ORIGINAL ARTICLE

Clinical characteristics of chemotherapy-induced alopecia in childhood

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Background: Chemotherapy-induced alopecia (CIA) is a frequent complication in patients with cancer. There are an increasing number of reports of permanent CIA.

Objective: We investigated the clinical characteristics of CIA, including permanent CIA in childhood.

Methods: We collected data on 159 pediatric patients who had undergone high-dose conditioning chemotherapy followed by hematopoietic stem cell transplantation and 167 control subjects, using a questionnaire, medical record reviews, and phototrichograms.

Results: Alopecia began at 1.5 ± 1.4 months and was sustained until 2.2 ± 1.6 months after chemotherapy initiation. Hair regrowth started 2.6 ± 1.6 months after chemotherapy ceased and lasted for 7.3 ± 4.9 months. The mean hair density and thickness were 198.3 ± 47.4/cm^2 and 76.3 ± 18.4 μm in the patient group and 229.6 ± 34.5/cm^2 and 79.5 ± 12.4 μm in the control group, respectively (both, $P < .001$). In all, 19 (12%) patients experienced permanent CIA. Thiotepa use was identified as a significant risk factor for permanent CIA (odds ratio 7.57, $P = .002$).

Limitations: Cross-sectional study in a single-center is a limitation.

Conclusion: CIA is common in pediatric patients. Use of thiotepa is strongly associated with permanent CIA. (J Am Acad Dermatol 10.1016/j.jaad.2013.10.034.)

Key words: alopecia; chemotherapy; chemotherapy-induced alopecia; childhood; hematopoietic stem cell transplantation; permanent; thiotepa.

Chemotherapy-induced alopecia (CIA) is frequently observed in patients with cancer, with an incidence of 65%.[1] Hair loss has a strong negative impact on body image and self-esteem.[1] As children are especially susceptible to the perceptions of others, they may be particularly affected, possibly reducing social interactions.[2] CIA

Abbreviations used:

CI:	confidence interval
CIA:	chemotherapy-induced alopecia
GPA:	global photographic assessment
HD:	hair density
HSCT:	hematopoietic stem cell transplantation
HT:	hair thickness

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has been studied in adult patients,[3,4] but little is known about pediatric CIA.

Permanent CIA usually occurs after high-dose conditioning chemotherapy and subsequent hematopoietic stem cell transplantation (HSCT).[5-7] Hematopoietic malignancies, which are common malignancies in children, are the main indication for HSCT.[8] Although permanent CIA is not uncommon among pediatric patients, its prevalence and features are not well studied. To date, only 1 study on permanent CIA in pediatric patients has been reported and this was conducted decades ago.[9] Since then, the development of chemotherapeutic agents and treatment protocols has progressed extensively. We investigated the clinical characteristics of CIA, including permanent CIA, and analyzed factors associated with the development of permanent CIA in pediatric patients who undergo HSCT.

CAPSULE SUMMARY

- Chemotherapy-induced alopecia is frequently observed in patients with cancer.
- This study of chemotherapy-induced alopecia in children undergoing hematopoietic stem cell transplantation found that thiotepa use is strongly associated with permanent hair loss.
- Pediatric patients should be informed about chemotherapy-induced hair changes and the risk of permanent chemotherapy-induced alopecia after hematopoietic stem cell transplantation.

METHODS

Patients

This study used questionnaire surveys, medical record reviews, and phototrichograms as the main data-gathering tools. From November 2011 to January 2013, a questionnaire survey was conducted of pediatric patients who had completed chemotherapy and were disease-free. Each patient had undergone high-dose conditioning chemotherapy, followed by HSCT, for various underlying diseases. The patients were evaluated at least 6 months after their last chemotherapy treatment. The questionnaire collected demographic information; onset and duration of CIA; onset and duration of hair regrowth after alopecia; and changes in hair density (HD), color, and texture. Clinical details, including diagnosis, age at diagnosis and HSCT, type of HSCT, conditioning chemotherapy regimen, history of cranial irradiation, and chronic graft-versus-host disease, were obtained from the medical records. To conduct a comparison with individuals with normal hair growth, 167 participants without scalp disease, hair loss problems, or a treatment history involving chemotherapy or HSCT were enrolled. This study was approved by the institutional review board of Seoul National University Hospital in Korea.

