CASE REPORT

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Undiagnosed, Untreated Acute Lymphoblastic Leukemia Presenting as Suspected Child Abuse

REFERENCE: McClain, J. L., Clark, M. A., and Sandusky, G. E., **"Undiagnosed, Untreated Acute Lymphoblastic Leukemia Presenting as Suspected Child Abuse,"** *Journal of Forensic Sciences*, JFSCA, Vol. 35, No. 3, May 1990, pp. 735–739.

ABSTRACT: Natural disease being mistaken for child abuse is rare. A two-year-old child was found unresponsive at home and transported to a local hospital, where she expired in the emergency room. Several cutaneous contusions were observed. Prior to the autopsy it was learned that an anonymous report of "child abuse" had been previously filed concerning this child. At autopsy there were multiple metasynchronous cutaneous contusions, but no radiologic or gross evidence of other injuries. A pericardial effusion, massive hepatosplenomegaly and generalized lymphadenopathy were apparent. The bone marrow, liver, spleen, lymph nodes, kidneys, pancreas, heart, stomach, and dura mater showed a monotonous lymphocytic infiltrate. Immunocytochemical studies confirmed the diagnosis of acute lymphoblastic leukemia of childhood. This case reaffirms the need for an objective examination of all cases by a forensic pathologist.

KEYWORDS: pathology and biology, child abuse, leukemia, acute lymphoblastic leukemia, monoclonal antibodies, autopsy

Child abuse homicide cases are not infrequent occurrences in busy medical examiners' offices, but cases of suspected child abuse which ultimately are determined to result from natural diseases are extremely rare. This report concerns a case of undiagnosed, untreated acute lymphoblastic leukemia presenting as suspected child abuse.

Case Report

A two-year-old white female was found unresponsive in bed by her mother, who, along with her live-in boyfriend, rushed the child to a local emergency room where the child died, despite vigorous resuscitation efforts. Numerous bruises of different colors were

Presented in part at the 41st Annual Meeting of the American Academy of Forensic Sciences, held in Las Vegas, Nevada, 13–18 Feb. 1989. Received for publication 22 May 1989; accepted for publication 16 June 1989.

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noted on the child's back and extremities and the police were notified. It was then discovered that an anonymous report had been filed one month prior to the child's death alleging that the child had been seen "covered with bruises" in a local restaurant. At the time of that report, investigating social workers concluded that the allegations of abuse were unsubstantiated because of the child's appropriate interaction with her mother and father surrogate. Investigators from the coroner's office interviewed the child's maternal grandmother, who felt that the mother's boyfriend was to blame for the numerous bruises on the child.

The child's past medical history was significant only in that she had been seen one week prior to her death by a local physician for "respiratory problems." No X-rays were taken and no laboratory studies were performed. The decedent was prescribed Septra suspension and Ventolin syrup, and the mother reported that the medication did little to alleviate the symptoms.

At autopsy, the deceased was a thin, dehydrated 2-year-old white female child who weighed 34 lb (15 kg) and measured 38 in. (96.5 cm) in length. This placed her in the 30th percentile for her age. Petechiae were present on the face, chest, abdomen, and right labia majora. Contusions of various ages (as judged by color) were found on the face, chest, abdomen, back, and lower legs. In addition, there were focal hemorrhages of the anal mucosa. The heart showed extensive epicardial hemorrhage, with extension of the hemorrhage into the regions of the sinoatrial and atrioventricular nodes. The liver was mottled in appearance, and the cortical surfaces of both kidneys displayed mottling and petechiae. Microscopic examination of hematoxylin- and eosin-stained sections of the liver, kidneys, heart, stomach, pancreas, and dura mater showed an extensive infiltration by lymphoblasts which were monotonous in appearance. Specifically, the lymphoblasts had a very high nucleus to cytoplasm ratio, prominent heterochromatin, and 2 to 3 oval nucleoli. In many sections, particularly in the kidneys, the normal architecture of the organ was totally obliterated by the lymphoblastic infiltrate (Fig. 1 through 4). Sections of bone marrow showed total effacement by the lymphoblastic infiltrate. Postmortem bacterial cultures of blood, lung tissue, and cerebrospinal fluid showed no growth, as was also the case for viral cultures of the lung and small intestine.

