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Acute myeloid leukemia type 2 revealed by acute pancreatitis (About a Case and Literature Review)

Zineb Amhaouch[1]*, Imane Tlamçani[1], Mariam Mahha[1], Majdouline El Khiyat[1], Fatima Aich[1], Amal Taghouti[1], Moncef Amrani Hassani[1]
[1]Department of Biological Hematology, Central Laboratory of Medical Analyzes, UHC Hassan II, Fez, Morocco

***Corresponding author**
Zineb Amhaouch

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Abstract: Acute myeloid leukemia (AML) is a very heterogeneous group of hematological malignancies, Characterized by clonal proliferation of abnormal myeloid precursors and altered normal hematopoiesis. The world Health organization (WHO) classification retains the diagnostic threshold the infiltration of the bone marrow by more than 20% of non-lymphoid blasts. AML 2 represents 30% to 40% of AML, the translocation (8; 21) is identified in 5% to 10% of all AML cases and 10% to 22% of AML2 cases. We report a case of AML 2 discovered in a 56-year-old woman, during a paraclinical assessment of acute pancreatitis. The hemogram showed a pancytopenia. The blood smear revealed the presence of circulating blasts estimated at 36%. The medullogram revealed a medullary invasion by undifferentiated blast cells estimated at 59%, Myeloperoxidase staining was positive. The patient was given antibiotic therapy and rehydration. An extra-renal treatment was performed due to the installation of acute renal failure. Evolution was marked by death following infectious complications.
Keywords: Acute myeloid leukemia, acute pancreatitis

INTRODUCTION

Acute myeloid leukemia type 2 (AML2) accounts for 30% to 40% of AML and occurs at all ages.

It is defined (according to the Franco-American-British FAB classification) by a rate of medullary blasts between 20 and 90% with a granular maturation greater than 10%. The karyotype shows a t (8; 21) in about one-third of the cases.

The incidence of AML in adults is 5 to 8 / 100,000 per year in Europe; it increases with age, especially after 50 years. The mortality rate is 4 to 6 / 100,000 per year. The median age at diagnosis is 65 years.

The diagnosis of AML requires examination of blood and medullary smears by trained cytologists.

The minimal assessment must include a morphological study (FAB criteria and signs of dysplasia) and cytochemical (peroxidase), a cytogenetic study of the marrow (karyotype and in situ hybridization in FISH fluorescence) and a study in molecular biology (gene rearrangements resulting from abnormalities chromosome).

We report in this study a case of AML 2 in a 56-year-old patient, revealed by acute pancreatitis, and we discuss it in the light of data from the literature.

OBSERVATION

This patient is 56 years old, with no significant pathological history, admitted for epigastric pain with vomiting.

Clinical examination found a dehydrated patient, blood pressure: 130/70 mmHg, abdominal examination revealed epigastric sensitivity, without splenomegaly or hepatomegaly, the ganglionic areas are free.

The neurological examination was normal eliminating a possible neuro-meningeal blastic infiltration, otherwise

The pulmonary examination was without peculiarities.

The biochemical assessment showed lipase activity at 249 IU / l [21-67], Blood Sugar: 1.16g / l [0.74-1.06] ; Renal insufficiency: urea: 2.62 g / l [0.17-0.43]; Creatinine: 82 mg / l [6.60-10.90]; Calcium: 63mg / l [88-108]; Phosphorus: 61 mg / l [25-45]; Uric acid: 365mg / l [26-60]; CRP: 114 mg / l [0-5]; LDH: 3325 U / L [0-247]; Total proteins: 63 g / l [66-83]; Albumin: 37g / l [35-52]; Serum iron: 2.1 mg / l [0.6-

1.8]; Ferritin: 4787µg / l [10-120]; CPK: 175 µl / l [0-145]; CPK-MB: 52 IU / l [0-24]; Triglycerides: 4.32g / l [0-1.5]; HDL cholesterol: 0.10g / l [0.4-1]; Tumor markers: CA19-9: 47.3U / ml [0-35]; CA125: 60U / ml [0-35]; CA15-3: 9.9U / ml [0-31.40].

HBV viral serology; HBC; CMV and HIV are negative; Syphilitic serology is also negative.

The hemogram showed a pancytopenia: anemia at 8 g / dl; VGM: 81.1fl; CCMH: 34.6 g / dl; Leukocytes: 2.93.10 ^ 3 / µl; Neutropenia at 90 / µl; Platelets at 24,000 / µl. The blood smear (FIG. 1) revealed the presence of circulating blasts estimated at 36%.

