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Transfusion characteristics and hemovigilance of pediatric cancer patients: A single-center observational study

Adriana Inés Urdiales Valarezo [ID] [1], Enmanuel Isidoro Guerrero Quiroz [ID] [1, 2]

1. Postgraduate Department of Pediatrics, Faculty of Medical Sciences, University of Cuenca, Ecuador
2. Hematology Service, SOLCA Institute, Núcleo de Cuenca, Ecuador.

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Abstract

Introduction: Transfusion therapy is not risk-free, and hemato-oncological patients are the most commonly transfused patients; hence, hemovigilance is needed. The objective of the present study was to identify the transfusion characteristics and hemovigilance of pediatric patients with cancer at the SOLCA Institute-Cuenca from January to December 2021.

Method: A descriptive study was carried out with all patients under 18 years of age who required transfusions, and all blood transfusions were performed at SOLCA-Cuenca 2021. The data were collected in a previously validated form and analyzed with the SPSS v25.0 program; the results are presented as the frequency, percentage, mean, and standard deviation.

Results: A total of 73 patients and 620 transfusions were studied; 45.2% were adolescents, 63% were male, 98.6% were mixed race, 76.7% were urban, and 83.5% were ORH+ patients. B-cell acute lymphoblastic leukemia (49.3%) and induction chemotherapy (41.1%) were used. A total of 58.9% had a transfusion history, and 4.1% had a previous reaction (urticaria). The average number of transfusions per patient was 8.49, and 7.1% of the patients were premedicated with steroids. Concentrated erythrocytes were mainly transfused (49%) for anemia (95.4%) at 9.32 ml/kg (mean) in 121 to 180 minutes (56.9%). Of the 3.1% of reactions detected, 100% were immediate, 84.2% were noninfectious (urticaria), definitive, and were treated with medications (84.2% steroid); 79% of the reactions were mild; they were secondary to erythrocyte concentrates (47.4%), apheresis (47.4%) and B-cell acute lymphoblastic leukemia (31.5%).

Conclusions: Patients with B-cell acute lymphoblastic leukemia required additional blood transfusions, mainly erythrocyte concentrates, while transfusion reactions were frequently associated with erythrocyte concentrates and apheresis.

Keywords:

MeSH: Blood Safety, Blood Transfusion, Transfusion Reaction, Neoplasms, Pediatrics.

* Corresponding author.

Email: < enmanuel.guerrero@ucuenca.edu.ec > Enmanuel Isidoro Guerrero Quiroz/Address: 32Q4+HR4, Pje. of Paradise, Cuenca. Faculty of Medical Sciences, Campus Paraíso, University of Cuenca, Cuenca-Ecuador. Telephone [593] 07 4051000 ext 3158.

Introduction

Adverse transfusion reactions (ATRs) constitute the unwanted effects that occur during transfusion and must be classified and analyzed to determine their cause and prevent possible subsequent responses. This set of procedures is known as hemovigilance. For a transfusion to be safe, the benefit/risk ratio must be assessed, and the correct prescription of the blood component must be monitored [1, 2].

González et al. estimated that 20% of hemotransfusions will cause some reactions, of which 0.5% are profound; hence, establishing a hemovigilance system is essential. With the incorporation of this system, the effectiveness and efficiency of the transfusion chain are expected to improve by implementing the required changes [3, 4].

Hemovigilance ranges from the indication to transfuse a component to stages after the transfusion act to ensure a correct prescription based on the clinical status of the patient, correct identification of the donor and recipient, adequate storage of the blood component, and monitoring. Other alternatives to transfusion must be considered to establish optimal treatment, such as granulocyte colony-stimulating factor and erythropoietin [5].

Transfusion practices are frequently used in most specialties. However, these procedures are not free of complications such as urticaria and disseminated intravascular coagulation (DIC), among others, without ruling out the possibility of death, implying great responsibility for staff health [4, 6].

The incidence of ATRs in adults is lower than in pediatric patients, with an average of 252 and 538-620/100,000 transfusions, respectively [7]. In medical practice, it has been shown that hemato-oncology patients are exposed to continuous transfusions due to the myelosuppression they suffer from their underlying disease or because of myeloablative and immunosuppressive treatment, reflecting spinal depression with low hemoglobin, platelet, and absolute neutrophil counts [8, 9].

