CASE REPORT

Unexpected infant death secondary to a pulmonary infiltration due to acute myelocytic leukaemia

Mehdi BEN KHELIL*** MD, Youssef CHKIRBENE*** MD, Mona MLIKA**** MD, Slim HAOUET***** MD and Moncef HAMDOU n*** MD

*Faculty of Medicine, University Tunis-Elmanar, **Department of Legal Medicine, Charles Nicolle Hospital, ***Department of Pathology, Ariana Hospital, and ****Department of Pathology, La Rabta Hospital, Tunis, Tunisia

Abstract

Acute myeloid leukaemia (AML) often presents with non-specific symptoms such as fatigue, anaemia or infection. Pulmonary involvement is uncommon in AML during the course of the disease and is usually caused by infection, haemorrhage, leukaemic pulmonary infiltrates and leukostasis. Lung localization of AML is very uncommon and potentially life threatening if not diagnosed and treated rapidly. The authors describe the sudden death of an asymptomatic five-month infant because of a misdiagnosed lung localization of AML. Autopsy examination followed by histopathological studies showed an extensive leukostasis and extramedullary leukaemic infiltrating the lungs. Special stains and immunohistochemical studies revealed findings consistent with acute myelogenous leukaemia. This case suggests that underlying acute leukaemia should be considered as a cause of flu-like symptoms in infants. Medical personnel are urged to be alert to fever, sore throat, weakness and dyspnea that may be characteristic of serious systemic diseases.

Keywords: unexpected infant death, infant, acute myeloid leukaemia, acute respiratory distress syndrome

INTRODUCTION

Although acute leukaemia is known to be the most frequent childhood cancer, it remains rarely observed in infants among whom it would also show a high mortality risk. In Tunisia, acute leukaemia is also the most common cancer in paediatric patients, and shows a rapid progress, representing 22% of paediatric cancer in Tunisia. Patients with acute myeloid leukaemia (AML) may present with diffuse pulmonary infiltration which can lead to death. A sudden death due to bilateral leukaemic pulmonary infiltrates is exceptionally uncommon and can pose diagnostic challenges. We present a case of sudden infant death with bilateral leukaemic pulmonary infiltrates due to undiagnosed acute myeloid leukaemia (AML).

CASE REPORT

Clinical summary

The patient was a five-month-old female infant, with no past medical history, and uncomplicated pregnancy and delivery. She presented with a three-day history of dyspnea, sore throat and weakness. A Streptococcic angina was diagnosed and the patient was then treated symptomatically. Two days later, the family noticed an exacerbation of dyspnea and a hacking cough. She was found unresponsive, in the third day, by a family member in supine position on her bed. A medico-legal autopsy was performed almost 12 h after death.

Autopsy findings

On external examination, considering her age, the body was well-built (weight 7 kg, height 59 cm, body mass index 20.19 kg/m², head circumference 39 cm). The external examination revealed central and peripheral cyanosis and blood stained secretions from nostrils. There was no visible injury on external examination of the body. The autopsy showed no subgaleal haemorrhage and no skull fracture. The brain weighed 560 g
with no lesion or injury. However, we noticed a pronounced congestion of the cerebral vessels without any haemorrhage. The heart weighed 25 g, and the coronary arteries were healthy with no cardiac malformation. The right and the left lungs were severely congested and weighed 40 and 55 g respectively. The bronchus contained thick secretions and the pulmonary arteries were free from emboli or tumour mass. Liver and spleen were enlarged and weighed 260 g and 20 g respectively. The kidneys weighed 25 g each and had no remarkable findings. All organs were severely congested without any other macroscopical abnormality.

Microbiological and viral analysis of cerebrospinal fluid did not show any sign of meningitis. Toxicological analysis was negative for alcohol and common drugs were not detected.

**Histopathology**

In the histological examination, the different fragments of the lung had a normal architecture. It showed an enlargement of the alveolar septa due to infiltration by large hyperchromatic atypical white cells. These cells had an abundant cytoplasm with an immature, apple-core nucleus, and heavily granulated cytoplasm consistent with myeloblast infiltration, without significant fibrosis or hyaline membrane formation.

The alveoli’s lumen were oedematous and occupied by a dense cell population, consisting of macrophages, neutrophils and myeloblastic cells. We observed a perivascular and interstitial infiltration with atypical cells, with a myeloblastic cell infiltration in the bronchi, bronchioles, alveolar and vascular lumen (Fig. 1).

Furthermore, similar cells were found in reticuloendothelial tissues like the liver (Fig. 2). Immunohistochemistry showed the tumour cells to express CD34 and myeloperoxidase antigens highlighting their immaturity and myeloid lineage.

The bone marrow was not sampled during autopsy as it was not included in the systematic sampling protocol and as leukaemia was not suspected at autopsy. Death was attributed to an acute respiratory failure caused by a pulmonary infiltration due to an acute myelocytic leukaemia. The manner of death was natural.

**DISCUSSION**

Acute leukaemia may occur at any age but is most common in young individuals. It is characterized by a severe extramedullary involvement and an aggressive clinical course that can cause sudden death in paediatric patients.

AML 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 leukaemias and are the primary determinants of the observed high early mortality (20% to 40%). AML can be revealed by uncommon symptoms or diseases such as pseudotumour cerebri, pulmonary complications, postpartum haemorrhage, polyarthritis, cutis infiltration and exophthalmia.

The case presented was particular because acute leukaemia was revealed by acute respiratory distress syndrome (ARDS) as the first symptom. Positive diagnosis was based on microscopical...
FATAL LEUKAEMIC PULMONARY INFILTRATION

and immunohistochemical findings, as there are no pathognomonic clinical or imaging signs of pulmonary leukaemic infiltration.

Noninfectious pulmonary complications occur during the course of the disease in nearly 8% of patients with leukaemia, and are a potential cause of death. Leukaemic pulmonary infiltration is not unusual at the late stages of both acute and chronic leukaemia.11

However, the initial presentation of acute leukaemia as symptomatic pulmonary infiltrates is uncommon. An autopsy study of the lung showed less than 10 percent of cases had leukaemic involvement of the lung.5,11,19,20 Lung infiltration can be due to leukaemic interstitial infiltration or intravascular leukostasis.

We highlighted that symptoms of leukaemia may mimic those of other “benign” disorders and misdiagnosis may lead to fatal issue in some instances. Therefore, it is very important to diagnose and initiate appropriate chemotherapy in the early stages.

Finally, we noticed the importance of collecting bone marrow in the autopsy activity as a routine manner to allow further testing and diagnosis mainly in sudden death.

In conclusion, a sudden death caused by lung localization of an asymptomatic leukaemia is uncommon, especially in infants. In spite of its rarity, such a diagnosis has to be kept in mind when dealing with vague flu-like symptoms in children. In the present case, the clinical features included were low grade fever, dyspnea, sore throat with hacking cough and weakness, without any haemorrhagic diathesis or tumoral lysis syndrome. AML may be considered as a differential diagnosis of sudden death with non-specific clinical features mainly in negative autopsy.

ACKNOWLEDGEMENT

The authors have no conflict of interest to declare.

REFERENCES

3. Green AL, Furutani E, Ribeiro KB, Rodriguez Galindo C. Death within 1 month of diagnosis in childhood cancer: an analysis of risk factors and

FIG. 2: Myeloblastic cell infiltration of the liver parenchyma (white arrow) (haematoxylin and eosin x40)