Scientific Research Publishing

Case Reports in Clinical Medicine, 2024, 13, 490-501
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Osteoarticular Manifestations of Pediatric Acute Lymphoblastic Leukemia: Study of an Observation and Review of the Literature

Fatou Sow Diouck[1*], Adama Bah[2], Harouna Ousmane Sow[3], Moustapha Niasse[1], Amy Thiam[4], Birahim Lo[5], Matar Ndiaye[5], Saidou Diallo[1]

[1]Department of Rheumatology, Aristide Le Dantec University Hospital, Dakar, Senegal
[2]Department of Rheumatology, Ignace Deen National Hospital, Conakry, Guinea
[3]Departement of Hematology Biology and Oncology Hematology, National Blood Transfusion Center, Dakar, Senegal
[4]Department of Clinical Hematology, Dalal Diam Hospital, Dakar, Senegal
[5]Department of Medical, Aristide Le Dantec University Hospital, Dakar, Senegal
Email: *fatsha8@gmail.com

How to cite this paper: Diouck, F.S., Bah, A., Sow, H.O., Niasse, M., Thiam, A., Lo, B., Ndiaye, M. and Diallo, S. (2024) Osteoarticular Manifestations of Pediatric Acute Lymphoblastic Leukemia: Study of an Observation and Review of the Literature. *Case Reports in Clinical Medicine*, **13**, 490-501.
https://doi.org/10.4236/crcm.2024.1311058

Received: September 19, 2024
Accepted: November 24, 2024
Published: November 27, 2024

Abstract

Introduction: Acute lymphoblastic leukemia (ALL) is a monoclonal hematological malignancy characterized by infiltration of the bone marrow by more than 20% of hematopoietic cells with blocked differentiation, called blasts, belonging to the lymphoblastic lineage of lymphoid nature (B or T lymphoblasts). Around 40% of childhood cancers are leukemias, and 85% of these are ALL. The first descriptions of osteoarticular involvement as an inaugural manifestation date back to 1913 with August Strauch. Our aim was to describe an isolated case of ALL with osteoarticular manifestations as an inaugural event supported by a review of the literature. **Observation:** A 14-year-old adolescent with no known pathological history was referred from pediatrics to investigate the etiology of a chronic peripheral polyarthritis that had been progressively evolving for about seven weeks. Clinically, he presented with chronic peripheral polyarthritis, polysynovitis, non-ankylosing deforming involving knees, shoulders, wrists, and proximal interphalangeals (PIP), and a leukemic facies (facial puffiness and periorbital erythema). Biological investigations revealed a non-specific inflammatory syndrome with a VS of 60 mm in the first hour and CRP increased to 45 mg/l (N ≤ 6 mg/l). The blood count showed hyperleukocytosis at 25,600/mm^3 with lymphocyte predominance at 18,660/mm^3, normocytic normochromic anemia with hemoglobin at 11 g/dl, and hyperplakettosis at 510,000/mm^3. The blood smear showed 37% blasts confirmed on the medullogram, with more than 20% blastic invasion and a predominance of common B-type lymphocytes on immunophenotyping with negative

Philadelphia. Immunological, renal, infectious, hepatic, lipid, and uricemia tests were normal. These clinical and paraclinical findings led to the diagnosis of B-type lymphocytic leukemia. The patient received multidrug therapy for induction, consolidation, and intensification. As part of the management of his osteoarticular disorders, infiltrations of the large painful joints were carried out with an adequate phosphocalcic intake. **Conclusion:** Leukemia is a diagnostic and therapeutic emergency, and osteoarticular damage may be the initial presentation.

Keywords

Acute Lymphoblastic Leukemia, Osteoarticular Manifestations

1. Introduction

Acute lymphoblastic leukemia (ALL) is a monoclonal hematological malignancy characterized by infiltration of the bone marrow by more than 20% of hematopoietic cells with blocked differentiation called blasts belonging to the lymphoblastic lineage of lymphoid nature (B or T lymphoblasts) [1]. Around 40% of childhood cancers are leukemias, and 85% of these are ALL [2]. In France, it affects between 400 and 500 children annually, making it the most common paediatric cancer [3]. Epidemiological data on the overall prevalence of osteoarticular involvement in pediatric lymphoblastic leukemia are still poorly known. Nevertheless, in Europe, the study by Pêcheux *et al.*, in Belgium, carried out over a period of 30 years, found 104 cases with 85% pre-B ALL and 12% T ALL, with 67% of patients having osteoarticular involvement, an average age of 5.9 years and a sex ratio of 1.6. [4] In Brazil, Teresa Robazzi reported 313 cases of leukemia over a 20-year period, with 54.7% osteoarticular involvement, a mean age of 6.8 years, and a sex ratio of 1.4 [5]. The first descriptions of osteoarticular (OA) involvement as an inaugural manifestation date back to 1913 with August Strauch. Nevertheless, this mode of presentation remains a diagnostic challenge, as the signs of such involvement are not specific to leukemias [6]. The onset of AO involvement in ALL is multifactorial: patient-, disease- or treatment-related [2]. Depending on their chronology, they may be inaugural, leading to erroneous and delayed diagnosis, as they are often confused with juvenile idiopathic arthritis or infectious causes. Or they may occur during or after treatment, mainly due to the toxicity of anti-leukemic drugs and corticosteroids. The mainstay of OA management is the etiological treatment of leukemia [7], but intra-articular corticosteroid infiltration, calcium, and vitamin D supplementation, the use of biphosphates in osteoporosis, and orthopedic and/or surgical treatment may also be used, especially in the case of osteonecrosis [2].

