Case Study
ISSN: 3051-8822
Journal homepage: https://www.harrisonacademicpress.com/index.php/IJCEHM
International Journal of Clinical and Experimental Human Medicine

Harrison Academic Press

Vincristine-Induced Peripheral Neuropathy and Its Correlation with Mucocutaneous Pigmentation Changes

Diaz C[1*], Kolev S[2] and Krumins M[3]

[1]*Department of Neurology, University of Valencia, Valencia, Spain*
[2]*Department of Medical Oncology, Medical University of Sofia, Sofia, Bulgaria*
[3]*Department of Dermatology, Riga Stradins University, Riga, Latvia*

ABSTRACT

Background: Vincristine-induced peripheral neuropathy (VIPN) is the classic dose-limiting toxicity of vincristine-containing chemotherapy, while mucocutaneous pigmentation changes-serpentine supravenous hyperpigmentation, melanoderma, and transverse melanonychia-are separately documented cutaneous accompaniments of the same regimens. Objective: To synthesize the peripheral neuropathy and mucocutaneous pigmentation literatures for vincristine-containing regimens and evaluate the evidence for a mechanistic and clinical correlation between the two toxicities. Methods: A narrative review of case reports, cohort studies, pharmacogenomic analyses, and systematic reviews addressing VIPN incidence, grading, and risk factors, and vincristine-associated cutaneous, nail, and oral pigmentation, with attention to regimen overlap, temporal course, and shared pharmacogenomic determinants. Findings: VIPN occurs in approximately one-third of patients by routine CTCAE grading but is identified in up to 86 percent using structured multi-domain instruments such as the pediatric-modified Total Neuropathy Score, and shows consistent cumulative-dose dependence and pharmacogenomic modulation by CYP3A5 and ABCB1 variants. Mucocutaneous pigmentation has been reported within the same vincristine-containing regimens-VAD, hyper-CVAD, R-CHOP, and pediatric leukemia consolidation-on a broadly similar timescale of weeks to months, and both toxicities plausibly arise from vincristine's disruption of microtubule-dependent intracellular transport in peripheral axons and melanocytes, respectively. No study has yet prospectively assessed both toxicities with validated instruments in the same cohort. Conclusions: The correlation between vincristine-induced peripheral neuropathy and mucocutaneous pigmentation is mechanistically plausible and supported by convergent shared-regimen, shared-timing, and shared-pharmacogenomic evidence, but remains a testable hypothesis rather than an established relationship; prospective studies pairing structured neuropathy scoring with systematic dermatologic assessment, stratified by CYP3A5/ABCB1 genotype, are needed.

Keywords: *vincristine-induced peripheral neuropathy; mucocutaneous hyperpigmentation; chemotherapy-induced neurotoxicity; CYP3A5 pharmacogenomics; melanonychia*

Citation: Diaz C, Kolev S and Krumins M (2025) Vincristine-Induced Peripheral Neuropathy and Its Correlation with Mucocutaneous Pigmentation Changes. Int J Clin Exp Hum Med, 3(2): 01-06.
DOI: 10.5281/zenodo.22644289

Corresponding Author: *Carmen Diaz*

E-mail Address: *carmen.diaz@universityofvalencia.edu*

Article History: *Received 10 July 2025 | Accepted 30 September 2025 | Published 26 December 2025*

Copyright: *© 2025 Carmen Diaz, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited (**https://creativecommons.org/licenses/by/4.0/**).*

Introduction

Vincristine remains a cornerstone vinca alkaloid in regimens for acute lymphoblastic leukemia, non-Hodgkin and Hodgkin lymphoma, multiple myeloma, and a range of pediatric solid tumors, almost always administered in combination with alkylating agents, anthracyclines, and corticosteroids [1,2]. Its dose-limiting toxicity is a length-dependent, predominantly sensory peripheral neuropathy that develops in roughly a third to the majority of treated patients depending on the diagnostic method used, frequently forcing dose reduction, dose delay, or early discontinuation of an otherwise curative regimen [3,4]. Far less clinically prominent, but recurrently documented across the same vincristine-containing regimens, is a spectrum of mucocutaneous pigmentary change—serpentine supravenous streaking, diffuse melanoderma, transverse melanonychia, and reticulate truncal hypermelanosis—that has been reported in case series spanning pediatric leukemia consolidation, multiple myeloma VAD therapy, and R-CHOP lymphoma treatment [5,6,7].