Analysis of hair regrowth

Hair regrowth was evaluated by global photographic assessment (GPA) and computer-assisted phototrichogram (Folliscope, Lead M, Seoul, Korea). The GPA was evaluated by 2 independent investigators using clinical photographs and a 5-point rating scale, with 1 being the absence of hair and 5 being more than 75% hair coverage. HD measurements for 2 adjacent scalp sites on the top of the head (at the cross-point of a line connecting the external auditory meati and the sagittal line) were averaged. To count precisely, we manually measured the HD in a 1-cm^2 area, under 50-fold magnification. The value for mean hair thickness (HT) was determined from phototrichogram images and measured using image analysis software (Image J, Version 1.24, National Institutes of Health, Baltimore, MD).

Definition of permanent CIA

Permanent CIA is defined as absent or incomplete hair regrowth at 6 months postchemotherapy.[6,10] The Olsen CIA scale was used to evaluate the CIA severity in our patients.[4] Briefly, this uses a 5-grade scale: minimal = grade 1 (1%-24% loss, compared with the pretreatment state); moderate = grade 2 (25%-49% loss), or grade 3 (50%-74% loss); extensive = grade 4 (75%-99% loss); and complete = grade 5 (100% loss). In this study, we defined permanent CIA as extensive and complete hair loss, by the Olsen criteria (grades 4 and 5, >75% loss) after more than 6 months, postchemotherapy.

Statistical analysis

We summarized the data using descriptive statistics and examined the association of CIA with each patient's demographics, diagnosis, type of HSCT, and type of chemotherapy regimen. In addition, to identify factors associated with permanent and nonpermanent CIA, between-group comparisons were conducted after adjusting for age and gender. We conducted univariate logistic regression analyses to assess the associations between each possible risk factor and permanent CIA. To estimate the relative risk of developing permanent CIA, we conducted multivariate logistic regression analyses

Table I. Demographic data of pediatric patients with chemotherapy-induced alopecia

	N (%) or mean ± SD
Overall	159
Gender	
Male	86 (54.1)
Female	73 (45.9)
Age, y	
At questionnaire	12.1 ± 5.3
At diagnosis	6.2 ± 4.7
At HSCT	7.4 ± 4.9
Diagnosis*	
Leukemia	85 (53.5)
Solid tumor	30 (18.9)
Nonmalignant disease	18 (11.3)
Brain tumor	15 (9.4)
Lymphoma	11 (6.9)
HSCT type	
Allograft	88 (55.3)
Autograft	71 (44.7)

HSCT, Hematopoietic stem cell transplantation.
*The diagnoses were grouped into 5 categories: leukemia (acute myeloid leukemia, acute lymphoblastic leukemia, acute biphenotypic leukemia, and juvenile myelomonocytic leukemia), lymphoma (anaplastic large cell lymphoma, Burkitt lymphoma, Hodgkin lymphoma, and non-Hodgkin lymphoma), brain tumor (choroid plexus carcinoma, ependymoma, medulloblastoma, pineoblastoma, primitive neuroectodermal embryogenic tumor, and intracranial germinoma), solid tumor (clear cell sarcoma, Ewing sarcoma, germ cell tumor, neuroblastoma, osteosarcoma, extrarenal malignant rhabdoid tumor, rhabdoid tumor of the kidney, and Wilms tumor), and nonmalignant disease (anaplastic anemia, chronic granulomatous disease, infection-associated hemophagocytic syndrome, idiopathic myelofibrosis, myelodysplastic syndrome, and Wiskott-Aldrich syndrome).

with variables identified in the univariate analyses as potential independent factors for the development of permanent CIA. Results were expressed as means ± SD and odds ratios with 95% confidence intervals [CI]). All analyses were performed using statistical software (SAS 9.2, SAS Institute, Cary, NC); *P* less than .05 was considered statistically significant.

RESULTS

Patient demographics and CIA clinical characteristics

A total of 159 patients (86 male, 73 female; mean age, 12.1 ± 5.3 [range, 3-24] years) were included in this study (Table I). The patients had various types of underlying disease; leukemia was the most common diagnosis (85 patients, 53.5%). Eighty-eight patients (55.3%) received allografts, and 71 patients (44.7%) received autografts. There were 167 (87 female) healthy control subjects (mean age, 8.1 ± 4.2 [range, 2-21] years).

