Clinical Case Report

Medicine®

OPEN

An unusual location of squamous cell carcinoma and a rare cutaneous infection caused by *serratia marcescens* on the tumoral tissue

A case report

Nurhayat Ozkan Sevencan, MD[a,*], Elcin Kal Cakmakliogullari, MD[b], Aysegul Ertinmaz Ozkan, MD[a], Burcak Kayhan, MD[a]

Abstract

Rationale: *Serratia marcescens (S. marcescens)* is an opportunistic pathogen of the Enterobacteriaceae family. Although *S. marcescens* is known to cause sepsis, meningitis, endocarditis, urinary system and ocular infections, skin infections are sporadic. Squamous cell carcinoma (SCC) is the most aggressive skin cancer type that is often located in the head and neck region, and rarely in the scalp tissue.

Patient concerns: An 89-years-old male patient was diagnosed with SCC three years ago. The frontal region of the skull showed an ulcerated tumor, irregular borders, and exophytic growth pattern. The destruction of the frontal bone made the vibrating brain tissue visible, and the lower part had haemopurulent flow.

Diagnoses: Gram staining showed the proliferation of gram (-) bacilli. Bacteria were identified as non-pigmented *S. marcessens* in the wound culture. To the best of our knowledge, there have not been any cases reported with *S. marcescens* causing cutaneous infections on SCC. Therefore, our report is the first case in the literature.

Interventions: According to the culture antibiogram, *S. marcescens* was ciprofloxacin sensitive. Consequently, 1000 mg/day ciprofloxacin was initiated for 14 days.

Outcomes: Purulent exudate in skin cancers may be caused by the nature of carcinoma tissue as well as the colonization of opportunistic pathogen microorganisms as seen in our patient.

Lessons: Examination of the wound cultures and elimination of infections are critical in these cases.

Abbreviations: BCC = basal cell carcinoma, EMB = eosin methylene blue, NMSCs = nonmelanoma, Serratia marcescens = *S. marcescens*, SCC = squamous cell carcinoma.

Keywords: cutaneous infection, elderly population, opportunistic pathogen, *serratia marcescens*, squamous cell carcinoma

1. Introduction

Approximately 75% of all skin cancers have been observed to affect the head and neck region mostly, and rarely the scalp.[1,2] Skin cancers can be broadly categorized into 2 groups: melanoma and nonmelanoma (NMSCs). Worldwide, nearly 40% of all cancers are NMSCs. NMSCs consists of 95% of all skin cancers.[3] Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are the 2 subgroups of NMSCs. Though SSC is the most aggressive type of skin cancer, it hardly ever occurs in the scalp. Moreover, intracranial invasion of SCC is extremely rare.[4–6]

Serratia (S) marcescens is a gram-negative, motile, facultative anaerobic bacillus from Enterobacteriaceae family. It may cause nosocomial infections, and rarely be the reason of cutaneous infections in immunosuppressed patients.[7] Some biotypes of *S. marcescens* produce a red pigment called prodigiosin. Both pigmented and nonpigmented biotypes may constitute pathogeny for humans. In recent years, there have been published reports suggesting that pigmented strains of *S. marcescens* may be used in the cancer treatment. Successful results were obtained after it was tested in the treatment of acute lymphoblastic leukemia and SCC.[8,9]

Since nonpigmented biotypes cause more serious and difficult-to-treat infections due to the cytotoxin production and antibiotic resistance, identification must be performed.[10] Many reports have been published in literature on this microorganism which is especially observed in immunosuppressed patients and may cause nosocomial infections. However, there are not any reports up to this date suggesting it causes cutaneous infections by colonization on the SCC tissue. The purpose of this report is to emphasize the

Editor: N/A.

This work was developed in Karabuk University, Training and Education Hospital, Karabuk, Turkey.

The authors have no conflicts of interest to disclose.

[a] Medical Faculty, Department of Internal Medicine, [b] Medical Faculty, Department of Microbiology, The University of Karabuk, Karabuk, Turkey.

[*] Correspondence: Nurhayat Ozkan Sevencan, Medical Faculty, The University of Karabuk, Karabuk 78100, Turkey (e-mail: dr_nurhayat@hotmail.com).