These two toxicities are conventionally discussed in separate literatures: neuro-oncology and clinical pharmacology have concentrated on quantifying and predicting peripheral neuropathy, while dermatology case reports have separately catalogued pigmentary findings, usually without systematic neurologic assessment of the same patients. Yet several lines of

indirect evidence motivate asking whether the two phenomena are mechanistically and temporally linked rather than coincidental co-travelers within the same multidrug protocols. Both processes depend on vincristine's canonical mechanism of tubulin binding and microtubule disruption—axonal transport in peripheral nerve and melanosome transport in epidermal melanocytes are both microtubule-dependent processes, raising the possibility that a single pharmacologic insult produces parallel injury in two very different cell types [1,8]. Both toxicities also show a cumulative-dose relationship and inter-individual variability that has been partly attributed to shared pharmacogenomic determinants of vincristine clearance, particularly CYP3A5 and ABCB1 polymorphisms [9,10,11].

This narrative review synthesizes the peripheral neuropathy literature and the mucocutaneous pigmentation literature for vincristine-containing regimens side by side, organized across five domains: the mechanistic basis for a shared vulnerability between peripheral nerve and pigment-producing cells; the epidemiologic burden and clinical course of vincristine-induced peripheral neuropathy (VIPN); the case-level evidence for pigmentary change in vincristine regimens and what is and is not known about its temporal relationship to neuropathy; the pharmacogenomic and metabolic determinants that may govern susceptibility to both toxicities; and the practical implications of treating visible pigmentary change as a bedside correlate warranting closer neurologic surveillance. Throughout, we are explicit about the evidentiary limits of this synthesis: with rare exceptions, the case reports describing pigmentation and the cohort studies quantifying neuropathy were not designed to test a correlation between the two, and the case for a mechanistic and clinical relationship rests on convergent indirect evidence rather than a single dataset that measured both outcomes concurrently in the same patients.

Mechanistic Convergence: Microtubule Disruption as a Shared Substrate for Neurotoxicity and Pigmentary Change

Vincristine binds tubulin dimers and prevents their polymerization into functional microtubules, arresting mitotic cells in metaphase; this is the basis of its antineoplastic activity, but the same disruption occurs in non-dividing, terminally differentiated cells that depend on microtubule-based transport rather than mitosis [1]. In peripheral sensory and motor axons, microtubules form the structural scaffold for fast axonal transport of mitochondria, vesicles, and trophic signaling complexes over distances that can exceed a meter; disruption of this transport produces a "dying-back" axonopathy that begins distally and progresses proximally, consistent with the classic glove-and-stocking distribution of VIPN [1,2]. Complementary mechanistic threads implicate endothelial injury—vincristine upregulates integrin expression on vascular endothelium, promoting macrophage infiltration and reactive oxygen species generation in the perineurium—and direct mitochondrial toxicity, with altered calcium handling across the mitochondrial membrane contributing to aberrant neurotransmitter release and further oxidative stress within the dorsal root ganglion and peripheral nerve [1].

Melanocytes and the keratinocytes that receive transferred melanosomes rely on an analogous, if distinct, microtubule- and motor-protein-dependent transport system to move melanosomes from the perinuclear region to the dendritic tips of the melanocyte for transfer to surrounding keratinocytes. Reviews of drug-induced pigmentation have proposed that antimitotic and cytotoxic agents can perturb this transport machinery, causing melanosomes to be retained, clumped, or aberrantly deposited within the epidermis and papillary dermis rather than distributed normally, producing the macular hyperpigmentation and melanophage-laden dermal infiltrates documented histologically in several vincristine-regimen case reports [8,7]. A second, regimen-specific mechanism operates in serpentine supravenous hyperpigmentation, where local endothelial and perivascular injury along the infused vein—conceptually parallel to the vascular injury proposed for VIPN—is thought to permit toxic concentrations of drug or its metabolites to diffuse into the adjacent dermis and injure resident melanocytes without frank extravasation [12,5].

Vincristine-containing regimens with independently reported mucocutaneous pigmentation and peripheral neuropathy findings, illustrating shared-regimen, shared-timing overlap without within-patient joint assessment.