Table II. Phenotypic changes of regrown hair after chemotherapy-induced alopecia

	Yes (%)	No (%)
Change in density	67.1	32.9
1%-25%	28	
26%-50%	2	
51%-75%	17	
76%-99%	28	
Change of color	58.3	41.7
Lightening	79.8	
Darkening	20.2	
Change of texture	78.8	21.2
Thinning	80.4	
Thickening	12.5	
Roughing	5.4	
Smoothening	1.8	

All patients had normal hair status before chemotherapy, and all lost their scalp hair during chemotherapy. Alopecia developed 1.5 ± 1.4 months after chemotherapy initiation and was sustained until 2.2 ± 1.6 months thereafter. Hair regrowth started 2.6 ± 1.6 months after chemotherapy ceased and stopped after 7.3 ± 4.9 months. When the hair regrew after chemotherapy, 67.1% patients experienced reduced HD compared with before chemotherapy; 45% patients who experienced a change in HD complained about the reduced density. More than half of the respondents (58.3%) demonstrated a change in hair color; most (79.8%) said their hair became lighter after chemotherapy. Of 78.8% patients who reported altered hair texture, 80.8% reported thinner hair (Table II).

We compared the onset and duration of CIA and the onset and duration of regrowth after alopecia according to gender, diagnosis, type of HSCT, and chemotherapy regimen. The nonmalignant disease group showed a significantly shorter duration of CIA ($P = .038$). The onset of hair regrowth appeared earlier for patients who received autografts, compared with those who received allografts ($P = .041$) (data not shown).

Quantitative analysis of hair status

Fig 1 demonstrates the differences in the values of the GPA, mean HD, and mean HT between the patient and control groups, with adjustments for age and gender. All parameters were significantly lower in the patient group compared with the control group. The patient group showed a significantly lower GPA score compared with the control group ($P < .001$). The mean HD and HT were significantly less in the patient group than in the control group (both, $P < .001$) (Fig 1).

