

Unexpected sudden death in a 14-year-old male: a case report and review of literature

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Citation

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Abstract

The rare case described in this report was of a 14-year-old male who was previously healthy and unexpectedly died due to a massive intracerebral hemorrhage caused by acute monoblastic leukemia. The acute monoblastic leukemia was undiagnosed until he was presented in the ER 12 hours prior to death. An autopsy was performed, which showed that the extensive leukostasis and extramedullary leukemic infiltrate involved multiple organs, including lungs, heart, liver, spleen, kidneys, GI tract, thymus, lymph nodes and skin. Diffuse lymphadenopathy and multiple organomegalies were also identified. This case suggests that underlying acute leukemia should be considered as a differential diagnosis with careful physical examination when pediatric patients present with flu-like symptoms. Medical personnel are urged to be alert to fever, sore throat and weakness that may be characteristic of serious systemic diseases.

BACKGROUND

Acute leukemia is the most common cancer in pediatric patients showing a rapid progress, representing 3.7% of cancer deaths in the United States. Acute monoblastic leukemia (AML) comprises 5-8% of cases of acute myeloid leukemia. It may occur at any age but is most common in young individuals. It is associated with severe extramedullary involvement, and follows an aggressive clinical course.^[1] The extensive extramedullary involvement is induced by the release of cytokine and proteinase from leukemic cells.^[2] AML may cause sudden unexpected death due to leukostasis and intracranial hemorrhage. The treatment of AML is with aggressive chemotherapy. Complete remissions are frequently achieved. Leukopheresis is routinely used for immediate leukocytoreduction.^[3,4,5]

CASE REPORT

The patient was a 14-year-old Caucasian male with no past medical history. He presented to his primary physician complaining on and off of low-grade fever with sore throat and weakness lasting one to two weeks. The strep throat was identified, and the patient was then treated with amoxicillin. Two days later, he felt weakness, numbness and tingling of his left arm and leg when he woke up in the morning. In the early afternoon, he was admitted to the ER, where he was found to have vomiting and photophobia but without nausea or bleeding. On physical examination, lymphadenopathy was

presented at cervical, axillary and inguinal areas. His spleen and liver were palpable and markedly enlarged. Laboratory tests showed that the white count was 328,000 with blast 92%, Seg 0%, Band 1%, lymph 6%, RBC 3.87, Platelets 90,000, HCT 32%, ESR 2, Calcium 10.1, bilirubin 1.8, AST 131, ALT 28, alkaline phosphate 246, total protein 6.9, albumin 4.0, BUN 13, creatinine 1.5, INR 2.55, APTT 39.7, PT 27.1, Fibrinogen 84, uric acid 13.2, and lactate dehydrogenase 4764. A CT scan of his head/brain found two frontal areas of hyperattenuation, which was suggestive of hemorrhage. He was diagnosed with likely AML, hyperleukocytosis, leukostasis, renal insufficiency, elevated uric acid and coagulopathy in the ER. Subsequently, he was treated with Vancomycin, Ceftaz, and Fosphenytoin. In the evening, the patient was transferred to the intensive care unit. Hematology, oncology and surgical teams were consulted. He was transfused with fresh frozen plasma. Later, he was taken to the MRI suite for MRI of the brain, head and spine. He seemed very agitated and kept on moving when he was in the MRI even though a dose of 4 mg of Versed was given by IV. Therefore, he was intubated. He died on the MRI table unresponsive to resuscitation in the later evening within 12 hours of presentation in the hospital. A complete autopsy was performed.