Regimen	Reported pigmentary finding	Independently reported neuropathy data for the same regimen	Key references
Vincristine + actinomycin D	Persistent serpentine supravenous hyperpigmentation	Vincristine cumulative-dose-dependent sensorimotor neuropathy (general VIPN literature)	Marcoux et al. 2000; Triarico et al. 2021
VAD (vincristine, adriamycin, dexamethasone)	Chromonychia, Beau's lines, diffuse melanoderma	Vinca-alkaloid-attributed neuropathy described in multiple myeloma treatment literature	Dasanu et al. 2006
Hyper-CVAD	Transverse nail-plate hyperpigmentation	Vincristine component retained despite dose-capping specifically to limit neuropathy	Lopes et al. 2013; Parakh et al. 2008
R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)	Diffuse lower-extremity, nail bed, and tongue hyperpigmentation	Genetic polymorphisms significantly associated with VIPN in an independent R-CHOP cohort	Yamamoto et al. 2024; Sawaki et al. 2020
Pediatric ALL consolidation (vincristine, methotrexate, cyclophosphamide, cytarabine, asparaginase)	Reticulate truncal and gluteal hyperpigmentation within one month of initiation	VIPN identified in 86% of vincristine-treated children by structured scoring	Kumar et al. 2021; Schouten et al. 2020

Neither cell type appears to be injured through an entirely novel pathway specific to pigmentation or to neurotoxicity; rather, both represent downstream consequences of the same core pharmacologic lesion—impaired microtubule-dependent intracellular transport—expressed differently according to the transport cargo and cell architecture involved. This convergence does not establish that the two toxicities must co-occur in a given patient, since local drug exposure (concentrated at the infusion

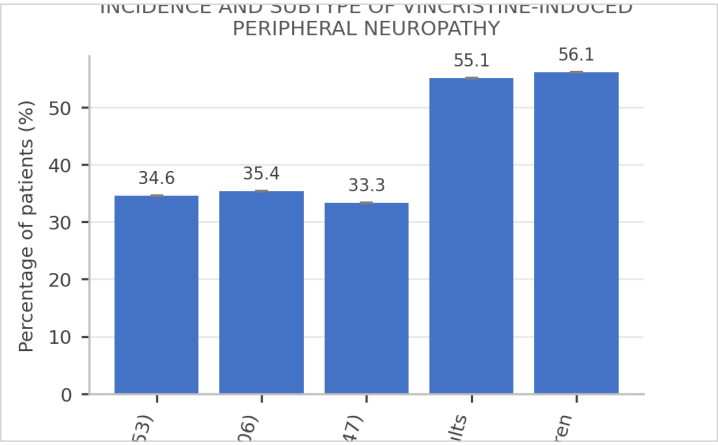
site for pigmentation, cumulative systemic exposure for neuropathy) and cell-intrinsic vulnerability differ substantially between peripheral neurons and cutaneous melanocytes. It does, however, provide a coherent biological rationale for why regimens and patients associated with more pronounced microtubule-transport disruption—whether through higher cumulative dose, impaired drug clearance, or individual pharmacogenomic susceptibility—might be expected to show a higher burden of both toxicities concurrently, a hypothesis explored further below.

The Clinical and Epidemiologic Burden of Vincristine-Induced Peripheral Neuropathy

VIPN is the most common non-hematologic dose-limiting toxicity of vincristine-containing chemotherapy, and its reported incidence varies substantially according to the diagnostic instrument used. A multicenter study of 353 vincristine recipients (206 adults and 147 children) treated for solid and hematologic malignancies found neuropathy in approximately one-third of patients overall, with autonomic neuropathy the single most common subtype—present in 55.1 percent of affected adults and 56.1 percent of affected children—while cranial neuropathy was disproportionately represented in the pediatric subgroup [3]. These figures, derived largely from clinician-graded CTCAE assessment, likely understate the true burden: a validation study of the pediatric-modified Total Neuropathy Score (ped-mTNS) administered to 56 vincristine-treated children and 56 matched healthy controls identified VIPN in 86 percent of patients compared with only 1.8 percent of controls, with patients scoring a median of 10.0 versus 0.0 on the ped-mTNS scale, demonstrating that a structured, multi-domain neurologic examination detects far more neuropathy than routine toxicity grading captures [4].