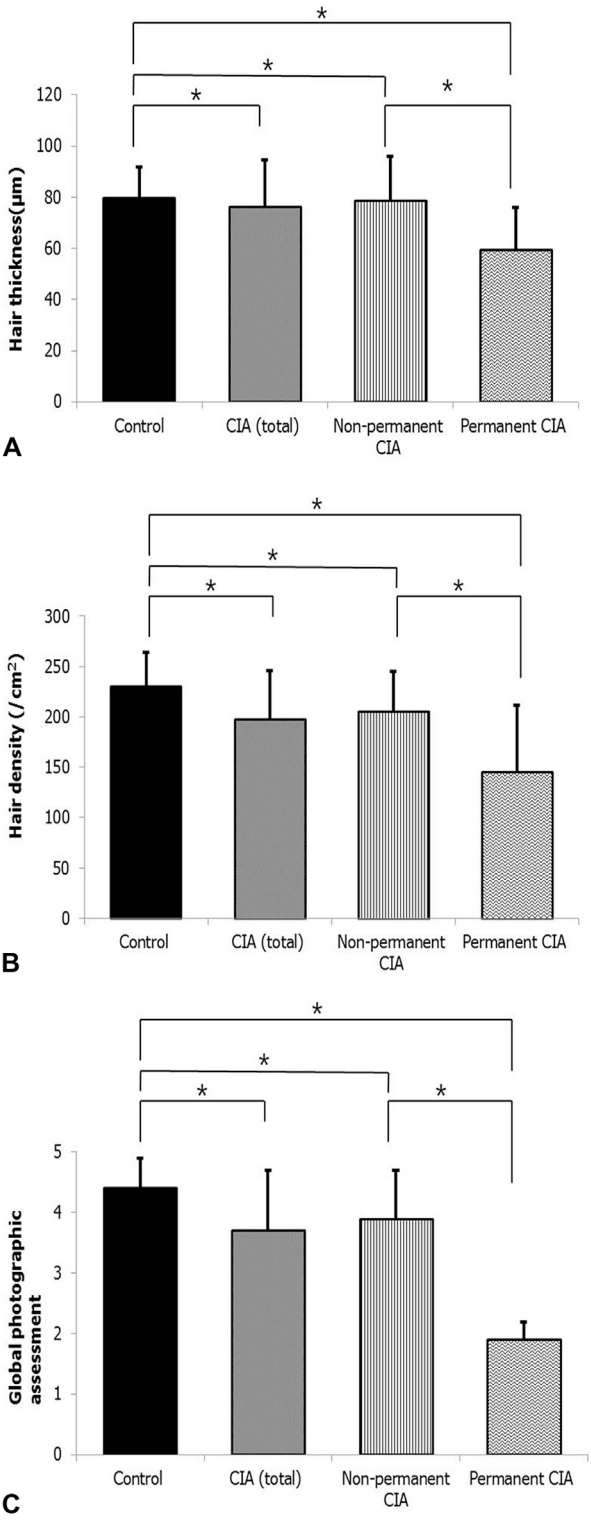

Fig 1. Chemotherapy-induced alopecia (*CIA*) in children. Comparison of hair thickness (**A**), hair density (**B**), and global photographic assessment (**C**) of patients and control subjects. All parameters were significantly lower in the CIA group compared with the control group. There were also significant differences comparing permanent CIA vs nonpermanent CIA, permanent CIA vs control, and nonpermanent CIA vs control in all parameters (*$P < .0001$).

Permanent CIA

Of the 159 patients, 19 (12%) had extensive or complete hair loss more than 6 months after discontinuing chemotherapy, namely permanent CIA. Physical examinations revealed diffuse hair loss, characterized by sparse, thin scalp hair without inflammation or scarring (Fig 2). Among the 19 patients, there were approximately equal (10 vs 9) numbers of male and female individuals, and autograft vs allograft recipients. No patient with permanent CIA developed chronic graft-versus-host disease, but 7 received cranial irradiation (Table III).

In the permanent CIA group, the mean age at the time of HSCT was significantly younger than that in the nonpermanent CIA group (5.2 ± 4.4 years vs 7.6 ± 4.9 years). There were no significant differences in the onset and duration of CIA or in the time to regrowth between the 2 groups (data not shown). In the quantitative analysis of the GPA, mean HD, and HT, significant differences ($P < .001$) were observed between the permanent and nonpermanent CIA groups (Fig 1). In the analysis by HSCT type, GPA, HT, and HD values for the permanent CIA group were lower than those of the nonpermanent CIA group, regardless of the HSCT type (data not shown).

The logistic regression analysis of risk factors for the development of permanent CIA versus nonpermanent CIA is shown in Table IV. The univariate analysis revealed a significant reverse correlation of increasing age at the time of HSCT and the development of permanent CIA, with a magnitude of 0.89-fold (95% CI, 0.79-0.99; $P = .042$). The risk of permanent CIA was statistically higher for subjects treated with thiotepa; the increased prevalence had a magnitude of 8.79-fold (95% CI, 3.02-26.00; $P < .0001$) in the unadjusted model and 7.57-fold (95% CI, 2.54-22.80; $P < .001$) in the adjusted model. Contrary to our expectations, significant statistical differences were not observed for the type of HSCT, a history of cranial irradiation, chronic graft-versus-host disease, or use of other chemotherapeutic agents, such as busulfan or cyclophosphamide. In the analysis by HSCT type, thiotepa was still a significant risk factor for permanent CIA in the autograft group, both with and without adjustment, whereas there was no relationship between permanent CIA and other factors in the allograft group.

DISCUSSION

We investigated the clinical characteristics of CIA and the prevalence and risk factors of permanent CIA in pediatric patients. All our patients experienced CIA and demonstrated significantly reduced GPA, HT, and HD values compared with control subjects.

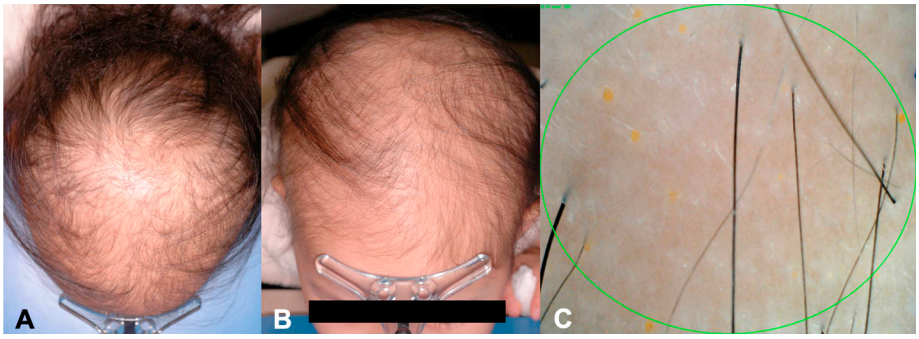

Fig 2. Clinical photographs of permanent chemotherapy-induced alopecia. An 8-year-old girl given the diagnosis of acute myeloid leukemia received an unrelated peripheral blood stem cell transplantation 3 years earlier. Diffuse decreased hair density with short, thin hairs (**A** and **B**); mean hair density, 25/cm^2; mean hair thickness, 64 μm (**C**).