The aim of this study is to describe an isolated case of ALL with osteoarticular manifestations and to review the literature in order to establish pathophysiological mechanisms.

2. Observation

A 14-year-old adolescent with no specific pathological history was referred to us from the pediatric department for the etiological investigation of chronic peripheral polyarthritis, which had been progressively evolving for about seven weeks. Clinical examination revealed chronic peripheral polyarthritis, polysynovitis, deforming but not ankylosing, with involvement of the knees, shoulders, wrists, and proximal interphalangeal (PIP) and dactylitis (Figure 1), associated with a leukemic facies (facial puffiness and periorbital erythema). (Figure 2)

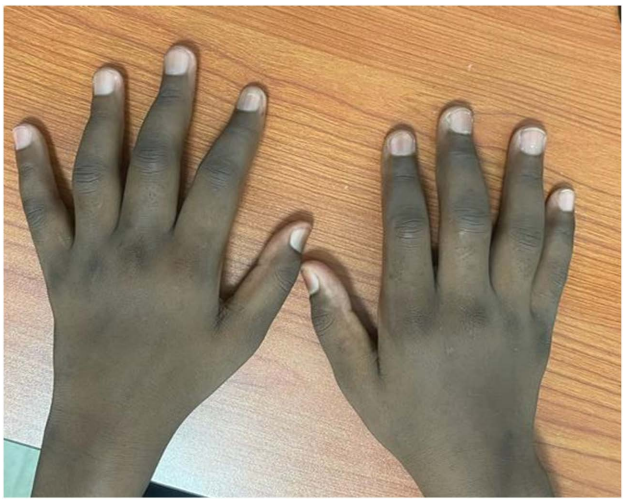

Figure 1. Dactylitis in acute lymphoblastic leukemia.

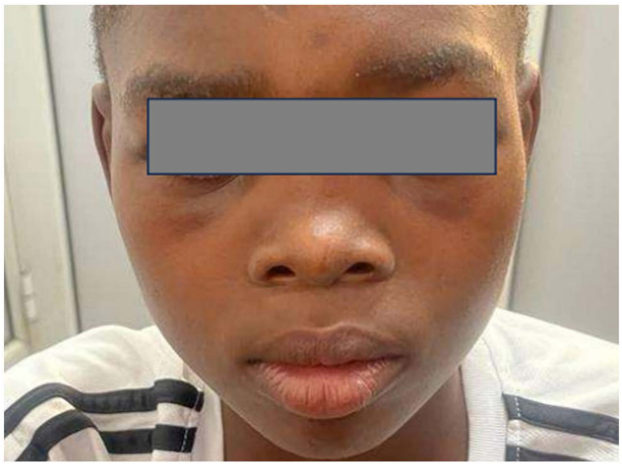

Figure 2. Periorbital erythema (leukemic facies).

Biological investigations revealed a non-specific inflammatory syndrome with a VS of 60 mm in the first hour and CRP increased to 45mg/l (N ≤ 6 mg/l). The blood count showed hyperleukocytosis at 25,600/mm^3 with lymphocyte predominance at 18,660/mm^3, normocytic normochromic anemia with hemoglobin at 11 g/dl and hyperplakettosis at 510,000/mm^3. The blood smear showed 37% blasts confirmed on the medullogram, with over 20% blastic invasion and a common B-

type lymphocytic predominance on immunophenotyping with negative Philadelphia. Renal (uremia, creatininemia and 24-hour proteinuria) and hepatic (blood glucose, lipids, uricemia, infectious diseases) tests were unremarkable. Hand X-rays (**Figure 3**) and abdominal ultrasound for organomegaly were also unremarkable. The diagnosis of B-type lymphocytic leukemia was made on the basis of these clinical and paraclinical arguments after eliminating: juvenile idiopathic arthritis, with negative immunological findings (rheumatoid factors, anti-CCP antibodies, antinuclear antibodies, and ASLO); paraneoplastic arthritis, with a normal thoraco-abdominopelvic CT scan and, above all, improvement after local infiltration with delayed corticosteroids and initiation of multidrug therapy within the first few weeks of treatment. The patient also received phosphocalcic supplementation in accordance with his needs.