Longitudinal characterization of VIPN in adults confirms that symptoms typically emerge within the first few cycles, evolve in character over the treatment course, and can persist well beyond treatment completion in a meaningful subset of patients, with numbness, paresthesia, and reduced deep tendon reflexes the most durable findings [13]. A systematic review of VIPN in hematologic malignancies similarly emphasizes that sensory symptoms typically precede motor involvement, that autonomic manifestations (constipation, paralytic ileus, orthostatic hypotension) are under-recognized relative to sensorimotor findings, and that no single grading instrument has achieved consensus status across pediatric and adult oncology, complicating cross-study comparison of incidence and severity [2]. A broader mechanistic and clinical review of VIPN in pediatric tumors situates these findings within the wider recognition that VIPN is cumulative-dose-dependent, generally reversible over months following treatment cessation, but occasionally irreversible, particularly when high single doses are administered to patients with unrecognized predisposing peripheral neuropathy such as hereditary motor and sensory neuropathies [1].

Reported incidence and clinical subtype distribution of vincristine-induced peripheral neuropathy (VIPN) among 353 solid-tumor and hematologic malignancy patients (206 adults, 147 children), showing overall incidence and the proportion of affected patients with autonomic involvement in each age group (Alwhaibi et al., 2023).

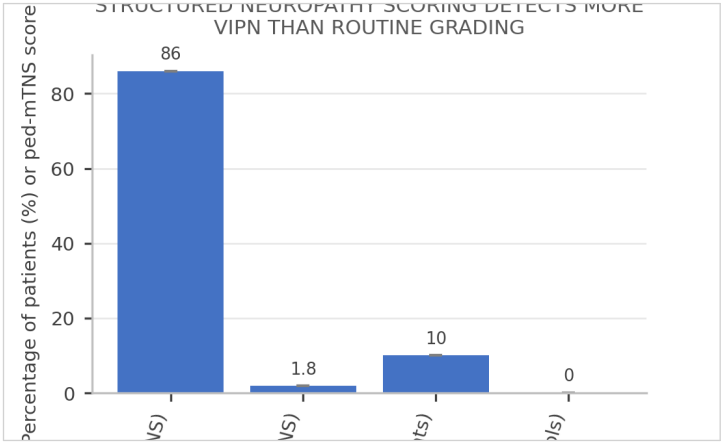


Efforts to predict which patients will develop clinically significant VIPN before it manifests have used metabolomic and genomic approaches. A pilot metabolomics study of 36 pediatric ALL patients stratified into high- and low-neuropathy groups identified serum metabolite panels that predicted subsequent VIPN with an area under the receiver operating characteristic curve of 0.93 at day 8 of treatment, 0.75 at day 29, and 0.91 at six months, suggesting that biologically measurable perturbations precede clinically apparent neuropathy by weeks [14]. Genomic approaches have converged on cytochrome P450 3A5 (CYP3A5) expression status and ABCB1 (P-glycoprotein) variants as the most consistently replicated pharmacogenomic determinants of VIPN risk, discussed in detail below, establishing a mechanistic and predictive framework onto which the pigmentation literature has yet to be systematically mapped [9,11].

Mucocutaneous Pigmentation in Vincristine-Containing Regimens: Patterns and Temporal Relationship to Neuropathy

The case-report literature describing pigmentary change in vincristine-containing regimens spans several distinct morphologies, each arising in a multidrug context that also places the patient at risk for VIPN, although few reports systematically documented neurologic findings alongside the dermatologic ones. The earliest and most specific report described persistent serpentine supravenous hyperpigmented eruption following combination therapy with actinomycin D and vincristine, establishing vincristine-containing regimens within an entity more commonly attributed to 5-fluorouracil [5,12]. A widely cited case of a multiple myeloma patient treated with vincristine, adriamycin, and dexamethasone (VAD) described three distinct nail alterations—transverse pigmented banding, transverse grooves, and diffuse leukonychia—together with diffuse forearm and palmar crease hyperpigmentation, all resolving within four months of treatment discontinuation; notably, VAD itself is well recognized in the pharmacology literature as a vincristine-containing regimen with an appreciable neuropathy burden, yet the dermatologic report did not include a structured neurologic assessment [6]. A comparable transverse nail pigmentation pattern was reported in a hyper-CVAD-treated leukemia patient, and a broader review of chemotherapy-induced nail changes lists vincristine among the recognized causes of chromonychia [15,16].

