

## CASE REPORT

# Eruptive acral lentiginosis following chemotherapy for acute lymphoblastic leukemia: A case series

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**Abstract**

Lentigines are brown macules which develop due to increased proliferation of melanocytes at the dermo-epidermal junction. We report three cases of acral lentiginosis in children following chemotherapy for acute lymphoblastic leukaemia (ALL) which have persisted following cessation of chemotherapy, despite avid photoprotection. Generalised eruptive naevi with subsequent development of dysplastic naevi and melanoma in situ have been reported following chemotherapy, highlighting the importance of continued clinical observation.

**KEYWORDS**

acral lentigines, chemotherapy, leukemia

## 1 | INTRODUCTION

Lentigines are brown macules which develop due to increased proliferation of melanocytes at the dermo-epidermal junction. They commonly occur in healthy people but can also be seen in genodermatoses such as Noonan syndrome with multiple lentigines. Eruptive lentigines have previously been described in the context of inflammatory dermatoses,<sup>1</sup> phototherapy,<sup>2</sup> and immunomodulatory therapy.<sup>3</sup> Acral eruptive lentigines have been described following chemotherapy<sup>4</sup> or as a paraneoplastic phenomenon.<sup>5</sup> We report three cases of acral lentiginosis

in children following chemotherapy for acute lymphoblastic leukemia (ALL) which have persisted following cessation of chemotherapy, despite avid photoprotection. All patients remain in remission from ALL.

## 2 | CASE SERIES

Patient one was a five-year-old Caucasian boy diagnosed with pre-B ALL in 2013 and treated as per the UKALL 2011 protocol regimen A. This regimen includes dexamethasone, vincristine, pegaspargase, methotrexate,

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FIGURE 1 Multiple lentigines on the dorsal surfaces of the feet



FIGURE 2 Multiple lentigines on the dorsal surfaces of the hands

mercaptopurine, doxorubicin, cyclophosphamide, and cytarabine. Following cessation of chemotherapy in 2016, multiple small brown macules were noted on the palmar and plantar surfaces of hands and feet (Figure 1). These have persisted for over 4 years.

Patient two was a nine-year-old Caucasian boy diagnosed with pre-B ALL in 2017 and treated as per the COG ALL 1131 protocol. This regimen includes prednisolone, vincristine, pegaspargase, methotrexate, mercaptopurine, anthracyclines, cyclophosphamide, and cytarabine. During maintenance chemotherapy in 2020, multiple small brown macules were noted on the dorsal surfaces of fingers and feet (Figure 2).

Patient three was a seven-year-old Caucasian boy diagnosed with pre-B ALL in 2018 and treated as per the

UKALL 2011 protocol regimen A. During maintenance chemotherapy in 2020, multiple small brown macules were noted on the palmar and plantar surfaces of hands and feet, as well as extensive macules on the trunk (Figure 3).

### 3 | DISCUSSION

Lentigines are the most basic form of melanocytic proliferation, on a spectrum that progresses to junctional, compound, and dermal nevi. Inflammation or immunosuppression can induce melanocyte hyperplasia. Cytotoxic agents may also induce lentigines via modulation of tumor-specific lymphocytes.<sup>4</sup> Eruptive lentigines



FIGURE 3 Multiple lentiginos on the feet and trunk

have been described in the context of psoriasis, atopic dermatitis, and drug eruptions, as well as secondary to both psoralen and ultraviolet A (PUVA) and ultraviolet B (UVB) phototherapy. Topical tacrolimus and topical immunotherapy with dibutyl squaric acid have also been associated with lentiginos. Drugs implicated in eruptive lentiginos include immunomodulatory therapy such as methotrexate, azathioprine, apremilast, etanercept, adalimumab, infliximab, ustekinumab, secukimumab, and ixekizumab, and cancer chemotherapy.

Acral lentiginos is characterized by eruptive lentiginos limited to the hands and feet. The predilection for acral sites may occur due to a combination of altered immunosurveillance and elevated local trophic factors present in acral skin.<sup>6</sup> Exposure to ultraviolet radiation may facilitate their development. Eruptive acral lentiginos has been reported following chemotherapy for ALL in children,<sup>7</sup> and following treatment with capecitabine<sup>4</sup> and tegafur<sup>8</sup> (both prodrugs of 5-fluorouracil).

There are obvious difficulties in ascertaining the culprit drug for lentiginos when multiple cytotoxic and immunosuppressive drugs are administered concomitantly as a part of a chemotherapeutic protocol. Anecdotally, we have also noted several cases of eruptive acral lentiginos in patients treated with high dose cytarabine for acute myeloid leukemia (C Ryan, personal observation). Development of lentiginos may depend on a complex milieu of cancer, immunosuppression, cytotoxic drug therapy, and UV exposure.

Generalized eruptive nevi with subsequent development of dysplastic nevi and melanoma in situ have been reported following chemotherapy,<sup>9</sup> highlighting the importance of continued clinical observation.

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#### CONFLICT OF INTEREST

None declared.

#### AUTHOR CONTRIBUTIONS

LAM suggested publication of the case series. COC reviewed all patients and wrote the initial draft. COC, CR, and LAM reviewed and edited the manuscript.

#### CONSENT

Consent for publication was provided by the parents of the children in this case series.

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