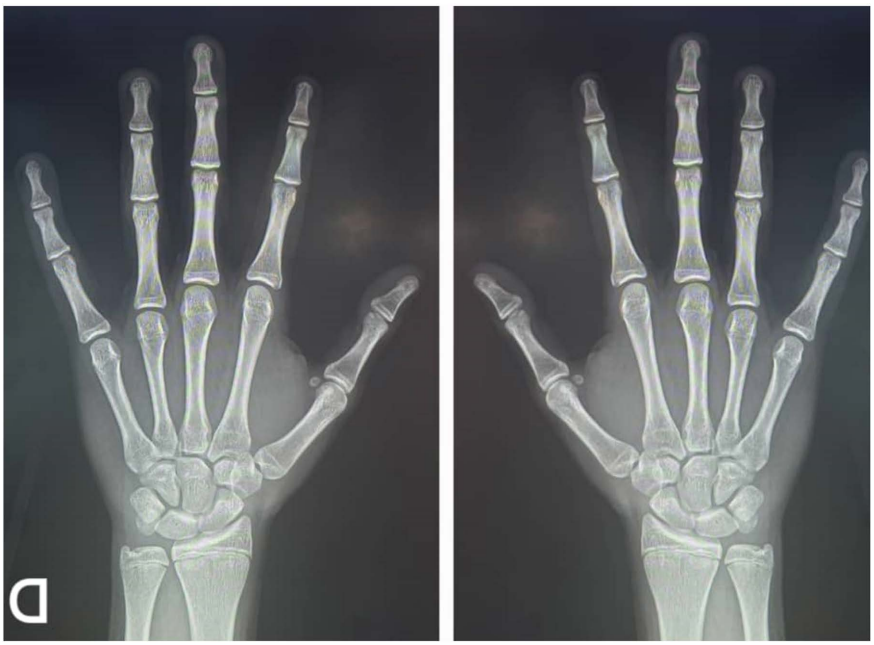

Figure 3. X-ray of the front hand.

3. Discussion

The osteoarticular manifestations of pediatric acute lymphoblastic leukemia are of physiopathological, epidemiological, diagnostic and therapeutic interest.

The hematopoietic system is organized hierarchically, with hematopoietic stem cells (HSCs) at the top, possessing self-renewal capacities and generating the progenitors of all mature blood elements [8]. As they differentiate, the differentiation potential of the progenitors is restricted until only one type of mature cell is generated [9]. If they are transformed, they acquire or retain self-renewal properties and resistance to apoptosis, with a modified response to proliferative and anti-proliferative signals. Schematically, there is an initiation phase, followed by promotion, progression and then metastasis. In leukemia, this translates into a block in differentiation. The result of a multi-stage transformation process is an accumulation of

genetic alterations affecting the main oncogenic/tumor suppressor pathways, blocking maturation, proliferation and survival. The genetic basis of cancers is already accepted, but it is a fact that in leukemia, the phenomena of recurrent acquired chromosomal translocations are to the fore. The cloning of chromosomal translocation breakpoints associated with human leukemias has identified fusion genes, including the BCR-ABL1 gene responsible for the Philadelphia chromosome, which are involved in the pathogenesis of the disease [10]. Several other genetic mutations have also been identified (**Table 1** and **Table 2**). Environmental factors underlie all chromosomal lesions, including exposure (benzene, pesticides, etc.), ionizing radiation, chemotherapy (alkylating agents, VP16), radiotherapy and infectious diseases (HIV, Epstein Barr Virus, HTLV1) [11]. The so-called de Novo primary in the absence of several identified causes.

Table 1. Examples of mutated or altered genes in B-ALL [9].

Affected genes	Type of anomaly	Remarks
TEL-RUNX1	Translocations	RUNX1 participates in the control of B lymphoid differentiation
E2A-PBX1	Translocations	
MLL Mergers	Translocations	
BCR-ABL1	Translocation	
PAX5	Mutations/deletions/translocations	Participates in the control of B lymphoid differentiation
IKZF1/IKAROS	Mutations/deletions	Participates in the control of B lymphoid differentiation
EBF1	Mutations/deletions	Participates in the control of B lymphoid differentiation
FOXP1	Translocations	
LEF1	Mutations/deletions	Participates in the control of B lymphoid differentiation
E2A	Mutations/deletions	Participates in the control of B lymphoid differentiation
CMYC	Translocations	
CEBPs	Translocations	
ID4	Translocations	Participates in the control of B lymphoid differentiation
CRLF2/TSLPR	Translocations/other rearrangements	Activating mutations associated with mutations in JAK family genes
CDNK2	Mutations/deletions	
RB1	Mutations/deletions	

Table 2. Examples of mutated or altered genes in T-ALL [9].