Sensitivity of a structured, multi-domain neuropathy instrument versus routine clinical assessment for detecting vincristine-induced peripheral neuropathy in 56 pediatric patients and 56 matched healthy controls, illustrating the diagnostic gap relevant to interpreting the timing of any correlate, including pigmentary change, against neuropathy onset (Schouten et al., 2020).



The report most directly bridging the two toxicity domains involves R-CHOP therapy (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone), in which a lymphoma patient developed diffuse hyperpigmented, xerotic plaques of the lower extremities together with pigmented nail bed and tongue macules; the authors implicated cyclophosphamide as the most probable causative agent but could not exclude vincristine [7]. Independently, a pharmacogenomic study of R-CHOP-treated lymphoma patients found that specific polymorphisms were significantly associated with the development of VIPN in this identical regimen, meaning that the pigmentation case and the neuropathy pharmacogenomic study, though never combined in a single cohort, describe the same drug combination acting on the same two vulnerable tissue types in parallel patient populations [17]. A pediatric case of reticulate truncal and gluteal hyperpigmentation arising one month into vincristine-containing consolidation therapy for T-cell ALL further extends the pigmentary spectrum into the population—children receiving multiagent leukemia protocols—in whom VIPN is most extensively documented and most frequently graded using sensitive instruments such as the ped-mTNS [18,4].

Because no identified study has prospectively screened the same vincristine-treated cohort for both a validated neuropathy score and a structured dermatologic pigmentation assessment, the "correlation" between the two toxicities at present is best characterized as a shared-regimen, shared-timing association rather than a demonstrated within-patient statistical correlation. What can be stated with reasonable confidence is that both toxicities cluster in the same regimens (VAD, hyper-CVAD, R-CHOP, pediatric ALL consolidation), emerge on a similar timescale of weeks to a few months into treatment, and share cumulative-dose dependence, all of which are necessary, though not sufficient, preconditions for a genuine biological correlation to exist [6,7,18].

Pharmacogenomic Determinants Common to Neurotoxicity and Pigmentary Susceptibility

Vincristine is metabolized principally by hepatic CYP3A5, with a smaller contribution from CYP3A4, and is a substrate of the ABCB1-encoded P-glycoprotein efflux transporter; genetic variation in both systems governs systemic and, plausibly, local tissue exposure to the parent drug and its metabolites. The low-CYP3A5-expresser genotype (CYP3A5*3/3*), which predominates in individuals of European ancestry, was associated with a significantly increased risk of grade 2 or higher VIPN in a cohort of children with acute lymphoblastic leukemia, establishing CYP3A5 genotype as one of the earliest and most reproducible pharmacogenomic predictors of VIPN severity [9]. A case study of an adult CYP3A5 nonexpressor with additionally reduced CYP3A4 activity who developed severe, treatment-limiting vincristine-induced neuropathic pain reinforced that combined impairment of both principal metabolic pathways can produce clinically severe toxicity even at otherwise standard dosing, and argued for pre-treatment pharmacogenomic screening in selected patients [19]. By contrast, a Kenyan pediatric cancer cohort in which 91 percent of participants carried the high-CYP3A5-expresser genotype found that, despite significantly higher vincristine exposure in the minority of low expressers, neuropathy was infrequent across the cohort as a whole, illustrating that population-level allele frequency substantially shapes the observed incidence of VIPN and that CYP3A5 genotype alone does not fully explain individual risk [10].

Pharmacogenomic determinants of vincristine clearance implicated in peripheral neuropathy risk, with the regimens in which each has been studied.

Gene/variant	Mechanism	Reported association with VIPN	Regimen/population studied	Key reference
CYP3A5*3/3* (low expresser)	Reduced hepatic vincristine metabolism	Significantly increased risk of grade ≥2 VIPN	Pediatric acute lymphoblastic leukemia	Egbelakin et al. 2011
CYP3A5 high-expresser (predominant genotype)	Enhanced vincristine clearance	Higher exposure but low neuropathy incidence in low-expresser minority	Kenyan pediatric cancer cohort (91% high expressers)	Skiles et al. 2018
Combined CYP3A4/CYP3A5 reduced activity	Impaired systemic vincristine clearance	Severe treatment-limiting neuropathic pain in a single nonexpressor	Adult case, standard-dose vincristine	Bosilkovska et al. 2016
ABCB1, CEP72 promoter, and other candidate variants	Altered drug efflux and pharmacokinetics	Multiple loci associated with variable VIPN risk	Pediatric acute lymphoblastic leukemia (systematic review)	Yang et al. 2021
Regimen-specific genetic polymorphisms	Altered vincristine handling within a multidrug regimen	Significant association with VIPN development	R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) lymphoma	Sawaki et al. 2020