Medicine (2018) 97:42(e12596)

Received: 26 April 2018 / Accepted: 3 September 2018

http://dx.doi.org/10.1097/MD.0000000000012596

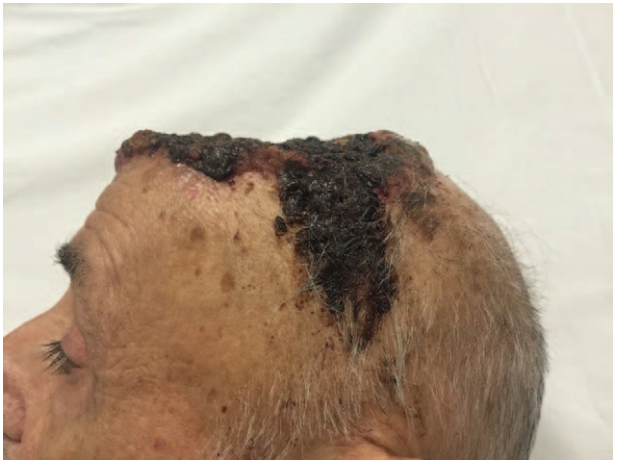

Figure 1. Loss of convexity in frontopariatel area due to bone destruction in cranium.

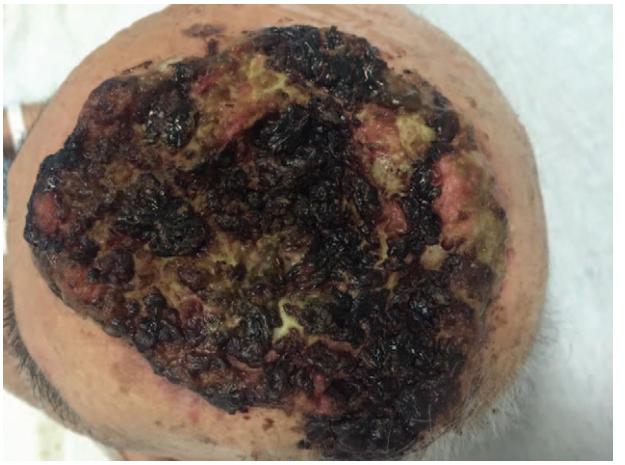

Figure 3. Hemopurulent exudate due to squamous cell carcinoma.

unusual location of skin cancer (SCC), and the co-occurrence of nonpigmented *S. marcescens*.

2. Case presentation

An 89-year old male patient applied to our clinic with fatigue and lack of appetite complaints. He had no history of cancer in the family and his past but had a 30 pack/y smoking history. He was under follow-up for the previously diagnosed hypertension and atherosclerosis. During the physical examination painful, bleeding, heterogeneous, ulcerated tumor in the frontal region of the scalp, which has irregular borders and an exophytic growth pattern was seen. The growth of the tumor was gradual over the last 3 years. However, in the last 6 months, it grew rapidly. The destruction of the frontal bone made the pulsating brain tissue visible (Figs. 1 and 2). The patient did not have hepatosplenomegaly or palpable lymph nodes. There were not any neurologic deficits, and all the other system examinations were normal. The patient was diagnosed with SCC 3 years ago but refused the surgical treatment. However, the option of surgery was not considered in this time because of the high risk caused by the tumoral invasion of the calvarium. The lower part of the tumor, that has grown rapidly in the last 6 months, had hemopurulent discharge (Fig. 3). The laboratory findings were as follows; hemoglobin:12 g/dL (14–18), leukocyte:14,700/mm^3 (4000–10,000), C-reactive protein: 9.0 mg/L (0–5), Sediment: 42 mm/h (0–20), glucose: 123 mg/dL (74–106), albumin: 3.1 g/dL (3.2–4.8), sodium: 131 mEq/L (132–146) and other laboratory parameters were regular. The samples obtained from this part of the tumor were cultured on blood agar, Eosin Methylene Blue (EMB) agar, and chocolate agar, and incubated at 37°C for 24 to 48 hours. Blood agar demonstrated nonhemolytic, nonpigmented bacteria while EMB agar demonstrated lactose (−) colonies. Gram staining showed the proliferation of gram (−) bacilli (Fig. 4). BD Phoenix automated microbiology system (Becton Dickinson Diagnostic Systems, Sparks, MD) was used for the