Affected genes	Type of anomaly	Remarks
NOTCH1	TCR/mutations	
TLX1	TCR	
TLX3	BCL11B/TCR	
HOXA	TCR/BCL11B	
TAL1/SCL, TAL2, LYL1	TCR/other changes	TAL1/SCL: important function in hematopoietic stem cells
LMO1, LMO2	TCR/other changes	LMO2: important function in hematopoietic stem cells
MYB	TCR/other changes	
CALM-AF10	Fusion gene translocations	

Continued

MLL Mergers	Translocations	
NUP218ABL1	Episome-fusion gene	
PTEN	Mutations/deletions	Inactivation
FBW7	Mutations/deletions	Inactivation
PHF6	Mutations/deletions	Inactivation
LEF1	Mutations/deletions	Inactivation
PTPN2	Mutations/deletions	Inactivation
CDKN2A	Mutations/deletions	Inactivation

In the pathophysiology of osteoarticular damage in leukemia, we haven't found a single cause established by the authors. Nevertheless, there are individualized gene mutations (**Table 1** and **Table 2**) [9], the most frequent of which is BCR ABL1, but what interests us most in this table is that of the RUNX genes involved in chromosomal translocations. They are involved in mesenchymal cell differentiation and control of B lymphopoiesis differentiation [9]. The crucial importance of this gene has been highlighted by experiments on mice [12]. In CBFβ-deficient mice, fetal hepatic hematopoiesis is absent before birth, and dwarfism, skeletal malformation, reduced calcification, and delayed ossification occur, hence its role in skeletal and mesenchymal cell development. Mice specifically deleting the Runx1 gene also show reduced ossification, bone density and mandibular defects, indicating an osteoporotic phenotype. Deletion of Runx1 impairs fracture healing. Core-binding factor β (CBFβ) is an essential binding partner for Runx1 [13], stabilizing Runx1 by forming heterodimers without which Runx1 can barely be detected. CBFβ provides Runx1 proteins with an inhibitory domain and enhances their DNA binding. Both act in different processes (**Table 3**) [12], most notably in cartilage and bone formation. As a working model, we have highlighted the particular role of Runx1 in bone formation and inhibition of adipogenesis at early stages, with late activation by RUNX 2 (**Figure 4**) [14].

Table 3. RunX functions [14].

System		Major function
Circulatory system	Hematopoiesis	Runx1 is essential for both definitive embryonic and adult hematopoiesis.
	Leukemia	More than 50 Runx1 mutations, including translocations and point mutations, have been identified as causative factors in multiple leukemias.
	Immune system	Runx1 is involved at multiple stages of the complex cell-fate decisions of T lymphocyte development in the thymus and is important for basophil development and lymphoid tissue inducer cells.
	Angiogenesis	Runx1 regulated the expression of angiogenic and adhesion molecules in endothelial cells (ECs) and increased the angiogenic activity of ECs.
Nervous system		Runx1 is crucial for the diversification of sensory neuron lineages, including sensory neurons in skin epidermis and hair follicles, PNS nociceptive neuron, the neuronal tissue of the olfactory system the homeostasis of glial populations of the CNS and the PNS.

Continued

Tumorigenesis	Runx1 has indirect and direct biological functions in modulating cancer metastasis, proliferation, angiogenesis, cancer stemness and chemoresistance to anticancer drugs.
Cartilage and bone	Runx1 is vital for the early stages of chondrogenesis and osteogenesis, and the homeostasis of skeleton system.
Hair follicles	Runx1 controls timely emergence of hair follicle stem cells and proper maturation during embryogenesis.
Mammary gland	Runx1 is required for the differentiation of luminal cells and is highly expressed in the epithelium of virgin females and post-lactation, but gradually decreases throughout pregnancy.

