Case Report

Metastatic Calcinosis Cutis: A Case in a Child with Acute Pre-B Cell Lymphoblastic Leukemia

Juan Pablo Castanedo-Cázares,1 Amalia Reyes-Herrera,1 Diana Hernández-Blanco,1 Cuauhtémoc Oros-Ovalle,2 and Bertha Torres-Álvarez1

1Department of Dermatology, Hospital Central Dr. Ignacio Morones Prieto, Universidad Autónoma de San Luis Potosí, 78210 San Luis Potosí, SLP, Mexico
2Department of Pathology, Hospital Central Dr. Ignacio Morones Prieto, Universidad Autónoma de San Luis Potosí, 78210 San Luis Potosí, SLP, Mexico

Correspondence should be addressed to Bertha Torres-Álvarez; torresmab@yahoo.com.mx

Received 11 June 2015; Revised 20 July 2015; Accepted 28 July 2015

Academic Editor: Marie-Christine Kyrtsonis

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Hypercalcemia in children with malignancy is an uncommon condition. It has been described in leukemia patients with impaired renal excretion of calcium or osteolytic lesions. Metastatic calcinosis cutis (MCC) may develop if hypercalcemia persists. We report the case of a 5-year-old girl with an atypical dermatosis and unspecific gastrointestinal symptoms. Considered clinical diagnoses were xanthomas, histiocytosis, molluscum contagiosum, and nongenital warts. Cutaneous histological analysis showed amorphous basophilic deposits in the dermis suggestive of calcium deposits. Extensive investigations such as bone marrow biopsy established the diagnosis of an acute pre-B cell lymphoblastic leukemia. Careful review of the literature fails to reveal previous reports of these peculiar cutaneous lesions of MCC in children with leukemia.

1. Introduction

Hypercalcemia usually results in nonspecific constitutional and gastrointestinal symptoms, such as nausea, vomiting, anorexia, and weight loss. Its presence in children with malignancy is very rare but has been linked to rhabdomyosarcoma, hepatoblastoma, Hodgkin’s and non-Hodgkin’s lymphoma, brain tumors, neuroblastoma, angiosarcoma, and acute lymphoblastic and myeloid acute leukemia [1]. Metastatic calcinos is cutis (MCC) occurs in undamaged tissues and is associated with elevated serum phosphate and/or calcium levels, most frequently in adults with end stage renal disease. It is an uncommon finding in pediatric leukemia patients [2, 3]. This case report highlights the importance of skin features in the diagnosis of a hematological disease in a child with nonspecific symptoms.

2. Case Presentation

A 5-year-old girl with a history of nausea, vomiting, abdominal pain, and diarrhea, who had been hospitalized without a definite diagnosis of her illness on multiple occasions before her consultation, was admitted because of diarrhea and moderate dehydration.

Physical examination revealed asymptomatic large plaques of confluent papules, reddish brown on the groins, pubis, and gluteus fold, firm, and well demarcated, approximately 2 × 7 cm in size of four-week duration (Figures 1 and 2). Neither hepatosplenomegaly nor palpable lymphadenopathies were detected. The clinical diagnosis of skin lesions was xanthomas, histiocytosis, molluscum contagiosum, or nongenital warts. Laboratory tests on admission were normal, including hemogram with hemoglobin level of 11.5 g/dL, a white cell differential count of 70% neutrophils, and 25% lymphocytes.
as well as phosphorous and parathyroid hormone levels, but an abnormal high level of serum calcium of 17.9 mg/dL. A 4-mm punch skin biopsy was taken, and subsequent hematoxylin and eosin stain revealed an amorphous and basophilic deposit in reticular dermis, highly suggestive of calcium deposits (Figure 3). Von Kossa staining was positive and the diagnosis of calcinosis cutis was confirmed. Chest X-ray was normal and kidney ultrasound suggested nephrocalcinosis; however renal function parameters remained normal. There was no evidence of other visceral calcifications.

