

Miliaria-rash after neutropenic fever and induction chemotherapy for acute myelogenous leukemia*

Miliária 'rash' após neutropenia febril e quimioterapia de indução para a leucemia mielóide aguda

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Abstract: Miliaria is a disorder of the eccrine sweat glands which occurs in conditions of increased heat and humidity. It can be associated with persistent febrile states as well as with certain drugs. We presented a 40 year-old female with myelodysplastic syndrome and progression to acute myelogenous leukemia who was admitted to the hospital for chemotherapy induction. The patient was treated with idarubicin and cytarabine. She became pancytopenic and developed neutropenic fever and was started on vancomycin and cefepime, but was persistently febrile with night sweats. Five days into her fevers, she developed diffuse, nonpruritic and fragile vesicles together with drenching nightsweats. The patient's exanthem was diagnosed as *Miliaria crystallina*, most probably induced by neutropenic fever and idarubicin exposure.

Keywords: Chemotherapy, cancer, regional perfusion; Drug eruptions; Drug therapy; Idarubicin; Miliaria

Resumo: Miliária é uma desordem das glândulas sudoríparas écrinas, que ocorre em condições de aumento de calor e umidade. Miliária pode ser associada com estados febris persistentes bem como com certos medicamentos. Apresentamos o caso de uma mulher de 40 anos com síndrome mielodisplásica e progressão para leucemia mielóide aguda que foi admitida no hospital para quimioterapia de indução. A paciente foi tratada com idarubicina e citarabina. Ela se tornou pancitopênica e desenvolveu neutropenia febril. Iniciou tratamento com vancomicina e cefepime, mas a febre com sudorese noturna continuou. Cinco dias depois a paciente desenvolveu vesículas difusas, não pruríticas e frágeis juntamente com a persistência de sudorese noturna. O exantema do paciente foi diagnosticado como *Miliária cristalina*, provavelmente induzida por neutropenia febril e exposição a idarubicin..

Palavras-chave: Quimioterapia, câncer, perfusão regional; Erupções por droga; Terapia medicamentosa; Idarubicina; Miliária

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INTRODUCTION

Miliaria, also known as heat rash, is a disorder of the eccrine sweat glands with unknown pathogenesis. It is a common finding in newborns, especially in warm climates, but it may also occur in older individuals. 3 types of miliaria exist: 'pustulosa', 'profunda' and 'crystallina', depending on the level at which obstruction of the sweat duct occurs. The latter appears in crops of vesicles within days to weeks of exposure to hot weather and disappears within hours or days. In adults, lesions tend to occur on the trunk.¹ Well-known causes are persistent febrile states and certain drugs such as bethanecol, salbutamol and clonidine.^{2,3} A link with doxorubicin exposure has also been reported.⁴ Our patient had neutropenic fevers and idarubicin exposure, both potential precipitants of miliaria crystallina. Miliaria crystallina is a benign, self-limited rash not requiring treatment. Management includes keeping the area cool and dry given that the condition is self-limited and asymptomatic.

CASE REPORT

A 40 year-old female with myelodysplastic syndrome and new progression to acute myelogenous leukemia was admitted for chemotherapy induction. On hospital Day 3, she began induction with idarubicin (Sicor, CA, USA) 26 mg IV for 3 doses and cytarabine (Hospira, IL, USA) 6600 mg IV every 12 hours for 12 doses. On Day 4, she was initiated on Acyclovir 400 mg PO every 12 hours. On Day 5, she was pancytopenic. On day 10, she developed neutropenic fever of 100.6°F and was placed on vancomycin (generic) 1.5 g IV every 12 hours and metronidazol (Pfizer, NY, USA) 500 mg PO every 8 hours for her complaints of diarrhea. Cefepime (generic) 2g IV every 8 hours was initiated on Day 11. Despite broad-spectrum coverage, she developed recurrent fever on Days 14 and 15 associated with drenching night sweats. On Day 15, it was noted that she had a nonpruritic skin rash. The Dermatology Department was consulted for further evaluation of her rash in a fever and neutropenia setting.

Examination revealed 1-3 mm vesicles located on the patient's upper chest and flanks (Figures 1 and 2), and not along a single dermatomal distribution. The lesions were not erythematous or tender. The vesicles were very fragile. There were no oral lesions.

The patient had a positive blood culture for methicillin resistant *staphylococcus aureus* (MRSA). Urine cultures were positive for *E. coli*. Clostridium difficile toxin was negative. Chest and abdominal plain films were normal.