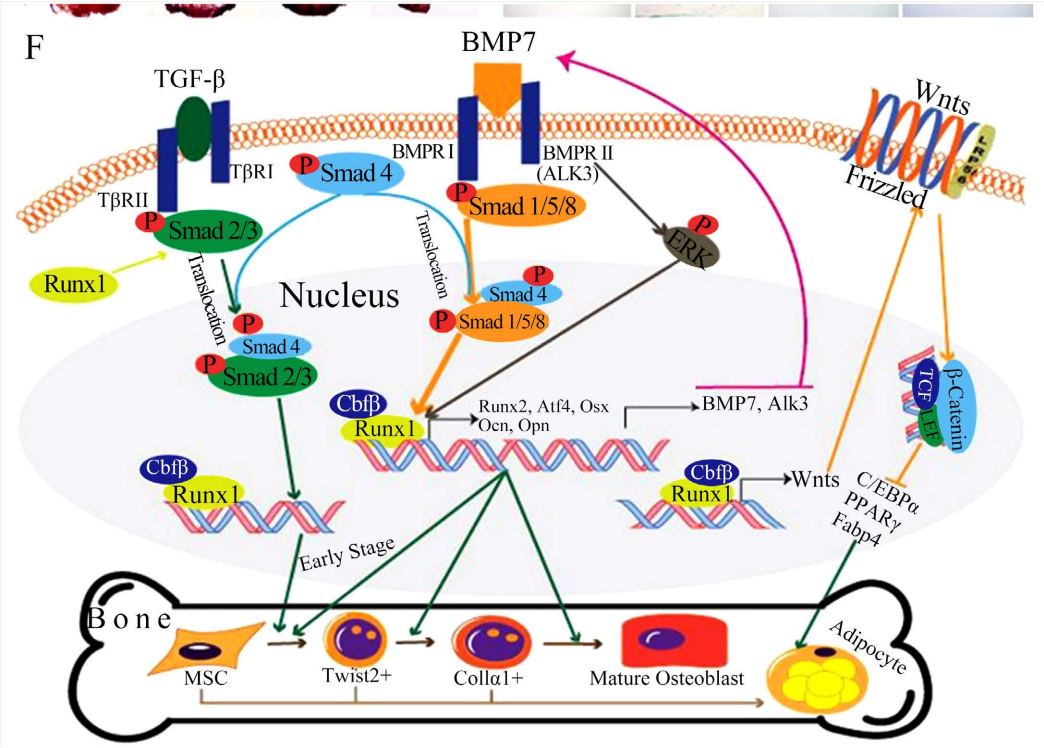

Figure 4. Specific role of Runx1 in bone formation and inhibition of adipogenesis in the early stages, with late activation by RUNX 2 [14].

This is achieved via signaling pathways aided by Smad proteins. Smad proteins are transcription factors to the cell nucleus, modulating target gene expression through Smad DNA-complex binding. Runx1 is a central regulator of osteogenesis and bone homeostasis, orchestrating the BMP, Wnt/*β*-catenin and TGF-beta signaling pathways, regulating early osteoblast differentiation and inhibiting Runx2 expression at later stages of osteoblast differentiation. Runx1 has great potential for the emergence of hematopoietic stem cells and for osteoblastic differentiation. At a much later stage of bone differentiation, we found a role for Runx2 with this modem overexpression in breast cancer-mediated bone metastases. High Runx2 expression was associated with higher metastatic risk and poorer overall survival, and activated osteoclasts (**Figure 5**) [15].

