

Acanthosis Nigricans in a Patient Treated With Palifermin

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Palifermin is a modified human keratinocyte growth factor (KGF) given to decrease the incidence and duration of severe oral mucositis in patients receiving myelotoxic chemotherapy followed by a hematopoietic stem cell transplant. We report a case of a 42-year-old man who developed acanthosis nigricans after taking palifermin.
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Case Report

A 42-year-old white man presented with a yolk sac tumor of the mediastinum. After having a hypersensitivity reaction to etoposide and failing a chemotherapy regimen of vinblastine sulfate, ifosfamide, and cisplatin, the patient underwent an autologous tandem stem cell transplant (a patient receives 2 sequential courses of high-dose chemotherapy followed by a stem cell transplant given several weeks to several months apart). The patient tolerated the treatment well and had a good response to the first stem cell transplant after a preparatory regimen of etoposide phosphate and carboplatin. Before the second stem cell transplant, palifermin was given to prevent oral mucositis. He initially received intravenous palifermin in a 60 µg/kg dosage daily for 3 consecutive days, then an etoposide phosphate and carboplatin preparatory regimen (similar to what he had received before the first stem cell transplant) for 3 consecutive days, and then intravenous palifermin again at a 5.8 mg daily dosage for 3 consecutive days. On the fifth day of receiving palifermin, the patient noticed asymptomatic darkening of the skin of his neck, axillae, flexor aspect of the elbows, and groin. The lesions persisted for 7 days and then started to lighten.

The patient had no other history of medical problems, including obesity, insulin resistance, or other endocrinopathies. Family history was negative for acanthosis nigricans. On review of systems, the patient reported that he noticed tingling and numbness in his mouth starting the second day of palifermin and resolving the day after it was stopped. On physical examination, the patient had ill-defined, velvety, papillomatous, hyperpigmented plaques at the base of the anterior neck, axillae, flexor aspect of the elbows, and groin that were consistent with acanthosis nigricans (Figure).

Comment

Palifermin is a modified human keratinocyte growth factor (KGF) given to decrease the incidence and duration of severe oral mucositis in patients receiving myelotoxic chemotherapy followed by a hematopoietic stem cell transplant. Keratinocyte growth factor has been shown to induce the proliferation and differentiation of epithelial cells.^{1,2} Mesenchymal cells produce endogenous KGF, which is increased in response to epithelial tissue injury.³

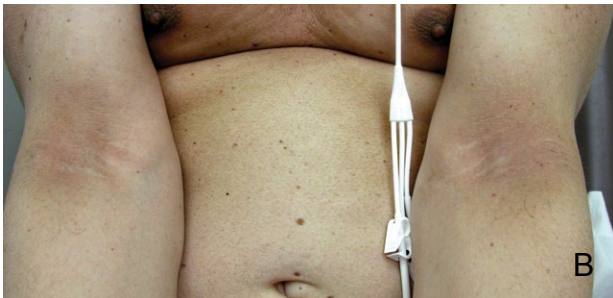
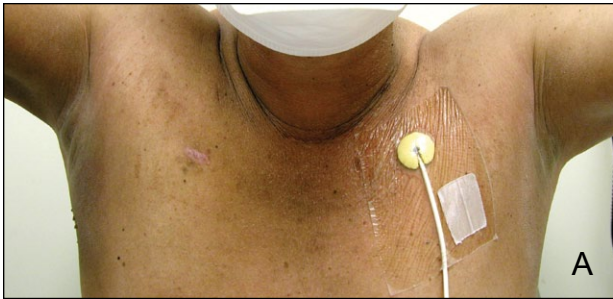
Research done in mice has revealed a connection between KGF and an acanthotic reaction similar to our case. Expression of KGF in transgenic mouse embryos caused them to have marked epidermal papillomatous acanthosis and hyperkeratosis in the skin.⁴ This same histologic finding is found in human patients with acanthosis nigricans.

According to a PubMed search of articles indexed for MEDLINE and data from the manufacturer's trials and postmarketing experience, an association between palifermin and acanthosis nigricans was not previously reported in the dermatology literature and was reported once in 2007 in the worldwide literature. In the previously reported case, a single autologous stem cell transplant was performed and acanthosis nigricans did not appear until 2 days after palifermin infusions were stopped.⁵

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Ill-defined, velvety, papillomatous, hyperpigmented plaques on the neck and axillae (A), elbows (B), and groin (C).

Although the presence of a malignancy may have been a contributing factor in the development of acanthosis nigricans in our patient, several

factors suggest a cause-and-effect relationship between palifermin and acanthosis nigricans. Our patient noticed the lesions after palifermin therapy was started and they began to resolve after the drug was stopped. The patient also had undergone a similar stem cell transplant just weeks prior with the same chemotherapeutic regimen and supporting medications except for palifermin and there was no development of acanthosis nigricans. There was no relation to the improvement or worsening of the patient's cancer. A potential mechanism of action exists, as palifermin has been shown to increase proliferation of epithelial cells. Research in mice also has reported a skin reaction with histologic findings similar to acanthosis nigricans.

Conclusion

Acanthosis nigricans may be brought about by the binding of palifermin to KGF receptors in the skin. It is unknown if the activation of these receptors is the etiologic factor in acanthosis nigricans.

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