The medullogram showed the presence of 59% of undifferentiated blasts and myeloblasts (Figure 2) with the positivity of myeloperoxidase activity (cytochemical staining) (Figure 3) and the presence of a granular maturation exceeding 10%, Leading to the diagnosis of acute myeloid leukemia versus LAM 2 according to the FAB classification.

The cytogenetic and biomolecular study could not be carried out due to the rapid and fatal evolution of the disease. Abdominal ultrasound is without anomalies; C-abdominal CT scan (performed after 48 hours of onset of symptomatology) returned normal, the injection of the contrast agent could not be achieved due to impaired renal function.

Acute pancreatitis (AP) was classified severely according to the Ranson score (Table I). At the end of this assessment, the diagnosis of AP associated with AML 2 was retained. The patient was rehydrated and received 3rd generation cephalosporin, paracetamol and antiemetics.

The progression was marked by the aggravation of renal function; Hence the indication for extra-renal purification. The patient secondarily introduced an infectious syndrome of fever with chills; the blood cultures were performed and were positive for *Enterococcus faecium* Sensitive to teicoplanin and vancomycin. The patient died as a result of septic shock on an immunocompromised terrain.

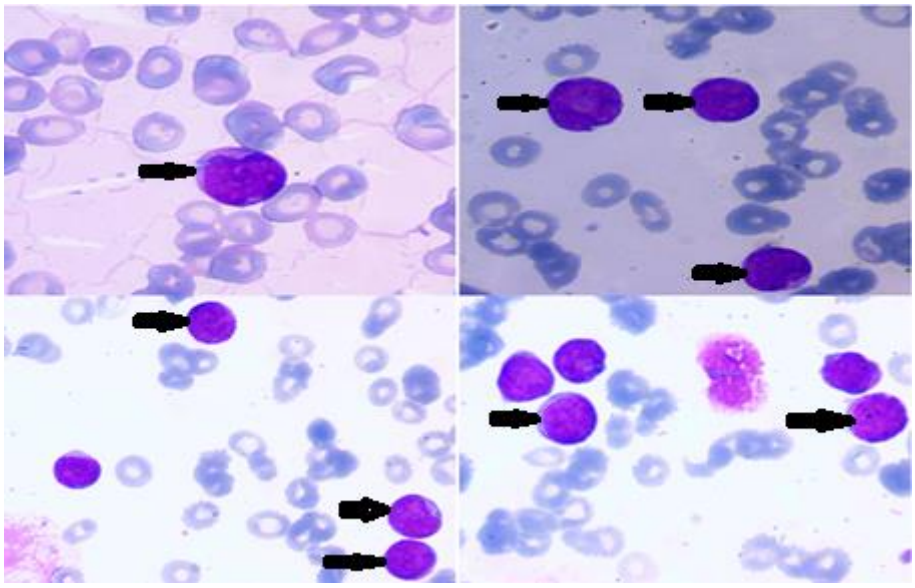

Fig-1: Blood smear (colored at May-Grünwald-Giemsa-objective x 100) showing two medium-sized blasts, Nucleus rounded to oval, basophilic cytoplasm with the presence of some azurophilic granulations

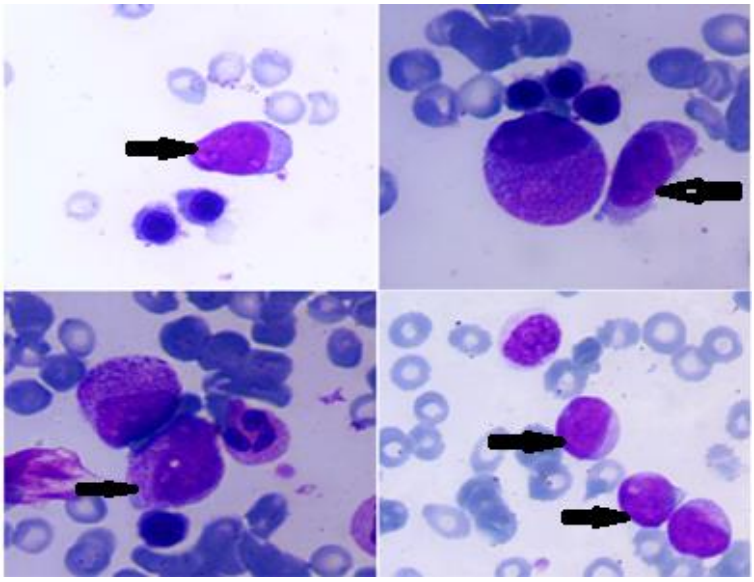

Fig-2: Myelogram (MGG staining, X 100) showing infiltration of bone marrow by undifferentiated blast cells and myeloblasts, Of medium size, a rounded or oval nucleus, With the presence of nucleoli, fine chromatin and more or less basophilic cytoplasm strewn with azurophilic granulations