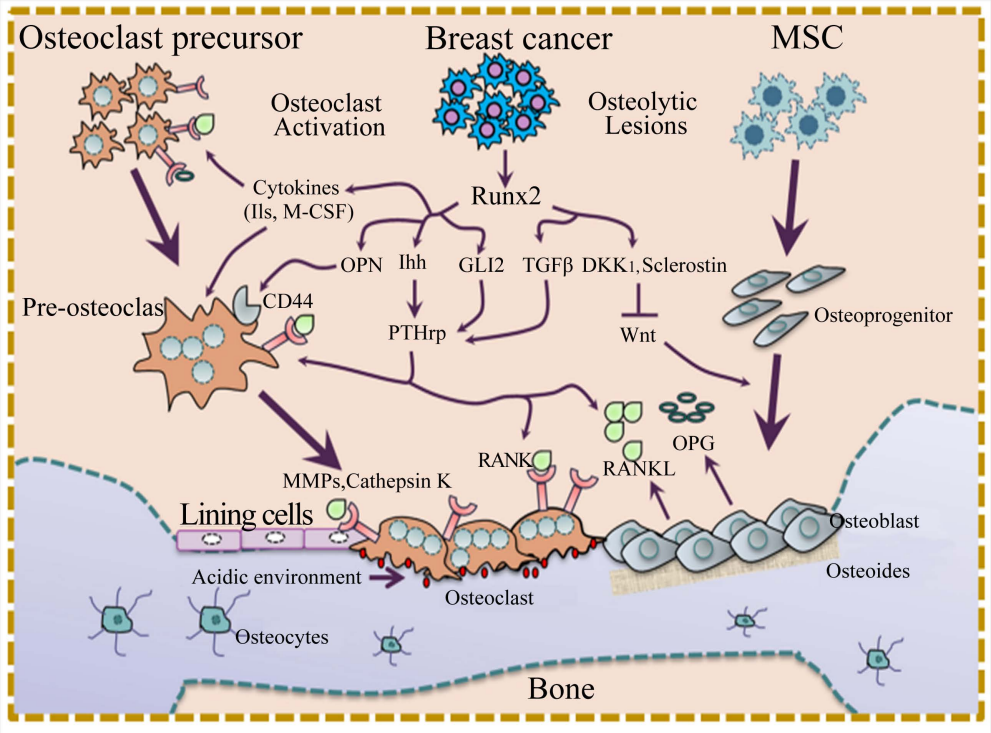

Figure 5. Role of RUNX2 in breast-cancer-mediated bone metastasis. (Image obtained with permission [15]).

So, it's easy to see how mutations in the Runx gene can lead to disturbances in both hematopoiesis and osteogenesis, which are at the root of the various osteo-articular disorders. This leads to a variety of radiological presentations. In our case study, the x-rays of the hands performed are normal, but several authors have found images of bone destruction [16]-[20].

Leukemic bone damage is linked to the pressure exerted by bone marrow infiltration on the periosteum, cytokine-mediated stimulation of osteoclasts, and weakening of the bone matrix, leading to fractures or vertebral compression. In addition to leukemic infiltration of the synovium or leukemic arthritis. Secondary non-specific arthritis, blastic infiltration of the juxtaarticular bone, subcapsular or intra-articular haemorrhage, complex immune deposits, microcrystalline or septic arthritis may also occur [2].

The growing skeleton can be weakened by bone toxicity of treatments, particularly glucocorticoids, which directly affect bone, modify the hormonal axis, and alter intestinal calcium absorption and renal calcium excretion. Glucocorticoids have also been incriminated in the pathogenesis of TAN by promoting the hypertrophy of medullary fat cells, generating an increase in intra-osseous pressure, compressing blood vessels and sinuses in the more fragile epiphyseal zones [21].

Epidemiologically, in Europe, we have the studies by Mathilde Louvigné and colleagues in France [4], Pécheux L and colleagues in Belgium [22], and Brix Nina and colleagues in Denmark [23], with 49, 104, and 286 cases, respectively. The annual incidence was higher in Denmark (12.4) than in Belgium (3.4). T-type lymphocytic

leukemia was predominant in all studies, with a mean age ranging from 7.3 in France to 4.4 in Belgium and a male predominance in all studies. In America, the studies by Isaias [5] in Missouri and Teresa [24] in Brazil, with 74 and 313 cases, respectively, showed a higher annual incidence in Brazil (15.6), with myeloid leukemia predominating in the Isaias study, which explains the later age of onset and the lower percentage of osteoarticular involvement than in the Brazilian study. In North Africa, S. El aichaoui [25] and Latifa Harzallah [26] reported more individual cases, with a later mean age, a predominance of males, and the disease being found in all cases. West Africa Paul Eloundou in Cameroon described an association of Still's disease with acute lymphoblastic leukemia [27]. Our case is a 14-year-old male. The clinicobiological data are in line with the literature.

Diagnostically, the circumstances of discovery were inaugural in the Pecheux, Teresa Robazzi and Ninna Birix studies, with 50%, 88%, and 100%, respectively. In the Pêcheux study, osteoarticular involvement was found during chemotherapy and 28% and 37% after treatment. The clinical course of leukemia is polymorphous, and osteoarticular disorders are diverse. After clinical suspicion, we look for hyperleukocytosis, sometimes associated with anemia, thrombocytopenia, and an inflammatory syndrome. Blood smears, medullograms, and cerebrospinal fluid studies confirm blastosis. Ultrasound-guided synovial biopsy with anapathic examination and examination of joint fluid also reveal blastosis. Imaging is used to explore osteoarticular damage through radiology, joint ultrasound, bone magnetic resonance imaging, and bone densitometry. **Table 3** summarizes the osteoarticular disorders found in the literature. [22] [26] [28] [29].

Therapeutically, intra-articular corticosteroid infiltrations have failed, according to the literature. Calcium and vitamin supplementation and the use of biphosphates are used mainly during and after treatment in conjunction with corticosteroid therapy. Orthopedic and surgical treatment are more common in the management of sequelae. In all cases, etiological treatment is the cornerstone in the management of osteoarticular disorders [22] [29]. Our patient benefited from polychemotherapy for the induction, consolidation, and intensification phases in an appropriate clinical hematology department. We performed infiltrations in the large joints, with improvement in joint pain and synovitis with adequate phosphocalcium intake. As part of our screening for treatment-related complications, we plan to carry out bone densitometry one year after the start of chemotherapy, and to use magnetic resonance imaging of painful joints to detect epiphyseal osteonecrosis at an early stage. He is currently waiting for a donor. Our case presents certain limitations linked to the sometimes precarious diagnostic tools available in our developing countries. We are particularly interested in synovial biopsy and genetic testing to identify mutations in the RUNX gene.