Approximately 12% developed permanent CIA, a markedly higher rate than reported in previous studies of adult patients.[5,6]

CIA results from direct damage to the hair matrix cell.[11] Because the affected hairs are those in the highly proliferative anagen phase, CIA is referred to as a type of anagen effluvium.[11] When the hair regrew after chemotherapy was terminated, most patients experienced changes in the density, color, and texture of their hair. The reasons for such phenotypic changes are unknown. One important determinant of hair shaft texture is presumably the hair follicle.[12] Chemotherapeutic agents affect the vasculature and sebaceous glands, damaging the function of the hair follicle.[13,14] Furthermore, chemotherapy induces oxidative stress to the pigmentary unit of the hair follicle, which is vulnerable to reactive oxygen species, possibly provoking a complicated change in melanocyte function.[15] These effects may impact the changes in hair characteristics observed during regrowth, but the precise mechanisms require further investigation.

In the quantitative analyses, using phototrichograms, the HD and HT in the CIA group were significantly lower than those in the control group, confirming the results from the questionnaire survey. In contrast to previous studies suggesting that HD fully recovers after chemotherapy,[3,16] our study demonstrated low values for GPA, HT, and HD of the regrown hair compared with the hairs of the healthy control group. Thus, we believe that pediatric patients should be informed about hair regrowth changes after chemotherapy.

Permanent CIA is common after high-dose conditioning chemotherapy for bone-marrow transplantation.[7,9,17] The reported incidence of permanent CIA ranges from 0.9% to 43% in adults and is 24% in children.[6,7,9] Based on the CIA grading system, hair loss of more than 50% had a psychosocial impact, and hair loss of more than 75% required the use of a wig.[4] According to our definition of extensive or complete hair loss (>75%) at least 6 months after chemotherapy discontinuation as permanent CIA, 12% of the patients had permanent CIA. A previous study of the incidence of permanent CIA in children defined mild hair loss ($\leq$ 25%, but less than pretransplant state) as permanent CIA and reported that 24.3% of pediatric patients who received bone-marrow transplantation did not subsequently demonstrate complete hair regrowth.[9] Because most research on the incidence of permanent CIA in adult patients labeled patients with "incomplete" hair regrowth as having permanent CIA, direct comparisons with this study are difficult.[5-7] Our data show that permanent CIA is not uncommon after high-dose conditioning chemotherapy and HSCT. Pediatric patients undergoing HSCT should be informed about the risks of permanent CIA.

Specific chemotherapeutic agents such as busulfan, cyclophosphamide, and docetaxel are widely known risk factors for permanent CIA.[6,7,10,18] Although most previous studies reported busulfan as the main causative agent,[7,17] it was not a significant factor for permanent CIA in our patient group. We found that thiotepa played an important role. Thiotepa-induced permanent CIA has been reported in patients treated with high-dose cyclophosphamide/thiotepa/carboplatin chemotherapy, and higher concentrations of carboplatin, thiotepa, and tepa, the active metabolite of thiotepa, increase the risk of permanent CIA.[19] Previous studies showed a higher incidence of permanent CIA in patients receiving allografts as opposed to autografts,[7,17] but our study did not demonstrate this difference. Unlike previous studies, we found an inverse association between increasing age at HSCT and the incidence of

Table III. Characteristics of pediatric patients experiencing permanent chemotherapy-induced alopecia

(A) Autograft

Patient	Gender	Age, y	Specific diagnosis	Conditioning regimen	Cranial irradiation
1	M	5	MBL	CarboThioVP/CyMEL	Yes
2	M	5	MBL	TopoThioCarbo/MEC	No
3	M	6	MBL	CarboThioVP/CyMEL	Yes
4	M	13	MBL	CarboThioTopo	Yes
5	M	14	MBL	CarboThioVP/CyMEL	Yes
6	F	5	MBL	CarboThioVP/CyMEL	Yes
7	F	5	NBL	CarboThioTopo/MEC	No
8	F	5	NBL	CarboThioVP/MEC	No
9	F	11	MBL	TopoThioCarbo/MEC	Yes
10	F	19	NBL	MelVP	No

