.
20. Iwahara Y, Ishii K, Watanabe S, Taguchi H, Hara H, Miyoshi I. Bloom's syndrome complicated by myelodysplastic syndrome and multiple neoplasia. Intern Med. 1993 May;32(5):399-402.
21. Arai Y, Hirose N, Yamamura K, Nagai M, Jang H, Hattori Y, et al. A patient with genetic deletion of glutathione-S-transferase T1 and M1 who developed non-small-cell lung cancer and myelodysplastic syndromes. Am J Med Sci. 1999 Dec;318(6):424-7.
22. Kamihara Y, Sato Y, Takada K, Okagawa Y, Iyama S, Sato T, et al. [Therapy-related myelodysplastic syndrome as a late adverse event of definitive chemoradiotherapy for esophageal and oropharyngeal cancer]. Nihon Shokakibyo Gakkai Zasshi. 2015;112(9):1664-73 .
23. Wang R, Zeidan AM, Yu JB, Soulos PR, Davidoff AJ, Gore SD, et al. Myelodysplastic syndromes and acute myeloid leukemia after radiotherapy for prostate cancer: A population-based study. Prostate. 2017 Apr;77(5):437-45.
24. Shenoy N, Mudireddy M, Vallapureddy R, Leung N, Pagliaro L, Witzig T, et al. Association between renal cell carcinoma and myelodysplastic syndromes: epigenetic underpinning? Clin Genitourin Cancer. 2018 Dec;16(6):e1117-22.
25. Liu L, Liu X, Sun Y, Zeng Y, Tang X, Li X, et al. Esophageal squamous cell cancer coincides with myelodysplastic syndrome/acute myelogenous leukemia: A case report and review of the literature. Oncol Lett. 2020 Nov;20(5):266.
26. Feng Y, Chen X, Jiang K, Zhang D, Tao F, Ni D, et al. Secondary myelodysplastic syndromes identified via next-generation sequencing in a non-small cell lung cancer patient. BMC Med Genomics. 2021 Dec;14(1):299.
27. Imamura H, Tamura S, Hattori H, Kidogami S, Mokutani Y, Kishimoto T, et al. Coexisting primary tumors from esophageal cancer and myelodysplastic syndromes: A case report. Clin Case Rep. 2021 Sep;9(9):e04872.