Beyond CYP3A5, a systematic review of genetic variation in pediatric VIPN identified additional candidate loci—including ABCB1 and CEP72 promoter variants and mitochondrially inherited variants—associated with altered VIPN risk, alongside microRNA and other regulatory variants influencing vincristine pharmacokinetics [11]. Most relevant to the correlation examined in this review, a study of R-CHOP-treated lymphoma patients—an

identical regimen implicated in the mucocutaneous pigmentation case discussed above—found that specific genetic polymorphisms were significantly associated with VIPN development, directly connecting a genotype-driven neurotoxicity risk factor to the same regimen in which pigmentary change has been separately documented [17,7].

These pharmacogenomic findings matter for the neuropathy-pigmentation correlation hypothesis because they identify a plausible shared upstream variable: a patient with reduced vincristine clearance capacity, whether from CYP3A5 genotype, ABCB1 variants, or combined CYP3A4/5 impairment, would be expected to experience higher systemic and local tissue drug exposure across every organ system through which vincristine or its metabolites pass, including both peripheral nerve and skin. No study to date has tested whether patients with high-risk CYP3A5 or ABCB1 genotypes are also more likely to develop cutaneous or nail pigmentation, but the pharmacologic logic is symmetrical with the neuropathy literature, and this represents a concrete, testable hypothesis for future pharmacogenomic-dermatologic collaboration rather than a claim already substantiated by existing data [9,11].

Clinical Implications: Using Pigmentary Change as a Bedside Correlate of Neurotoxic Risk

Given the current state of evidence, clinicians should not treat the appearance of vincristine-associated mucocutaneous pigmentation as a validated biomarker that reliably predicts or accompanies clinically significant peripheral neuropathy; no prospective study has established this relationship with adequate sensitivity or specificity. However, several practical inferences follow reasonably from the material synthesized here. First, because both toxicities share cumulative-dose dependence and a plausible common mechanistic substrate in microtubule-dependent transport, the new appearance of pigmentary change during vincristine therapy is a reasonable prompt for a more thorough neurologic history and examination at that same visit, particularly using a structured instrument such as the ped-mTNS rather than routine CTCAE grading alone, given the marked sensitivity gap demonstrated between the two approaches [4,3].

Second, in regimens with documented reports of both toxicities—VAD, hyper-CVAD, and R-CHOP among adults, and multiagent consolidation protocols among children—clinicians managing patients who develop early pigmentary signs might reasonably lower their threshold for proactive dose modification discussions or pharmacogenomic testing where available, especially in patients with additional risk factors such as pre-existing peripheral neuropathy, hepatic impairment affecting CYP3A metabolism, or concomitant use of strong CYP3A4/5 inhibitors such as azole antifungals, which have independently been reported to potentiate vincristine neurotoxicity by impairing its clearance [1,19]. Third, oral mucosal and nail pigmentation are both readily assessed without additional cost during a scheduled infusion visit, and incorporating a brief combined dermatologic-neurologic check into routine chemotherapy surveillance imposes minimal burden while potentially improving early detection of both toxicities [7,13].

Finally, patient and family counseling should distinguish clearly between the two toxicities in terms of clinical significance: VIPN is a genuine dose-limiting toxicity that can necessitate treatment modification and, in a meaningful minority, produces persistent symptoms, whereas the pigmentary changes reviewed here are overwhelmingly benign, self-limited, and rarely influence treatment decisions on their own, consistent with broader reviews of cytotoxic dermatologic adverse events concluding that pigmentary reactions are cosmetically significant but rarely dose-limiting [13,6,20]. This asymmetry is worth emphasizing given that antineoplastic agents as a class are implicated in a substantial proportion of all drug-induced hyperpigmentation reported in aggregated pharmacovigilance cohorts, a baseline prevalence that should temper any inclination to treat an individual pigmentary finding as inherently alarming [21]. Framing pigmentation as a visible, reassuring sign that treatment is having a measurable biological effect, while reserving genuine clinical concern for neurologic symptoms, allows clinicians to use the correlation discussed in this review constructively without overstating its current evidentiary basis or causing undue alarm over a generally cosmetic finding.