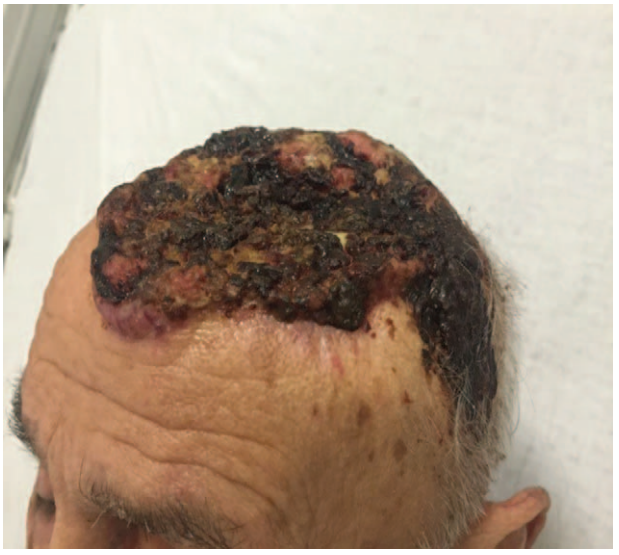

Figure 2. Loss of convexity in frontopariatel area due to bone destruction in cranium.

Figure 4. Nonpigmented *S marcescens* colonies in blood agar.

identification of bacteria and the antibiotic sensitivity test. The bacteria were identified as *S marcescens* According to the antibiogram results, 14-day ciprofloxacin treatment was initiated, and the patient was discharged from our clinic and followed up by the outpatient clinic. Informed consent was obtained from the patient for publication of this case report and accompanying images. This work was approved by the Karabuk University Ethics Committee, date: August 31, 2016, issue: 17.

3. Discussion

SCC is the most aggressive type of skin cancer, which is generally located on the head and neck region, and it is rarely located on the scalp unlike we observed in our case. Nevertheless, calvarium invasion is also rare.[4–6] Malignant tumors of the scalp grow and spread progressively, and they even may reach calvarium. High rates of cure may be provided in localized SCC. While SCC with calvarium metastasis was considered inoperable and incurable in the past, it is possible to obtain successful results in recent years with the advanced novel surgical methods.[11] However, the fact that our case was 89-years old and evaluated in the high-risk group, surgical treatment was not possible.

S marcescens is the most commonly isolated Serratia species that affect the human race. Being the cause of cutaneous infections is rare for this bacteria since it generally causes nosocomial infections, and the first reports of cutaneous infections caused by *S marcescens* were published in 1973.[12] The most frequent skin infections caused by *S marcescens* are necrotizing fasciitis and cellulitis. The limited number of case reports have indicated *S marcescens* as the cause of skin infections, and these situations may occur by forming superinfection with other microorganisms. These are severe infections with a fatal course that are mostly observed in immunosuppressed patients.[13–16] We also observed *S marcescens* proliferate in the culture originating from the hemopurulent exudate sample that was taken from the SCC lesion.

In recent years, some studies have been conducted to investigate the effect of *S marcescens* on cancer treatment. Cheng et al[9] tested a naturally red pigment named prodigiosin which is present in human oral squamous carcinoma cells as a secondary metabolite of this bacteria. Prodigiosin was shown to stimulate apoptosis and cause the cell cycle to stop in cancer cells in various concentrations and time periods.[9]

Mostly, *Serratia* isolates are resistant to ampicillin and first-generation cephalosporins. However, many isolates of *S marcescens* are resistant to other cephalosporins, aminoglycosides, and even carbapenems. Hence, the treatment of infections caused by *S marcescens* is complex.[17] According to the wound culture results of our patient, it was determined to be susceptible to amikacin, gentamycin, piperacillin/tazobactam, cefepime, ceftriaxone, ciprofloxacin, imipenem, meropenem, ertapenem, and trimethoprim-sulfamethoxazole and resistant to ampicillin, amoxicillin-clavulanate, colistin, and cefuroxime. We initiated ciprofloxacin treatment.

Nonpigmented *S marcescens* biotypes are more fatal due to the cytotoxin production and antibiotic resistance.[10] Identification must be correct since nonpigmented biotypes as we observed in our case cause severe and complicated infections. Thus, the treatment is more difficult and challenging, and the mortality and morbidity rates of immunosuppressant patients are already high. We consider that the colonization of bacteria on the cancerous skin tissue facilitated both the spread of carcinoma tissue and bone invasion. However, it is not possible to make this conclusion depending on only 1 case; it may just be a co-occurrence.