The present work aimed to determine the transfusion characteristics and hemovigilance of pediatric patients with cancer at the SOLCA-Cuenca Institute from January to December 2021.

At the Latin American level, in 2017, 57% of the patients were diagnosed with concentrated red blood cells (RBCs), 21.6% with platelet concentrates (PCs), 14% with fresh frozen plasma (FFP), 3% with cryoprecipitates and 3.5% with platelets obtained by apheresis [10]. In the European survey, 15,367 oncological patients were evaluated; at six months, the prevalence of anemia was 39%, and the incidence was 53.7%, with 14.9% requiring transfusion [8].

As mentioned, transfusion can trigger unwanted effects; Bossa & Valenzuela reported the relationship of ATRs with RBCs (40%), PCs (32%), and FFP (27%) [11]. According to the documentation issued by France and the United Kingdom, the primary reaction associated with high rates of morbidity and mortality is acute lung injury (TRALI). Moreover, errors in the administration of components (EAC) can occur due to failures in donor/recipient identification or the administration of the derivative [4].

Cando Cruz (2016) suggested that the impact of transfusion decreased by complying with the transfusion request and relegating part of the responsibility to each health team member [12]. Therefore, because of the importance of incorporating a surveillance system and, based on this context, we propose the following research question: What are the transfusion characteristics and hemovigilance of pediatric patients with cancer at the SOLCA Cuenca Institute, January-December 2021? This study aimed to describe the clinical characteristics and ATRs of pediatric neoplastic patients who received transfusion therapies.

Materials and methods

Type of study

The study was observational and descriptive. The source was retrospective. The observation is transversal.

Scenery

The study was conducted in the Department of Pediatrics of the SOLCA Institute-Cuenca, a fourth-level reference health facility for the country's southern region in zone 6 in Azuay, Cuenca, Ecuador. The study period was from January 1, 2021, to December 31, 2021.

Participants

Pediatric patients under 18 years of age who were hospitalized with an established diagnosis of neoplasia and required blood transfusions were included in the study. All incomplete records were excluded from the analysis.

Variables

The variables analyzed in this study included the following:

Age, sex, ethnicity, origin, transfusion history, previous ATR, blood group, type of cancer, treatment phase, indication for transfusion, premedication, blood component, volume, duration and frequency of transfusion, identification of the reaction in time, infectivity (acute and late infectious or not), severity and degree of imputability, medical and laboratory procedure carried out against the response and incidents that occurred.

Data sources/measurements

The observational method and survey technique were used through a form designed for data collection, facilitating the capture of information directly from the medical records. To ensure the quality of the data, a review and comparison were carried out with the original medical records of the Softcase® system.

Academic supervision: The development of the study was under the supervision of a hematologist attending the institution's hematology service.

Study Procedure

As part of the institutional protocol, health personnel registered all blood-transfused patients in their clinical history and via the Softcase system; in this way, the transfused patients were identified, and their respective follow-up was carried out. The questionnaire information was transcribed and statistically analyzed to obtain aggregate results. The confidentiality and protection of the data collected in the questionnaire were maintained.

Control of sources of bias

To minimize interviewer, information, and memory biases, the researchers rigorously followed a guide and records established in the research protocol. The strict application of participant selection criteria reduced observation and selection biases. All clinical and paraclinical variables recorded during the study period were documented. Two researchers examined each record independently and in parallel, ensuring consistency before inclusion in the database.

Universe and Sample

The universe comprised all the patients registered in the institution. The sample size was nonprobabilistic and discretionary since all incident cases in the study period were included.

Quantitative variables

Inferential statistics were used. Categorical results are expressed as frequencies and percentages.

Statistical analysis

The collected data were entered into a database developed in Microsoft Excel 2019, which allowed them to be organized according to specific variables. The descriptive results are shown as absolute frequencies and percentages. For numerical variables, means and

standard deviations were calculated and are presented in tables. The interpretations and discussions of these findings were compared to those of the academic literature and similar studies published in peer-reviewed scientific journals. The SPSS 25.0 statistical package was used for the analysis (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Results

Study participants

A total of 73 patients who received 620 transfusions were included in the study.