(B) Allograft

Patient	Gender	Age	Specific diagnosis	Allograft type	Conditioning regimen	Graft-versus-host disease	Total body irradiation	Cranial irradiation
1	M	3	ALL	CBT	BuFluVPATG	No	No	No
2	M	5	ALL	UPBSCT	BuFluVPATG	No	No	No
3	M	5	AML	DCBT	BuFluATG	No	No	No
4	M	6	AML	UPBSCT	BuFluATG	No	No	Yes
5	M	19	AML	RBMT	Little BuCyATG	No	No	No
6	F	3	ALL	RPBSCT	BuFluVPATG	No	No	No
7	F	8	AML	UPBSCT	BuFluATG	No	No	No
8	F	18	AML	RBMT	BuCyATG	No	Yes	No
9	F	22	MDS	RBMT	Little BuCyATG	No	No	No

ALL, Acute lymphoblastic leukemia; *AML*, acute myeloid leukemia; *ATG*, antithymocyte globulin; *Bu*, busulfan; *Carbo*, carboplatin; *CBT*, cord blood transplantation; *Cy*, cyclophosphamide; *DCBP*, double cord blood transplantation; *F*, female; *Flu*, fludarabine; *M*, male; *MBL*, medulloblastoma; *MDS*, myelodysplastic syndrome; *MEC*, melphalan + etoposide + carboplatin; *MEL*, melphalan; *NBL*, neuroblastoma; *RBMT*, related bone-marrow transplantation; *RPBSCT*, related peripheral blood stem cell transplantation; *Thio*, thiotepa; *Topo*, topotecan; *UPBSCT*, unrelated peripheral blood stem cell transplantation; *VP*, etoposide.

permanent CIA.[17] A positive correlation between age and permanent CIA is reported; however, these studies mostly targeted busulfan-induced permanent CIA, suggesting that the association was more closely related to blood concentrations of busulfan, which increased with age, rather than with increased age itself. However, blood concentrations of drugs differ, based on their pharmacokinetics, and are determined by not only the type of drug, but also its dose, administration regimen, age, and patient characteristics. The reasons why some patients develop irreversible permanent alopecia remain unclear. Direct toxicity of high-dose chemotherapy agents may permanently damage epithelial hair follicle stem cells.[16] The relationship between permanent CIA and various factors requires further, large-scale research, to provide an individualized prognosis for each patient.

Our study has some limitations. First, as the design was cross-sectional and involved a questionnaire, we could not exclude bias because of inaccurate patient/family memory. Second, a selection bias existed because patients and parents concerned about hair status were more likely to participate in the survey. In addition, there were some protocol modifications among different patients. These comprised differences in the chemotherapeutic agent(s) used and the dosage. Patients were treated

Table IV. Univariate logistic regression (A) and multivariate logistic regression (B) of risk factors for permanent chemotherapy-induced alopecia in children

(A) Univariate logistic regression

	Unadjusted OR	95% CI	*P*
Total patients			
Age	0.89	0.80-0.98	.018
Age at HSCT	0.89	0.79-0.99	.042
Thiotepa (yes/no)	8.79	3.02-26.00	<.001
Autograft patients			
Thiotepa (yes/no)	14.7	2.79-76.92	.002

(B) Multivariate logistic regression

	Adjusted OR	95% CI	*P*
Total patients			
Thiotepa (yes/no)	7.57	2.54-22.80	<.001
Autograft patients			
Thiotepa (yes/no)	14.7	2.79-76.92	.002

CI, Confidence interval; *HSCT*, hematopoietic stem cell transplantation; *OR*, odds ratio.

with various types of chemotherapeutic agents, at conventional doses, before conditioning chemotherapy and HSCT. However, conventional doses of chemotherapy are rarely related to permanent CIA, and we assumed that the involved chemotherapy regimens did not have a significant effect on the results of this study. To overcome these limitations, patient cohorts need to be organized before chemotherapy treatment. Lastly, scalp biopsy for histopathologic examination was not performed in all subjects. A large, prospective study needs to be conducted to consistently observe changes in hair status, including histopathologic features. The lack of a clear standard definition of permanent CIA increases the difficulty of investigating clinical features or determining the accurate prevalence. Considering the increasing number of reports of this complication, the development of a uniform and standardized classification of permanent CIA is required.