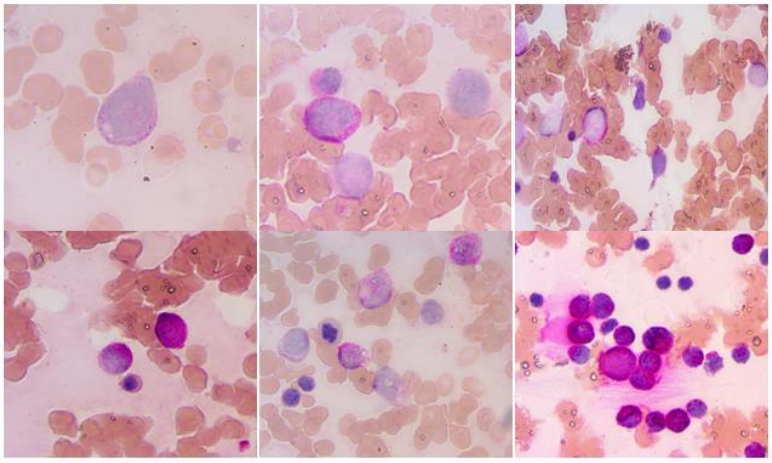

Fig-3: Medullary smear (MPO staining; X100) showing positive MPO blast cells

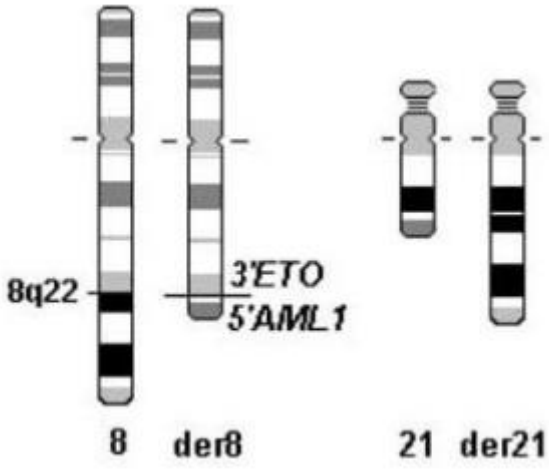

Fig-4: Scheme of t (8; 21) 5q22; q22) showing fusion of the ETO and AML1 genes [8]

Table-I: Ranson score [21]

At the admission	Between admission and 48 hours
Age> 55 years old Leukocytes >16 000/mm3 LDH> 1.5 times normal ASAT > 6 times normal Blood Sugar > 11mmol/L	Falling hematocrit > 10 points Elevation of blood urea > 1.8 mmol/L Serum Calcium < 2 mmol/L PaO2 < 60 mmHg Fall of bicarbonates > 4 meq/L Liquid sequestration > 6 L*

*: This means that more than 6 liters of solute have to be perfused within the first 48 hours to maintain a satisfactory hydro-electrolytic balance.

Number of signs	Mortality risk %
0-2	0.9
3-4	16
5-6	40
7-8	100

Each parameter is side 1 when present. Pancreatitis is considered severe if the score is greater than or equal to 3.

Table-II: Main causes of acute pancreatitis [21]

Common causes	Migration of a biliary calculation in the main bile duct (approximately 40% of AP) Chronic and significant alcoholism (approximately 40%)
Rare Causes	Malignant +++ or benign tumors of pancreas Postoperative Endoscopic retrograde cholangio-pancreatography
Exceptional causes	hypertriglyceridemia (>10 mmol/l) Hypercalcemia regardless of cause Drugs (chronology +++) Infectious (viral, bacterial, mycotic, parasitic) Autoimmune Pancreas divisum
Without cause	idiopathic

DISCUSSION

Acute pancreatitis is a common complication, which occurs in patients with gall bladder stones or chronic alcoholism. Hypercalcemia can cause acute pancreatitis, its causes being multiple: primary or secondary hyperparathyroidism, metabolic diseases of bone, bone metastases, as well as lymphoproliferative syndromes. (Table II).