Patient characteristics

Table 1 shows the sociodemographic characteristics of the transfused patients, where adolescents, males, individuals of mixed ethnicity, and individuals of urban origin predominated (Table 1). Table 2 shows that most transfused patients had ORH+ blood cells, had B-cell ALL, and were in the induction phase. Of the 73 patients studied, 43 (58.9%) had a history of transfusion, and 3 (4.1%) had previous ATRs (urticaria). The mean transfusion frequency per patient was 8.49 ± 13.19 (Table 2).

Transfusions

Based on the 620 transfusions, Table 3 reported that steroids were the most commonly used premedication agent. Red blood cells (RBCs) were the most widely used transfusion agent, followed by apheresis; the main indications for transfusion were anemia and thrombocytopenia.

The mean volume (ml/kg) administered was 9.32 ± 5.06 for RBCs, 8.38 ± 4.15 for PCs, 4.19 ± 2.86 for cryoprecipitates, 11.54 ± 8.30 for FFP and 7.38 ± 3.83 for apheresis.

Table 4 shows that the RBC was transfused most frequently at > 2 hours to 3 hours, PC and apheresis at <30 minutes, and cryoprecipitation and FFP at > 30 minutes to 1 hour (Table 4).

Table 1. Frequency and percentages of pediatric neoplasm patients requiring transfusions.

Characteristics	Frequency	%
Age		
<2 years	7	9.6
From 2 to 5 years	19	26.0
From 6 to 9 years	14	19.2
From 10 to 17 years	33	45.2
Sex		
Male	46	63.0
Female	27	37.0
Ethnicity		
Hispanic	72	98.6
Indigenous	1	1.4
Origin		
Urban	56	76.7
Rural	17	23.3

Table 2. Clinical characteristics of the patients.

Variable	Frequency	%
Typing		
Or HR+	61	83.5
Or RH -	1	1.4
A RH +	8	11.0
A RH -	3	4.1
Type of cancer		
Acute lymphoblastic L. B cells	36	49.3
Bone tumors	6	8.2
Acute myeloid leukemia	5	6.8
Hepatoblastoma	4	5.5
Hodgkin 's disease	3	4.1
Hodgkin lymphoma	3	4.1
Acute promyelocytic leukemia	3	4.1
Acute lymphoblastic leukemia T cells	2	2.7
Central nervous system tumor	2	2.7
Germ cell tumor	2	2.7
Others [1]	7	9.8
Treatment phase		
Induction	30	41.1
Consolidation	3	4.1
Maintenance	13	17.8
Adjuvant	5	6.8
Neoadjuvant	8	11.0
Rescue	14	19.2

[1] Others: Wilms tumor, Chronic myeloid leukemia, Thymus carcinoma, Acute leukemia mixed phenotype B/myeloid, Esthesioneuroblastoma , Rhabdomyosarcoma, Nasoangiofibroma.

Table 3. Transfusion characteristics.

Variable		Frequency n=620	%
Premediation			
Steroid		44	7.1
Antihistamines		4	0.6
Acetaminophen		2	0.3
Transfused blood component			
RBC		304	49.0
Aphaeresis		213	34.4
PC		76	12.3
FFP		24	3.9
CHILD		3	0.5
Transfusion indication			
RBC	Anemia	290	95.4
	Bleeding	14	4.6
Afer	Thrombocytopenia	195	91.5
	Bleeding	18	8.5
PC	Thrombocytopenia	70	92.1
	Bleeding	6	7.9
FFP	D.I.C.	17	70.8
	Bleeding	7	29.2
CRYO	Hypofibrinogenemia	2	66.7
	D.I.C.	1	33.3

RBC: concentrated red blood cell; PC: platelet concentrate; CRYO: cryoprecipitate; FFP: fresh frozen plasma; DIC: disseminated intravascular coagulation.

Table 4. Duration of transfusion.