DISCUSSION

The differential for fever and rash in a neutropenic patient is broad and requires an extensive work-

up given the high morbidity and mortality rates. It includes chest, abdomen and pelvic computed tomography (CT) with contrast, together with potentially nephrotoxic antimicrobials. Skin biopsies are both painful and risky in the setting of thrombocytopenia. Evaluation of the skin may therefore provide a quicker diagnosis and may be lifesaving.^{5,6}

In this case, the differential diagnosis of the patient's exanthem included zoster and drug reaction. Given her bacteremia, endocarditis was considered. Optimally, there is one unifying diagnosis, but one must always consider associated processes and diagnoses. Given this patient's fever and immunosuppressed state, an infectious etiology was of high concern.⁴ However her rash was unique in that it did not appear to be inflammatory. The key points were that it was nonpruritic, fragile, and associated with drenching night sweats. The exanthem was distributed mainly along areas of eccrine sweat glands and not in a dermatomal region. The patient's exanthem was eventually diagnosed as Miliaria crystallina (MC).

The exact pathogenesis is unclear, but in the setting of excessive heat and humidity such as in tropical climates, the eccrine sweat glands become obstructed, resulting in the rupture and leakage of contents into the surrounding skin. This is referred to as miliaria.⁶ The clinical presentation depends on where the occlusion is within the gland in relation to the surrounding dermal and epidermal layers. Miliaria profunda occurs with obstruction at or below the dermoepidermal junction, presenting as a flesh-colored or pale papule. These lesions are asymptomatic. Miliaria rubra occurs with obstruction within the prickle cell layer (stratum malpighii), presenting as an erythematous macule or papule that may contain a central vesicle. Pustules are possible. The rash is pruritic and may sting.⁷

Miliaria crystallina occurs when there is obstruction within the stratum corneum and subsequent formation of a vesicle just below the skin surface.⁶ MC is characterized by diffuse 1-2mm vesicles primarily located on the trunk. The vesicles are extremely fragile and rupture with friction. The surrounding skin is noninflamed. These lesions are asymptomatic and occur after days of excessive heat and humidity.²

Although common in the pediatric setting, MC is uncommonly observed in adults. It is seen in association with persistent febrile states and certain drugs that induce sweating. Previous case reports have linked Miliaria crystallina with the use of cholinergic drugs such as bethanecol.² More recent observations within the intensive care setting has linked excessive sweating associated with use of adrenergic drugs such as salbutamol and clonidine.³



FIGURE 1: Miliaria crystallina induced by chemotherapy with idarubicin and cytarabine for acute myelogenous leukemia (panoramic picture)



FIGURE 2: Miliaria crystallina induced by chemotherapy with idarubicin and cytarabine for acute myelogenous leukemia (close-up)

In the medical literature, there is no report relating MC to idarubicin and cytarabine therapy. Nevertheless, there is a reported link with doxorubicin treatment.⁶ Doxorubicin is known for its multiple dermatologic side effects such as hyperpigmentation, urticaria, radiation recall phenomenon, extravasation and angioedema. The exact mechanism of how doxorubicin precipitates MC remains unknown and there has been only one case report of doxorubicin-associated MC to date.⁴

Miliaria has a very clinically distinct appearance and diagnosis does not require a skin biopsy.^{2,7} Our patient had neutropenic fevers and idarubicin exposure, both of which are potential precipitants of MC. Miliaria crystallina is a benign, self-limited rash and does not require treatment. Management includes keeping the area cool and dry.^{2,7} Our patient's rash desquamated on its own after 4 days and the skin returned to normal appearance. □

REFERENCES

1. Ishimine P. Hyperthermia. In: Pediatric Emergency Medicine. Baren JM, Rothro SG, Brennan JA, Brown L, editors. Saunders Elsevier: Philadelphia; 2008. p.992.
2. Rochmis PG, Koplon BS. Iatrogenic miliaria crystallina due to bethanochol. Arch Dermatol. 1967;95:499-500.
3. Haas N, Martens F, Henz BM. Miliaria crystallina in an intensive care setting. Clin Exp Dermatol. 2004;29:32-4.
4. Godkar D, Razaq M, Fernandez G. Rare skin disorder complicating doxorubicin therapy: Miliaria crystallina. Am J Ther. 2005; 12: 275-6.
5. Donowitz GR. Fever in the compromised host. Infect Dis Clin North Am. 1996;10: 129-48.
6. Wolson JS, Sober AJ, Rubin RH. Dermatologic manifestations of infections in immunocompromised patients. Medicine (Baltimore) 1985;64:115-33.
7. Wenzel FG, Horn TD. Nonneoplastic disorders of the eccrine sweat glands. J Am Acad Dermatol. 1998;38:1-17.

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