4. Conclusion

Leukemia is a diagnostic and therapeutic emergency. Osteoarticular involvement is often the initial presentation linked to the patient, the disease, or the treatments.

They may also reveal a relapse of acute leukemia, or the accusation of chronic leukemia, which requires multidisciplinary management.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Snodgrass, R., Nguyen, L.T., Guo, M., Vaska, M., Naugler, C. and Rashid-Kolvear, F. (2018) Incidence of Acute Lymphocytic Leukemia in Calgary, Alberta, Canada: A Retrospective Cohort Study. *BMC Research Notes*, **11**, Article No. 104. https://doi.org/10.1186/s13104-018-3225-9

[2] Pécheux, L., Forget, P., Geurten, C., Rausin, L., Nicolescu, R. and Hoyoux, C. (2018) Atteintes osseuses des leucémies lymphoblastiques aiguës pédiatriques: Expérience monocentrique et revue de la littérature. *Revue Med Liege*, **73**, 575-582.

[3] Geurten, C., Piette, C. and Hoyoux, C. (2016) Schéma d'administration des glucocorticoïdes et risque d'ostéonécrose chez les enfants traités pour leucémie lymphoblastique aiguë où en sommes-nous? *Revue d'Oncologie Hématologie Pédiatrique*, **4**, 182-187. https://doi.org/10.1016/j.oncohp.2016.06.005

[4] Louvigné, M., Rakotonjanahary, J., *et al.* (2020) Persistent Osteoarticular Pain in Children: Early Clinical and Laboratory Findings Suggestive of Acute Lymphoblastic Leukemia (A Multicenter Case-Control Study of 147 Patients). *Rhumatologie pédiatrique*, **18**, Article No. 1.

[5] Spilberget, I., *et al.* (1992) The Arthritis of Leukemia. *Arthritis and Rheumatism*, **15**, Article No. 6.

[6] Strauch, A. (1913) Acute Lymphatic Leukemia in Early Life. *Archives of Pediatrics & Adolescent Medicine*, **5**, 43-57. https://doi.org/10.1001/archpedi.1913.04100250046006

[7] Adam de Beaumais, T., Baruchel, A. and Jacqz-Aigrain, E. (2015) Approches méthodologiques en pharmacogénétique: Le modèle des leucémies aiguës lymphoblastiques de l'enfant. *Revue d'Oncologie Hématologie Pédiatrique*, **3**, 215-220. https://doi.org/10.1016/j.oncohp.2015.06.007

[8] Danlos, F.-X., Papo, M. and Micol, J.-B. (2019) L'hématopoïèse clonale: Un concept émergent à la croisée des spécialités. *La Revue de Médecine Interne*, **40**, 684-692. https://doi.org/10.1016/j.revmed.2019.05.005

[9] Bernard, O. (2010) Mécanismes de la leucémogenèse. *Bulletin du Cancer*, **97**, 1381-1388. https://doi.org/10.1684/bdc.2010.1210

[10] Kelly, L.M. and Gilliland, D.G. (2002) Genetics of Myeloid Leukemias. *Annual Review of Genomics and Human Genetics*, **3**, 179-198. https://doi.org/10.1146/annurev.genom.3.032802.115046

[11] Ducassou, S. (2018) Traitement des leucémies aiguës de l'enfant: Aujourd'hui et demain. *Perfectionnement en Pédiatrie*, **1**, 185-191. https://doi.org/10.1016/j.perped.2018.07.005

[12] Liu, Y., Huang, C., Bai, M., Pi, C., Zhang, D. and Xie, J. (2022) The Roles of Runx1 in Skeletal Development and Osteoarthritis: A Concise Review. Heliyon, 8, e12656. https://doi.org/10.1016/j.heliyon.2022.e12656

[13] Ito, Y. (2004) Oncogenic Potential of the RUNX Gene Family: 'Overview'. *Oncogene*, **23**, 4198-4208. https://doi.org/10.1038/sj.onc.1207755

[14] Chen, Y., *et al.* (2021) Runx1 Is a Central Regulator of Osteogenesis for Bone Homeostasis by Orchestrating BMP and WNT Signaling Pathways. *Tang Journal PLOS GENETICS* 2021, **21**, 1-30.