Variable		Frequency n=620	%
Prescribed time			
RBC n=304	<30 minutes	2	0.7
	>30 minutes to 1 hour	4	1.3
	>1 hour to 2 hours	105	34.5
	>2 hours to 3 hours	173	56.9
	>3 hours to 4 hours	18	5.9
	>4 hours	2	0.7
Afer n=213	<30 minutes	175	82.2
	>30 minutes to 1 hour	35	16.4
	>1 hour to 2 hours	1	0.5
	>2 hours to 3 hours	2	0.9
PC n=76	<30 minutes	1	33.3
	>30 minutes to 1 hour	2	66.7
FFP n=24	<30 minutes	8	33.3
	>30 minutes to 1 hour	9	37.5
	>1 hour to 2 hours	7	29.2
CRYO n=3	<30 minutes	1	33.3
	>30 minutes to 1 hour	2	66.7

RBC: concentrated red blood cell; PC: platelet concentrate; CRYO: cryoprecipitate; FFP: fresh frozen plasma.

Table 5. Management of adverse reactions.

Variable	Frequency n=19	%
Medical procedure		
Medicine administration	19	100
Discontinuation of transfusion	2	10.5
Oxygen replacement	1	5.3
Intravenous fluid administration	1	5.3
Medications administered		
Steroid	16	84.2
Antihistamine	10	52.6
Analgesic	2	10.5
Antipyretic	1	5.3

Adverse Transfusional Reactions (ATRs)

Among the blood transfusions performed, ATRs were identified in 3.1% (19 patients) of the patients and were classified as immediate (100%) or acute (noninfectious): urticaria in 84.2% (16), anaphylaxis in 10.5% (2) and RTFNH in 5.3% (1). Among them, 79% (15) had mild disease, 10.5% (2) had moderate disease, and 10.5% (2) had severe disease. In addition, a degree of imputability of 100% was assessed as a definitive reaction. No infectious ATRs were identified.

As shown in Table 5, all patients with ATRs received medication, with steroids predominating. Notably, no laboratory tests were performed immediately after the reaction, and the related blood components were red blood cells (RBCs) or apheresis agents (47.4% each), followed by a PC (5.2%).

Table 6 shows that patients with B-ALL and AML after induction required more RBC transfusions and apheresis, followed by those with hepatoblastoma after neoadjuvant chemotherapy, which required more RBCs and PCs. ATR was observed more frequently in patients with B-cell ALL and was associated with apheresis (47.3% urticaria), RBC (36.8% urticaria, 5.3% anaphylaxis, 5.3% RTFNH), and PC (5.3% anaphylaxis). Notably, there were no EACs.

Discussion

Pediatric cancer patients frequently require blood transfusions. This research was carried out with 73

patients and 620 transfusions, and we showed that the majority of the individuals in the transfusion population were adolescents and that the men suffered from B-ALL and were in the induction phase. In addition, more than half of the patients had a history of transfusion, which agrees with the results of Jati et al. [13] and Freitas et al. [14]. Epidemiologically, this occurs because after the age of 15, cancer is 2.7 times more common, and men are more susceptible to developing oncological pathologies from their genetic basis. Likewise, ALL is the most common type of cancer in pediatrics and requires the most transfusions, as it directly affects the bone marrow and its hematopoiesis. Likewise, Alcayed et al. [15] and Velasquez [16] agree that during induction, more transfusions are performed due to the myelosuppression resulting from intensive treatment in this phase; hence, Freitas et al. [14] and Gallardo et al. [17] reported more than 60% of previous transfusions, as described in their work.

Table 6. Classification is according to the type of cancer and treatment phase with the kind of blood component, frequency of administration, and reactions.