The patient was lost during the follow-up after the initiation of the antibiotic treatment. Therefore we were unable to assess his response to treatment and to prove our estimation that nonpigmented *S marcescens* facilitated the expansion of SCC and its spread to calvarium.

4. Conclusion

Purulent exudate in skin cancers may be due to the nature of carcinoma tissue and the colonization of opportunistic pathogen microorganisms as it was in our case. Wound cultures and elimination of infectious agents are important in these cases. Otherwise, the success of treatment on the primary tumor may be affected in elder, immunosuppressed patients with comorbidities as in our case, and it may cause increased mortality and morbidity.

Author contributions

Data curation: Nurhayat Ozkan Sevencan, Aysegul Ertinmaz Ozkan.
Investigation: Nurhayat Ozkan Sevencan.
Methodology: Nurhayat Ozkan Sevencan.
Project administration: Nurhayat Ozkan Sevencan.
Resources: Elcin Kal Cakmakliogullari, Aysegul Ertinmaz Ozkan, Burcak Kayhan.
Writing – original draft: Nurhayat Ozkan Sevencan.
Nurhayat Ozkan Sevencan orcid: 0000-0001-9013-3517.

References

[1] Cobanoglu HB, Constantinides M, Ural A. Nonmelanoma skin cancer of the head and neck: molecular mechanisms. Facial Plast Surg Clin North Am 2012;20:437–43.
[2] Franceschi S, Levi F, Randimbison L, et al. Site distribution of different types of skin cancer: new aetiological clues. Int J Cancer 1996;67:24–8.
[3] Cakir BÖ, Adamson P, Cingi C. Epidemiology and economic burden of nonmelanoma skin cancer. Facial Plast Surg Clin North Am 2012;20:419–22.
[4] Abo MS, Amin A, Rifaat M, et al. Locally advanced tumors of the scalp: the Egyptian National Cancer Institute experience. J Egypt Natl Canc Inst 2006;18:250–7.
[5] Ahn JH, Abu-Serriah M, Ameerally P. Multiple synchronous cutaneous squamous cell carcinomas of the head and neck: a case report. J Oral Maxillofac Surg 2011;69:e317–23.
[6] Etlik Ö, Bay A, İzmirli M, et al. Deep intracranial extension of squamous cell carcinoma of the scalp. Pediatr Blood Cancer 2005;45:994–6.
[7] Veraldi S, Nazzaro G. Skin ulcers caused by Serratia marcescens: three cases and a review of the literature. Eur J Dermatol 2016;26:373–6.
[8] Sam M, Pourpak RS. Regulation of p53 and survivin by prodigiosin compound derived from Serratia marcescens contribute to caspase-3-dependent apoptosis in acute lymphoblastic leukemia cells. Hum Exp Toxicol 2018;37:608–17.
[9] Cheng MF, Lin CS, Chen YH, et al. Inhibitory growth of oral squamous cell carcinoma cancer via bacterial prodigiosin. Mar Drugs 2017;15: E224.
[10] Roy P, Ahmed NH, Grover R. Non-pigmented strain of Serratia marcescens: an unusual pathogen causing pulmonary infection in a patient with malignancy. J Clin Diagn Res 2014;8:DD05.
[11] Baker N, Webb A, Macpherson D. Surgical management of cutaneous squamous cell carcinoma of the head and neck. Br J Oral Maxillofac Surg 2001;39:87–90.
[12] Epstein E, Carson TE. Serratia granuloma. JAMA 1973;223:670–1.
[13] Majumdar R, Crum-Cianflone NF. Necrotizing fasciitis due to Serratia marcescens: case report and review of the literature. Infection 2016;44:371–7.

[14] Lakhani NA, Narsinghani U, Kumar R. Necrotizing fasciitis of the abdominal wall caused by Serratia marcescens. Infect Dis Rep 2015;7:5774.
[15] Vano-Galvan S, Álvarez-Twose I, Moreno-Martín P, et al. Fulminant necrotizing fasciitis caused by Serratia marcescens in an immunosuppressed host. Int J Dermatol 2014;53:e57–8.
[16] Wen YK. Necrotizing fasciitis caused by Serratia marcescens: a fatal complication of nephrotic syndrome. Renal Fail 2012;34: 649–52.
[17] Mahlen SD, Morrow SS, Abdalhamid B, et al. Analyses of ampC gene expression in Serratia marcescens reveal new regulatory properties. J Antimicrob Chemother 2003;51:791–802.