[15] Vimalraj, S. and Sekaran, S. (2023) RUNX Family as a Promising Biomarker and a Therapeutic Target in Bone Cancers: A Review on Its Molecular Mechanism(s) behind Tumorigenesis. *Cancers*, **15**, Article 3247. https://doi.org/10.3390/cancers15123247

[16] Bahadi, N., Biyi, A., *et al.* (2016) Diagnostics différentiels d'images d'hypofixations sur une scintigraphie du squelette: À propos d'un cas de leucémie aigue lymphoblastique. *Pan African Medical Journal*, **24**, Article 146.

[17] Xu, D., Xu, G., Xu, L., Cao, H., Xu, B., Chen, W., *et al.* (2015) Acute Lymphocytic Leukemia Mimicking Spondyloarthritis in an Adolescent: A Case Report and Review of the Literature. *Oncology Letters*, **11**, 1143-1145. https://doi.org/10.3892/ol.2015.4026

[18] Hbibi, M., Atmani, S., Abourazzak, S., Kamaoui, I., Chaouki, S., Bouharrou, A., *et al.* (2011) Tassement vertébral révélant une leucémie aiguë chez un enfant. *Archives de Pédiatrie*, **18**, 597-599. https://doi.org/10.1016/j.arcped.2011.01.012

[19] El aichaoui, S., Bahiri, R., Benbouazza, K., Bzami, F., Amine, B., Allali, F., *et al.* (2006) Polyarthrites révélatrices d'une leucémie. *La Revue de Médecine Interne*, **27**, 555-557. https://doi.org/10.1016/j.revmed.2006.04.004

[20] Lefèvre, Y., Ceroni, D., Läedermann, A., de Rosa, V., de Coulon, G., Ayse, H.O., *et al.* (2009) Boiterie aiguë conduisant au diagnostic de leucémie aiguë. À propos de quatre cas initialement pris en charge aux urgences chirurgicales pédiatriques. *Revue de Chirurgie Orthopédique et Traumatologique*, **95**, 79-84. https://doi.org/10.1016/j.rcot.2008.09.004

[21] Kunstreich, M., Kummer, S., Laws, H., Borkhardt, A. and Kuhlen, M. (2016) Osteonecrosis in Children with Acute Lymphoblastic Leukemia. *Haematologica*, **101**, 1295-1305. https://doi.org/10.3324/haematol.2016.147595

[22] Pêcheux, L., *et al.* (2018) Bone Damage in Leukemia Acute Lymphoblastic Pediatric: Single-Centric Experience and Literature Review. *Revue Médicale de Liège*, **73**, 575-582.

[23] Brix, N., Rosthøj, S., Herlin, T. and Hasle, H. (2015) Arthritis as Presenting Manifestation of Acute Lymphoblastic Leukaemia in Children. *Archives of Disease in Childhood*, **100**, 821-825. https://doi.org/10.1136/archdischild-2014-307751

[24] Robazzi**,** T.J., *et al.* (2007) Osteoarticular Manifestations as Initial Presentation of Acute Leukemias in Children and Adolescents in Bahia, Brazil. *Pediatric Hematology and Oncology*, **29**, Article No. 9.

[25] El aichaoui, S., Bahiri, R., Benbouazza, K., Bzami, F., Amine, B., Allali, F., *et al.* (2006) Polyarthrites révélatrices d'une leucémie. *La Revue de Médecine Interne*, **27**, 555-557. https://doi.org/10.1016/j.revmed.2006.04.004

[26] Harzallah, L., Bouajina, E., Ghannouchi, M., Amara, H., Ben Chérifa, L. and Kraiem, C. (2005) Lombosciatique révélatrice d'un neurinome se développant en regard du cône médullaire: Apport de l'IRM. *Revue du Rhumatisme*, **72**, 264-266. https://doi.org/10.1016/j.rhum.2004.09.007

[27] Eloundou, P., Bebey, F.S., Mbono, R.C., Kamissoko, A.B., Tiogouo, E., Fozeu, L., *et al.* (2022) Maladie de Still de l'enfant et Leucémie aigüe lymphoblastique, une association exceptionnelle: À propos d'un cas. *Pan African Medical Journal*, **43**, Article 156. https://doi.org/10.11604/pamj.2022.43.156.33476

[28] Xu, D.Y., *et al.* (2016) Acute Lymphocytic Leukemia Mimicking Spondyloarthritis in

an Adolescent: A Case Report and Review of the Literature. *Oncology Letters*, **11**, 1143-1145.

[29] Kunstreich, M., Kummer, S., Laws, H., Borkhardt, A. and Kuhlen, M. (2016) Osteonecrosis in Children with Acute Lymphoblastic Leukemia. *Haematologica*, **101**, 1295-1305. https://doi.org/10.3324/haematol.2016.147595