PATHOLOGY FINDINGS

The peripheral blood smear with Giemsa staining showed

92% of the blasts. The blasts were monotonous large cells with abundant eosinophilic cytoplasm and round to oval nuclei with dispersed chromatin and prominent nucleoli consistent with monoblasts. (Figure 1). The bone marrow smear displayed a complete replacement by a population of blasts (Figure 2), which were strongly positive for non-specific esterase staining. On the bone marrow section the blasts showed 40-50% of intensive staining for Ki-67, while they were negative for CD117. Autopsy showed that the extensive leukostasis and extramedullary leukemic infiltrate involved multiple organs, including lungs, heart, liver, spleen, kidneys, GI tract, thymus, lymph nodes and skin. The monoblasts filled in blood vessels and extravasated into tissues. Diffuse lymphadenopathy (1-5 cm in diameter) involved cervical, superclavicular, axillar, pulmonary hilar, mesentery and inguinal nodes. These lymph nodes were completely replaced by infiltrating monoblasts. The lungs showed a diffuse monoblastic infiltrate associated with parenchymal hemorrhage and formation of small thromboemboli. The liver (2700g) was filled with blasts in the sinusoids and portal tracts. The spleen (720g) was infiltrated with blasts in the sinusoids and white pulps. The spleen and kidneys demonstrated focal infarcts because of the blockage of arteries by the blasts. The heart demonstrated multiple foci of blast infiltrate in the myocardium. In the small and large intestines numerous nodules were seen on the mucosal surface. Microscopically, these nodules were composed of aggregates of blasts in the mucosa and submucosa underlying the epithelium. The thymus was much enlarged (43.5 g), and filled with monoblasts. On a random section of the skin clusters of blasts were surrounding the vessels in the dermis and subcutaneous tissue. The brain weighed 1610 g. Multiple foci of massive intracerebral hemorrhage were presented in the bihemispheres (mainly right side) and left lateral ventricle as well as focal subarachnoid space. In summary, the patient died of acute monoblastic leukemia (AML subtype, M5a by FAB classifications) with extensive leukostasis, extramedullary involvement of virtually every organ and massive intracranial hemorrhages.

Figure 1

Figure 1: The peripheral blood smear with Giemsa staining showed monotonous large cells with abundant eosinophilic cytoplasm and round to oval nuclei with dispersed chromatin and prominent nucleoli consistent with monoblasts. (The original magnification x 400).

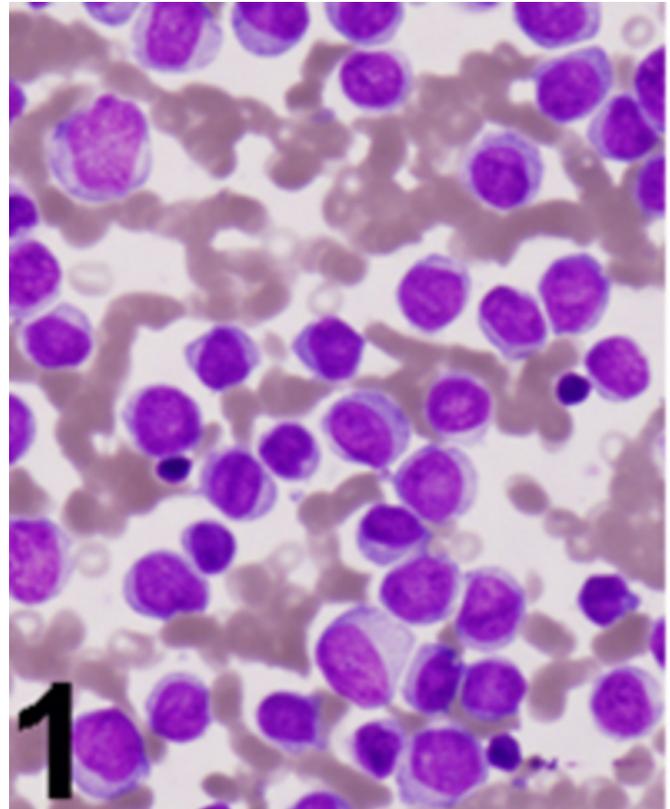
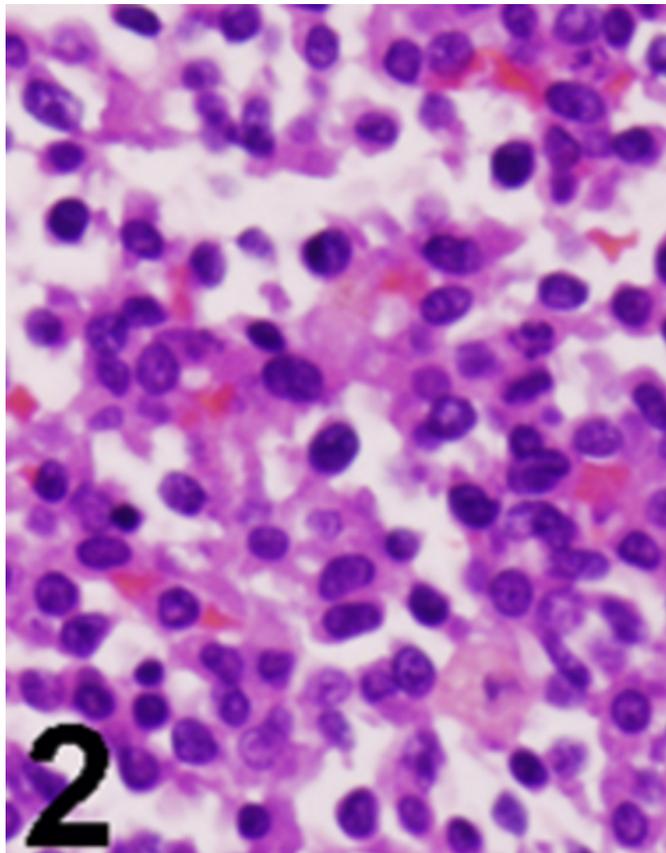