Finally, a bone marrow biopsy revealed a significant hypercellularity with over 90% blasts with L1 morphology (Figure 4). Immunohistochemical exam detected neoplastic cells positive for CD20 and CD79a indicating an infiltrate of B cell precursors (Figure 5). Flow cytometry of bone marrow was also consistent with early pre-B cell lymphoblastic leukemia as immunolabeling was negative for surface immunoglobulin but positive for CD10, CD20, and CD19 [4]. Two weeks after admission, follow-up blood work revealed hemoglobin 9.2 g/dL with a white blood count of 2710/μL, with 82% neutrophils and 15% lymphocytes and an elevated level of lactate dehydrogenase (LDH, 2440 U/L; normal < 213 U/L) was detected. The patient was treated with three cycles of vincristine, daunorubicin, and L-asparaginase. After that the level of serum calcium was 9.4 mg/dL and the level of lactate dehydrogenase was reduced to a normal level. Skin lesions did not regress but they did not expand either, as no particular treatment was offered for these lesions. One month after the last chemotherapy cycle, the patient developed central nervous system leukemia and intrathecal methotrexate was given; however there was no response for that and treatment with cranial radiotherapy was started. Four months after her diagnosis the patient presented pancytopenia and died from sepsis.
3. Discussion

Calcinosis cutis is classified as metastatic, dystrophic, idio-
pathic, or iatrogenic. Dystrophic calcinosis cutis is the most
common form; it appears secondary to tissue damage in a
setting of underlying disease associated with normal serum
calcium and phosphate levels [3]. Idiopathic type generally
occurs in childhood or adolescence and can be classified
as solitary or multiple, sporadic or associated with Down
syndrome [4, 5]. The iatrogenic type occurs following treat-
ment in the setting of intravenous extravasation of calcium
carbonate, calcium gluconate, or phosphate [6].

Hypercalcemia is defined as total serum calcium concen-
tration greater than 12 mg/dL, but clinical symptoms usually
appear when concentration is 15 mg/dL or greater [7].

MCC occurs when there is hypercalcemia or hyper-
phosphatemia secondary to abnormal calcium, phosphate
metabolism, or both leading to spontaneous calcium/phos-
phate deposits [6]. Characteristically, calcifications appear
at periarticular sites, and their size and number seem to
correlate with the degree of hyperphosphatemia or hyper-
calcemia [3]. Metastatic calcification (MC) may occur not
only within the cutaneous and subcutaneous tissues, but also
within other organs or tissues such as the kidneys, lungs,
stomach, and blood vessels [5, 8]. MC is more common
among adults, particularly in those affected by chronic renal
failure. Other conditions related to its occurrence are hyper-
vitaminosis D, the milk-alkali syndrome, Albright hereditary
osteodystrophy, neoplasms associated with bony destruction
(lymphomas, leukemias, multiple myeloma, and metastatic
carcinomas), sarcoidosis, and pseudohyperparathyroidism
[6]. Apparently there are only four cases in the literature of
MC in children; two of them presented also MCC: one child
with end-stage renal disease, metastatic calcinosis of lungs,
and cutaneous necrosis of buttocks and legs [9] and the
other case was an 18-month-old infant with massive
metastatic pulmonary calcification in a leukemic monocytic
leukemia [10]. The third case occurred in a newborn girl
with congenital acute monocytic leukemia, leukemia cutis,
and MCC [11]; and the last one was a pediatric hemodialysis
patient who presented with metastatic brain calcifications
and severe neurological manifestations secondary to uncon-
trolled hyperparathyroidism [12]. The clinical presentation
of MCC is indistinguishable from other conditions such as
xanthomas, xanthoma disseminatum, and diffuse plane
xanthomatosis [13], or common conditions such as molluscum contagiosum
as in the present case.

In children with malignancy, hypercalcemia is uncom-
mon. McKay and Furman reported that, over a period of
29 years, 25 out of 6,055 children treated for cancer were
identified with hypercalcemia (0.4%) [1]. Kerdudo et al.,
over a period of 7 years, found 16 cases of hypercalcemia and
reported a prevalence of 1.3% [14]. Recently, Moayeri et al.
described a prevalence of hypercalcemia in 5.4% of patients,
in which half of them were associated with acute lymphoblas-
tic leukemia (ALL) [15].

There is no specific treatment; intense hydration, biphos-
phonates, and corticosteroids to reduce calcium levels
are usually indicated [13]. Skin lesions could be resolved
following a good control of the calcium and phosphate levels
after a varied period of time [16].

To the best of our knowledge, this case may represent
the first pediatric patient with pre-B cell ALL and MCC,
as no case with similar skin lesions has previously been
informed in the literature. Its presentation highlights the
importance of skin features in the diagnosis of a potentially
severe hematologic disease. It was clear that an accelerated
hypercalcemia in children with ALL can confuse the clinician
due to nonspecific symptoms that may delay its diagnosis
and treatment. Although cutaneous lesions represent a later
sign of involvement, they are indistinguishable from other
conditions such as xanthomas; thus, the histological analysis
plays an important role for its recognition. In conclusion,
although hypercalcemia with MCC is infrequent, it can be the
initial manifestation of ALL.

Conflict of Interests

All authors declare no conflict of interests.

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