Pancreatic infiltration with leukemic cells is a rare manifestation of acute lymphoblastic leukemia (LAL) [1]. Acute pancreatitis in LAL is either due to hypercalcemia or chemotherapy, but direct damage to the pancreas by leukemic cells is rarely observed. [2, 3]. Acute myeloid leukemia type 2 according to the FAB classification is associated with the translocation t (8; 21) (q22; q22), And is part of the AML with recurring genetic abnormalities according to the WHO 2008 classification.

The diagnosis of acute pancreatitis is based on the association of typical abdominal pain with an elevation of lipasemia above 3 times normal. The place of the imagery is reserved for the cases of diagnostic doubt and for the diagnosis of gravity (classification of Balthazard). It is based on the abdominal CT scan with contrast agent injection from 48 hours after the onset of symptomatology.

The incidence of AML with recurrent cytogenetic abnormalities decreases with age [4; 5]. The translocation t (8; 21) is present in about 5% to 10% of all AML cases and 10% to 22% of AML 2 cases [6; 7]. This is a translocation affecting chromosomes 8 and 21. A part of the long arm of chromosome 8 containing the ETO gene is reciprocally translocated on the long arm of chromosome 21 at the level of the AML1 gene (FIG. 4) [8].

The consequence of the translocation results in a fusion gene between the AML-1 gene and the ETO gene in its CBFb part. The fusion gene called AML1 / CBFb is no longer able to regulate cell functions [8].

In 75% of cases, there are other associated chromosomal abnormalities, the most common being the loss of a sexual chromosome, the interstitial deletion of the long arm of chromosome 9, and trisomy 8 [9].

A second translocation has been described in AML 2 and AML4, associated with medullary basophilia and often preceded by dysmyelopoiesis. This is the translocation t (6; 9) (p23; q34). It is rare (less than 2% of abnormal karyotypes) and poor prognosis.

Furthermore, t (9; 22) (q34; q11), more commonly known in association with CML (Chronic myeloid leukemia), is also found in 3% of AML 1 and 2 and in 1% of AML in children with poor prognosis. [10]

Several studies have concluded that t (8; 21) tends to form at the myeloid cells [11]. In our patient, the diagnosis of acute pancreatitis associated with acute myeloid leukemia type 2 (according to the FAB) was quickly established, but the severity of acute pancreatitis classified according to the Ranson score (Table II) and the appearance of infectious complications on a site of acute leukemia do not provide a favorable evolution.

But the question remains: is there a link between these two pathologies? In the rare cases of association between acute leukemia and acute pancreatitis (AP), it is either an acute lymphoblastic leukemia leading to a hypercalcaemia at the origin of the AP, which is not the case of our patient suffering from a hypocalcemia, or iatrogenic pancreatitis, post-drug pancreatitis or post-chemotherapy based on Cytarabine, or L-asparaginase [12-16]. Renouncing the hypothesis of a Cause-effect relationship between AML 2 and PA, a standard etiological survey was undertaken, beginning with the most frequent etiologies of AP, it was thus that the medicinal origin was first dismissed by interrogation; the lithiasic etiology or compression of the main bile duct through a tumor process has been sought through abdominal CT scan that is normal income, consolidated by a biological assessment which did not show a peak of the transaminases nor of elevation of the bilirubin.

The patient benefited from a syphilitic and viral serology (HIV, HBV, HBC, and CMV) returning negative. The biological evaluation revealed a high triglyceride level at 4.32 g / l (4.88 mmol/l); the most common definition of HTG-AP (acute pancreatitis secondary to hypertriglyceridaemia) in the literature is triglyceridemia greater than or equal to 1000 mg/dl (11.3 mmol / l) [17, 18-20]. It was then that the diagnosis of acute pancreatitis secondary to hypertriglyceridemia was ruled out.

Two causes are likely to explain the etiological origin of acute pancreatitis: a pancreatic infiltration by the leukemic cells, a rare but possible etiology, or an idiopathic origin.

CONCLUSION

Acute pancreatitis is a severe pathology due to its complications, and its association with acute myeloid leukemia is quite rare. In our observation, the presence of a pancytopenia with circulating blasts was an alarming biological sign leading to a rapid diagnosis of AML 2. The cause-effect relationship could not be established, the evolution was fatal following infectious complications.

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