Conclusion

Vincristine-induced peripheral neuropathy and vincristine-associated mucocutaneous pigmentation are documented, respectively, by a mature quantitative clinical-pharmacology literature and a scattered case-report dermatology literature, and this review is among the first to examine them side by side rather than in isolation. The two toxicities share a plausible common mechanistic root in microtubule-dependent intracellular transport, cluster within the same multidrug regimens—VAD, hyper-CVAD, R-CHOP, and pediatric ALL consolidation—and emerge on a broadly overlapping timescale of weeks to months into treatment [1,6,17,7]. Pharmacogenomic determinants of vincristine clearance, principally CYP3A5 and ABCB1 variants, are well established as neuropathy risk factors and offer a testable, symmetrical hypothesis for pigmentary susceptibility that has not yet been directly examined [9,11]. At present, however, no study has prospectively assessed both toxicities with validated instruments in the same vincristine-treated cohort, and the correlation proposed here should be understood as a well-motivated hypothesis grounded in convergent indirect evidence rather than an established clinical or statistical relationship. Prospective studies pairing structured neuropathy grading (such as the ped-mTNS) with systematic dermatologic examination in vincristine-treated cohorts, ideally stratified by CYP3A5 and ABCB1 genotype, represent the most direct and clinically actionable next step toward confirming or refuting the relationship this review has synthesized.

References

1. Triarico S, Romano A, Attinà G, Capozza MA, Maurizi P, Mastrangelo S, Ruggiero A (2021) Vincristine-Induced Peripheral Neuropathy (VIPN) in Pediatric Tumors: Mechanisms, Risk Factors, Strategies of Prevention and Treatment. International Journal of Molecular Sciences, 22(8):4112, DOI:10.3390/ijms22084112.

2. Lindhard Madsen M, Due H, Ejskjær N, Jensen P, Madsen J, Dybkær K (2019) Aspects of vincristine-induced neuropathy in hematologic malignancies: a systematic review. Cancer Chemotherapy and Pharmacology, 84(3):471-485, DOI:10.1007/s00280-019-03884-5.

3. Alwhaibi AM, Alshamrani AA, Alenazi MA, Altwalah SF, Alameel NN, Aljabali NN, Alghamdi SB, Bineid AI, Alwhaibi

M, Al Arifi MN (2023) Vincristine-Induced Neuropathy in Patients Diagnosed with Solid and Hematological Malignancies: The Role of Dose Rounding. Journal of Clinical Medicine, 12(17):5662, DOI:10.3390/jcm12175662.

4. Schouten SM, van de Velde ME, Kaspers GJL, Mokkink LB, van der Sluis IM, van den Bos C, Hartman A, Abbink FCH, van den Berg MH (2020) Measuring vincristine-induced peripheral neuropathy in children with cancer: validation of the Dutch pediatric-modified Total Neuropathy Score. Supportive Care in Cancer, 28(6):2867-2873, DOI:10.1007/s00520-019-05106-3.

5. Marcoux D, Anex R, Russo P (2000) Persistent serpentine supravenous hyperpigmented eruption as an adverse reaction to chemotherapy combining actinomycin and vincristine. Journal of the American Academy of Dermatology, 43(3):540-546, DOI:10.1067/mjd.2000.106239.

6. Dasanu CA, Vaillant JG, Alexandrescu DT (2006) Distinct patterns of chromonychia, Beau's lines, and melanoderma seen with vincristine, adriamycin, dexamethasone therapy for multiple myeloma. Dermatology Online Journal, 12(6):10, DOI:10.5070/D321m795kv.

7. Yamamoto J, Fujimura T, Asano Y (2024) Atypical bilateral hyperpigmented macules on the lower legs possibly due to cyclophosphamide. Case Reports in Dermatology, 17(1):14-18, DOI:10.1159/000543124.

8. Tisack A, Mohammad TF (2024) Drug-Induced Pigmentation: A Review. Drugs, 84(9):1071-1091, DOI:10.1007/s40265-024-02062-z.