Figure 2

Figure 2: The bone marrow smear displayed a complete replacement by a population of monoblasts (The original magnification x 200. H.E. staining).



DISCUSSION

Acute leukemia is the most common cancer in pediatric patients, and shows a rapid progress, representing 3.7% of cancer deaths in the United States. Acute monoblastic leukemia (AML) comprises 5-8% of cases of acute myeloid leukemia. It may occur at any age, but is most common in young individuals. It is associated with severe extramedullary involvement, follows an aggressive clinical course and may cause sudden death in pediatric patients. [1,23] It may present with extremely high blast counts; a phenomenon known as hyperleukocytosis in children and adults. Respiratory failure, intracranial bleeding, and severe metabolic abnormalities frequently occur in acute hyperleukocytic leukemias, and are the primary determinants of the high early mortality (20% to 40%) observed.[2] In 1997, Yamauchi et al found that 38 (20%) of 194 patients with acute myeloid leukemia were diagnosed as having intracranial hemorrhage by a study of the CT and autopsy findings in patients with symptomatic intracranial haemorrhage in acute myeloid leukaemia. [4] More recently, Barton et al in 2006 reported that hyperleukocytosis

occurred in 7.3% of 547 pediatric patients with acute leukemia. These patients had a significantly increased early mortality rate due to intracerebral hemorrhage when compared to the nonhyperleukocytic group.[5] In the same year, Gino et al revealed 7 cases of sudden unexpected death due to clinically undiagnosed neoplasia in infancy and children among 4926 autopsies for sick children. Two cases of acute leukemia (1 myelogenous, 1 lymphoblastic) and 2 cases of mediastinal lymphoblastic lymphoma (pre-T cell type) were among these 7 cases. [6] Similar to the case reported here, Sakai et al in 2007 described a 15-year-old male who unexpectedly died due to a cerebral hemorrhage caused by underlying undiagnosed acute promyelocytic leukemia within 12 hours after presentation in a hospital.[7] Not only as in pediatric patients, a 51-year-old man with chronic lymphocytic leukemia suddenly died in hospital although he presented with respiratory distress. Autopsy revealed pulmonary leukostasis and a large intracardiac mass containing mostly mature lymphocytes and fibrin. The intracardiac mass might have been the cause of the patient's sudden death.[8] Also in 2007 a sudden death due to an undiagnosed acute myelogenous leukemia was reported although the original cause of death was determined to be cardiomyopathy.[9]

There were less than two weeks of time including only half a day in the ER from the beginning of flu-like symptoms to the numbness and weakness of his left extremities, and to his sudden death due to an extensive leukostasis and massive cerebral hemorrhage caused by AML. The AML was undiagnosed before the patient was sent to the ER. Unfortunately, a cytogenetical analysis was not performed. Otherwise, it might have shown the associations with abnormalities of 11q23, which is frequently seen in the acute monoblastic leukemia.[3] Treatment of AML is with chemotherapy and complete remissions are frequently achieved. Leukopheresis is routinely used for immediate leukocytoreduction, and it can effectively reduce the blast count in many patients with acute hyperleukocytic leukemias. [2,3,4,5] This case suggests that underlying acute leukemia should be considered as a differential diagnosis along with careful physical examination when pediatric patients present with flu-like symptoms. Medical personnel are urged to be alert to fever, sore throat and weakness that may be characteristic of serious systemic diseases.

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