In conclusion, CIA is common in pediatric patients and permanent CIA has a higher incidence in children than in adults. We hope our study will raise awareness of CIA, including permanent CIA, in this population.

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REFERENCES

1. Cash TF. The psychology of hair loss and its implications for patient care. Clin Dermatol 2001;19:161-6.
2. Harrison S, Sinclair R. Optimal management of hair loss (alopecia) in children. Am J Clin Dermatol 2003;4:757-70.
3. Chon SY, Champion RW, Geddes ER, Rashid RM. Chemotherapy-induced alopecia. J Am Acad Dermatol 2012;67:e37-47.
4. Olsen EA. Chemotherapy-induced alopecia: overview and methodology for characterizing hair changes and regrowth. In: Oliver IN; Multinational Association of Supportive Care in Cancer, editors. The MASCC textbook of cancer supportive care and survivorship. New York: Springer; 2011. pp. 381-8.
5. Palamaras I, Misciali C, Vincenzi C, Robles WS, Tosti A. Permanent chemotherapy-induced alopecia: a review. J Am Acad Dermatol 2011;64:604-6.
6. Machado M, Moreb JS, Khan SA. Six cases of permanent alopecia after various conditioning regimens commonly used in hematopoietic stem cell transplantation. Bone Marrow Transplant 2007;40:979-82.
7. Baker BW, Wilson CL, Davis AL, Spearing RL, Hart DN, Heaton DC, et al. Busulphan/cyclophosphamide conditioning for bone marrow transplantation may lead to failure of hair regrowth. Bone Marrow Transplant 1991;7:43-7.
8. Gratwohl A, Baldomero H, Aljurf M, Pasquini MC, Bouzas LF, Yoshimi A, et al. Hematopoietic stem cell transplantation: a global perspective. JAMA 2010;303:1617-24.
9. Vowels M, Chan LL, Giri N, Russell S, Lam-Po-Tang R. Factors affecting hair regrowth after bone marrow transplantation. Bone Marrow Transplant 1993;12:347-50.
10. Tallon B, Blanchard E, Goldberg LJ. Permanent chemotherapy-induced alopecia: case report and review of the literature. J Am Acad Dermatol 2010;63:333-6.
11. Paus R, Cotsarelis G. The biology of hair follicles. N Engl J Med 1999;341:491-7.
12. Thibaut S, Gaillard O, Bouhanna P, Cannell DW, Bernard BA. Human hair shape is programmed from the bulb. Br J Dermatol 2005;152:632-8.
13. Selleri S, Seltmann H, Gariboldi S, Shirai YF, Balsari A, Zouboulis CC, et al. Doxorubicin-induced alopecia is associated with sebaceous gland degeneration. J Invest Dermatol 2006;126:711-20.
14. Amoh Y, Li L, Katsuoka K, Hoffman RM. Chemotherapy targets the hair-follicle vascular network but not the stem cells. J Invest Dermatol 2007;127:11-5.
15. Wood JM, Decker H, Hartmann H, Chavan B, Rokos H, Spencer JD, et al. Senile hair graying: H2O2-mediated oxidative stress affects human hair color by blunting methionine sulfoxide repair. FASEB J 2009;23:2065-75.
16. Paus R, Haslam IS, Sharov AA, Botchkarev VA. Pathobiology of chemotherapy-induced hair loss. Lancet Oncol 2013;14:e50-9.
17. Ljungman P, Hassan M, Bekassy AN, Ringden O, Oberg G. Busulfan concentration in relation to permanent alopecia in recipients of bone marrow transplants. Bone Marrow Transplant 1995;15:869-71.
18. Kluger N, Jacot W, Frouin E, Rigau V, Poujol S, Dereure O, et al. Permanent scalp alopecia related to breast cancer chemotherapy by sequential fluorouracil/epirubicin/cyclophosphamide (FEC) and docetaxel: a prospective study of 20 patients. Ann Oncol 2012;23:2879-84.
19. de Jonge ME, Mathot RA, Dalesio O, Huitema AD, Rodenhuis S, Beijnen JH. Relationship between irreversible alopecia and exposure to cyclophosphamide, thiotepa and carboplatin (CTC) in high-dose chemotherapy. Bone Marrow Transplant 2002;30:593-7.