Variable		Homocomponent transfused										ATR	
Type of cancer	Phase tto	RBC		PC		CRYO		FFP		Aphaeresis			
		n=304	%	n=76	%	n=3	%	n=24	%	n=213	%	n=19	%
LLA cells b	Induction	48	15.8	17	22.4	---	---	---	---	31	14.6	2	10.5
	Consolidation	17	5.6	1	1.3	---	---	---	---	21	9.9	---	---
	Maintenance	28	9.2	5	6.6	---	---	---	---	24	11.2	2	10.5
	Rescue	37	1.,2	12	15.8	1	33.3	10	41.7	7	3.3	2	10.5
LLA cells T	Induction	12	3.9	3	4	---	---	---	---	7	3.3	1	5.3
	Consolidation	5	1.6	---	---	---	---	---	---	---	---	---	---
Disease of Hodgkin	Induction	6	2	1	1.3	---	---	1	4.2	1	0.5	1	5.3
Lymphoma not Hodgkin	Induction	10	3.3	3	4	---	---	1	4.2	11	5.2	4	21
Tumor of Wilms	Neoadjuvant	1	0.3	---	---	---	---	---	---	---	---	1	5.3
	Rescue	9	3	3	4	---	---	---	---	5	23	3	15.7
Tumor of the CNS	Adjuvant	8	2.6	---	---	---	---	---	---	5	23	---	---
Tumors bone	Adjuvant	1	0.3	---	---	---	---	---	---	---	---	---	---
	Neoadjuvant	7	23	1	1.3	---	---	2	8.3	---	---	1	5.3
	Rescue	7	23	---	---	---	---	---	---	---	---	---	---
Leukemia acute myeloid	Induction	3. 4	11.2	6	7.8	---	---	2	8.3	35	16.4	1	5.3
	Consolidation	15	4.9	2	2.6	---	---	---	---	26	12.2	---	---
	Maintenance	9	3	3	4	---	---	---	---	16	7.5	---	---
	Rescue	1	0.3	2	2.6	---	---	---	---	3	1.4	---	---
Myeloid leukemia chronicle	Induction	5	1.6	1	1.3	---	---	---	---	---	---	1	5.3
Leukemia acute promyelocytic	Induction	15	4.9	4	5.3	---	---	2	8.3	10	4.7	---	---
	Rescue	---	---	---	---	---	---	---	---	1	0.5	---	---
Tumor of germ cells	Adjuvant	2	0.7	---	---	---	---	---	---	---	---	---	---
	Neoadjuvant	3	1	2	2.6	---	---	---	---	1	0.5	---	---
Carcinoma of thymus	Rescue	2	0.7	---	---	---	---	---	---	---	--	---	---
ALMP B/myeloid	Rescue	2	0.7	---	---	---	---	---	---	2	0.9	---	---
Hepatoblastoma	Neoadjuvant	17	5.6	9	11.8	2	66.7	6	25	7	3.3	---	---
Esthesioneuroblastoma	Rescue	2	0.7	---	---	---	---	---	---	---	---	---	---
Rhabdomyosarcoma	Rescue	---	---	1	1.3	---	---	---	---	---	---	---	---
Nasoangiofibroma	Adjuvant	1	0.3	---	---	---	---	---	---	---	---	---	---

ALL: acute lymphocytic leukemia. CNS: Central Nervous System. ALMP: acute leukemia mixed phenotype.

In the present study, less than 10% of premedication for transfusions was carried out, whereas Gallardo et al. [17] reported less than 30% premedication for transfusions; this is probably because, in the Institution's protocol, premedication is carried out only in the case of a significant previous ATR, positive Coombs or emergency transfusions involving blood components from a different blood group than the patient to avoid hiding immune pictures. On the other hand, the present investigation reported that approximately half of the transfusions involved RBC, followed by apheresis, similar to the findings of Alcayed et al. [15]. Pedrosa et al. [19] contrast with those of Jati et al. [13] and Kohorst et al. [18], who concluded that more than 50% of patients were transfused with PC. This depends on the degree of myelosuppression and condition of the cell lines, as well as the complications and comorbidities present, such as hemorrhages, surgical pathologies, and sepsis. Therefore, we also assessed the indications for transfusion, highlighting anemia and thrombocytopenia in more than 90% of the patients, agreeing with what was expressed by Pardo et al. [8] and Flores [20], who also indicated that oncological pathology alone suppresses hematopoiesis, triggering anemia and thrombocytopenia. Additionally, it was determined that the RBCs were transfused at an average volume close to 10 ml/kg, mostly at 121-180 minutes; however, there are no studies based on these variables, but the transfusions carried out were carried out following established protocols, such as those detailed by the Spanish Society of Blood Transfusion and Cellular Therapies [2].