Several days after the autopsy was performed, the results were received from laboratory studies performed on blood drawn from the victim in the emergency room during re-

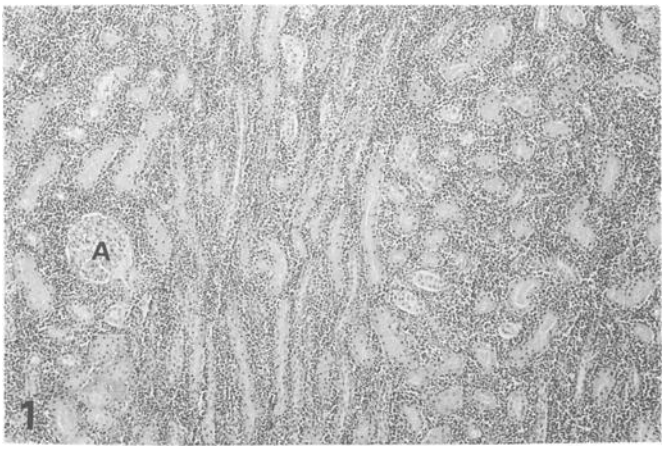

FIG. 1—*This section of kidney shows an interstitium filled with a lymphoblastic leukemic infiltrate. A single glomerulus* (A) *is visible (stain, hematoxylin and eosin; original magnification, ×20).*

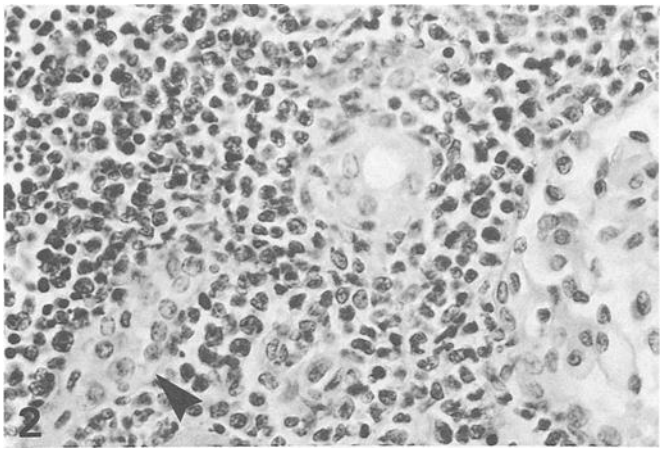

FIG. 2—*This higher power view of a kidney shows expansion of the interstitium by the leukemic infiltrate. Focally, there is infiltration of the tubule walls* (arrow) *(stain, hematoxylin and eosin; original magnification, ×250).*

suscitative attempts. Of particular relevance were the results of a complete blood count (CBC), which showed a hemoglobin of 1.8 g/dL, a hematocrit of 4%, a red blood cell count of 0.43 million/mm^3, and a white blood cell count of 39.3 thousand/mm^3. A peripheral blood smear showed 100% lymphocytes, and the platelet count was 87 thousand/mm^3.

Immunoperoxidase Studies

Sections of kidney which displayed a heavy infiltration by leukemic cells were further studied using a monoclonal antibody panel. Unstained sections were deparaffinized and stained using the avidin biotin complex method described by Hsu et al. [*1*]. Staining of 1% or less of the cells was disregarded. A monoclonal antibody panel, consisting of the

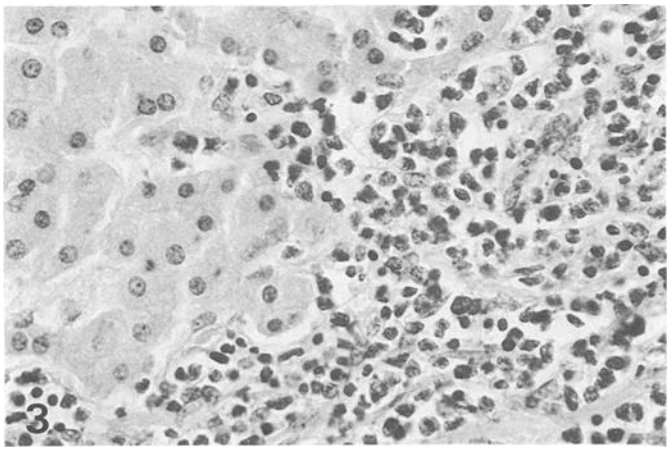

FIG. 3—*Portal areas of the liver massively expanded by the leukemic infiltrate. An island of normal-appearing hepatocytes is seen at the upper left (stain, hematoxylin and eosin; original magnification, ×250).*