9. Egbelakin A, Ferguson MJ, MacGill EA, Lehmann AS, Topletz AR, Quinney SK, Li L, McCammack KC, Hall SD, Renbarger JL (2011) Increased risk of vincristine neurotoxicity associated with low CYP3A5 expression genotype in children with acute lymphoblastic leukemia. Pediatric Blood & Cancer, 56(3):361-367, DOI:10.1002/pbc.22845.

10. Skiles JL, Chiang C, Li CH, Martin S, Smith EL, Olbara G, Jones DR, Vik TA, Mostert S, Abbink F, Kaspers GJ, Li L, Njuguna F, Sajdyk TJ, Renbarger JL (2018) CYP3A5 genotype and its impact on vincristine pharmacokinetics and development of neuropathy in Kenyan children with cancer. Pediatric Blood & Cancer, 65(3):e26854, DOI:10.1002/pbc.26854.

11. Yang QY, Hu YH, Guo HL, Xia Y, Zhang Y, Fang WR, Li YM, Xu J, Chen F, Wang YR, Wang TF (2021) Vincristine-Induced Peripheral Neuropathy in Childhood Acute Lymphoblastic Leukemia: Genetic Variation as a Potential Risk Factor. Frontiers in Pharmacology, 12:771487, DOI:10.3389/fphar.2021.771487.

12. Shan J, Obiakor BC, Cheng J, Francois RA, Dobry AS (2024) Serpentine supravenous hyperpigmentation induced by chemotherapy: a systematic review. Archives of Dermatological Research, 316(6):215, DOI:10.1007/s00403-024-03057-2.

13. Li T, Trinh T, Bosco A, Kiernan MC, Goldstein D, Park SB (2024) Characterising vincristine-induced peripheral neuropathy in adults: symptom development and long-term persistent outcomes. Supportive Care in Cancer, 32(5):278, DOI:10.1007/s00520-024-08484-5.

14. Verma P, Devaraj J, Skiles JL, Sajdyk T, Ho RH, Hutchinson R, Wells E, Li L, Renbarger J, Cooper B, Ramkrishna D (2020) A Metabolomics Approach for Early Prediction of Vincristine-Induced Peripheral Neuropathy. Scientific Reports, 10(1):9659, DOI:10.1038/s41598-020-66815-y.

15. Lopes M, Jordão C, Grynszpan R, Sodré C, Ramos-e-Silva M (2013) Chromonychia secondary to chemotherapy. Case Reports in Dermatology, 5(2):163-167, DOI:10.1159/000351874.

16. Parakh A, Gupta A, Dubey AP (2008) Chemotherapy induced nail changes. Indian Journal of Dermatology, 53(4):204, DOI:10.4103/0019-5154.44804.

17. Sawaki A, Miyazaki K, Yamaguchi M, Takeuchi T, Kobayashi K, Imai H, Tawara I, Ono R, Nosaka T, Katayama N (2020) Genetic polymorphisms and vincristine-induced peripheral neuropathy in patients treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone therapy. International Journal of Hematology, 111(5):686-691, DOI:10.1007/s12185-020-02832-x.

18. Kumar S, Bhattacharjee R, Kambhampati SB, Narang T, Kanwar AJ, Vinay K (2021) Chemotherapy-induced reticulate pigmentation in three Indian patients including a case in the pediatric age group. Indian Journal of Dermatology, Venereology and Leprology, 87(3):386-388, DOI:10.25259/IJDVL_216_20.

19. Bosilkovska M, Ing Lorenzini K, Uppugunduri CRS, Desmeules J, Daali Y, Escher M (2016) Severe Vincristine-induced Neuropathic Pain in a CYP3A5 Nonexpressor With Reduced CYP3A4/5 Activity: Case Study. Clinical Therapeutics, 38(1):216-220, DOI:10.1016/j.clinthera.2015.10.017.

20. Deutsch A, Leboeuf NR, Lacouture ME, McLellan BN (2020) Dermatologic Adverse Events of Systemic Anticancer Therapies: Cytotoxic Chemotherapy, Targeted Therapy, and Immunotherapy. American Society of Clinical Oncology Educational Book, 40:485-500, DOI:10.1200/EDBK_289911.

21. Alharithy R, Alotaibi K, Bin Salamah R, Altamimi R, Alqntash N, Alsarhan R, Khosyfan L, Alrowais S (2026) Drug induced hyperpigmentation: systematic review and meta-analysis. Frontiers in Medicine, 13:1674278, DOI:10.3389/fmed.2026.1674278.