We reported a low percentage of transfusions that led to ATRs, all of which were immediate and classified as acute noninfectious: urticaria, anaphylaxis, or RTFNH; these findings are similar to what was published by Kohorst et al. [18] and Reina [21], whose reactions were between 2 and 2.5%. Furthermore, Bossa et al. [11], Freitas et al. [14], Pedrosa et al. [24], and Guo et al. [26] agree that immediate reactions are predominant and that late reactions are infrequent, with allergic reactions and RTFNH prevailing; these effects occur because the immune system of cancer patients is depressed and unable to reject the antigen from transfusion. Now, from the unwanted impacts resulting in our study, the majority of the adverse effects were mild and entirely treated with medications (mainly steroids), similar to the findings of Jati et al. [13], Pedrosa et al. [24], and Grandi et al. al. [25]; Likewise, Freitas et al. [14] and Ghataliya et al. [22], with the difference that their management was based on the use of antihistamines; therefore, it is essential to mention that the majority of reactions are mild and resolve after the administration of medications; at the Institute, the most commonly used protocol is steroids.

We also appreciate that a large portion of the reactions was associated with RBC and apheresis, similar to the findings of Bossa et al. [11]. and Grandi et al. [25], where RBC prevailed and, with those of Kracalik et al. [26], where apheresis predominated, unlike those reported by Freitas et al. [14], Lemssahli et al. [23] and Pedrosa et al. [24], who associated it mainly with platelets. This peculiarity is because both erythrocytes and platelet concentrates can contain leukocytes and proinflammatory cytokines that trigger reactions; as we observed, most transfusions were performed with RBCs and apheresis (they contain platelets). In addition, the results indicated that approximately 30% of patients with B-ALL developed ATRs, which was also observed in the studies of Jati et al. [13] and Guo et al. [25] and may be secondary to greater exposure. to transfusions, as well as the leukocytes and cytokines of the transfused blood components.

Finally, it is essential to note that among solid tumors, hepatoblastoma requires the most transfusions; however, there are no studies in the literature that support this phenomenon; therefore, it must be remembered that some coagulation factors are produced at the liver level. These findings can be altered by the presence of tumors triggering coagulopathies, bleeding, etc., but these results must be corroborated with other studies.

This research allowed us to determine the characteristics of patients who required more transfusions, the most commonly used blood component, ATRs, and their management.

Limitations

This research has limitations in the data collection since some variables that limited the increase in cases due to incomplete data were not recorded in the system.

Conclusions

- Adolescents, males, mestizos, and patients from the urban sector predominated in the study group.
- More than half of the population had a transfusion history, and urticaria was the only previous ATR reported. The most common were the ORH+ blood group, patients with B-cell ALL, and patients in the induction phase. Steroids and red blood cells (RBCs) are the most commonly used drugs and blood components. The transfusion volume and time were within the recommended parameters.
- An immediate transfusion reaction was the most common reaction. No infectious reactions were recorded; the majority of the reactions were mild and Grade 3.
- All adverse reactions were treated with medications, and no immediate laboratory tests were performed.
- The blood components that produced the most severe adverse reactions were red blood cells (RBC) and apheresis.
- Patients with B-ALL or AML in the induction phase require additional RBC transfusions and apheresis. Its frequency was higher than other pathologies; the most frequent ATR was urticaria.
- There were no EACs, and the only incidents recorded were related to ATRs.

Abbreviations

DIC: disseminated intravascular coagulation.
RBC: concentrated red blood cell.
PC: platelet concentrate.
CRYO: cryoprecipitate.
ALL: acute lymphoblastic leukemia.
ALMP: Acute leukemia mixed phenotype.
FFP: fresh frozen plasma.
ATR: adverse transfusion reaction;
CNS: central nervous system
Treatment: treatment.

Supplementary information

No supplementary materials are declared.

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Author contributions

Adriana Inés Urdiales Valarezo: Conceptualization, data curation, formal analysis, acquisition of funds, research, writing - original draft.
Enmanuel Isidoro Guerrero Quiroz: Conceptualization, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing - Review and Editing.
All the authors read and approved the final version of the manuscript.

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Availability of data and materials

The data were collected from medical archives and are not publicly available due to patient confidentiality but are available through the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

The study obtained approval from the Health Research Bioethics Committee (COBIAS) of the University of Cuenca and the Research Headquarters of the SOLCA Cuenca Institute. Informed consent was not obtained because the study did not involve direct interaction with the patient. We also worked with the information recorded in the clinical history and the Softcase 2.0 system.

Publication consent

Specific images of patient photographs, X-rays, ultrasounds, or MRIs were not available.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Author information

Not declared

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