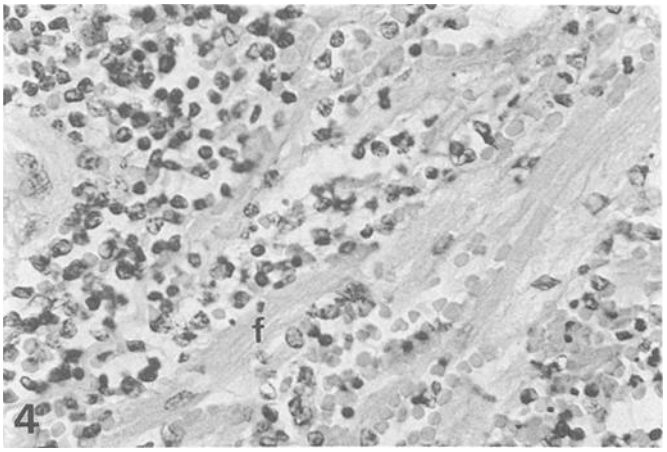

FIG. 4—*Leukemic infiltrate in the interstitium of the myocardium. The myofibers* (f) *appear to be spread apart by the infiltrate (stain, hematoxylin and eosin; original magnification, ×250).*

kappa and lambda light chains markers and the LN-1, LN-2, and LN-3 antibodies, was used for lymphocyte identification. Scattered immunocytochemical staining for LN 3 was observed in the leukemic lymphoblasts in the kidney. The LN-3 staining was localized to the cell membrane and cytoplasm of the positive-staining cells. No staining was seen with the kappa and lambda light chains or the LN-1 and LN-2 tumor markers. Some nonspecific staining was seen in the interstitial renal connective tissue. This staining pattern is diagnostic of the acute lymphoblastic leukemia of childhood or CALLA.

Discussion

Every pediatric death occurring outside a hospital setting is suspicious until proven otherwise and, in this particular case, the child's external appearance was consistent with child abuse. It is the duty of the forensic pathologist to perform an impartial autopsy in all such circumstances and to collect appropriate samples for diagnostic studies. Forensic pathology is a dynamic medical specialty and has a history of incorporating technical advances in order to make more accurate diagnoses. In this particular case, the authors were able to classify an undiagnosed acute leukemia using immunoperoxidase staining procedures. The autopsy showed this to be a case of previously undiagnosed and untreated acute lymphoblastic leukemia, which is rarely seen today. Recently, Kaplan has used the term "pseudoabuse" to describe natural diseases which were mistakenly diagnosed as child abuse [*2*]. A case of panhypogammaglobulinemia masquerading as child abuse has also been reported [*3*]. In this case, the child was being followed at a local hospital for pneumonia, failure to thrive, and possible child abuse/neglect. Only at autopsy was a correct diagnosis of panhypogammaglobulinemia obtained. This type of case again points out the importance of a thorough autopsy, including microscopic examination to protect innocent people from unwarranted prosecution for child abuse.

The use of monoclonal antibodies has resulted in significant advances in the identification of various lymphoid disorders. Commercially available monoclonal antibodies directed against B-cell- and T-cell-specific antigens have, until quite recently, generally required the use of frozen sections or cell suspensions, since these antigens are destroyed by the paraffin embedding process [*4*]. More recent technology allows the staining of specific antigens on paraffin-embedded tissue sections. LN 1, LN 2, and LN 3 represent a comprehensive B-cell-specific panel which may be used to identify normal and malignant

B lymphocytes by immunoperoxidase methods. Monoclonal LN 1 antibody recognizes a surface membrane antigen found primarily on germinal center B lymphocytes and T cells while histiocytes are negative. Monoclonal LN 2 antibody recognizes a nuclear membrane protein expressed in the mantle zone and germinal center of B lymphocytes as well as in interdigitating histiocytes in reactive lymph nodes. Monoclonal antibody LN 3 recognizes the human lymphocyte antigen DR (HLA-DR) (I^A-like), which is seen in the CALLA type of acute lymphoblastic leukemia. The T-cell leukemias do not display the HLA-DR (I^A-like) antigen. Null cell acute lymphoblastic leukemia (ALL) can occasionally display the HLA-DR-type antigen [*4*]. The kappa and lambda antigens are also specific for B lymphocytes. Taking into account the child's age, the staining pattern represents a CALLA-type ALL. Acute lymphoblastic leukemia accounts for approximately 80% of the cases of leukemia seen in the pediatric population [*5*]. The presenting symptoms in children with ALL include fever, pallor, petechiae, purpura, lymphadenopathy, hepatosplenomegaly and bone pain [*4*]. Acute lymphoblastic leukemia is generally characterized as either CALLA, T-cell, or B-cell derived. In childhood ALL, CALLA accounts for 60 to 70% of the cases and is considered the most readily treatable of the childhood leukemias [*5,6*]. T-cell ALL accounts for 14 to 20% of ALL cases and B-cell ALL accounts for 2 to 3% of the cases [*5*].

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