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Juvenile Myelomonocyte Leukemia Associated with Type 1 Neuro fibromatosis with Late Revelation: About a case in a hematology and oncology unit of the Rabat child hospital

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Abstract

Juvenile myelo Monocytic leukemia's (LMMJ) are rare Myeloproliferative and melody's plastic syndromes, mostly affecting very young children, but serious, which can lead to massive Monocytic infiltration of all organs and death from multiple organ failure. Their occurrence in a context of predisposing genetic syndrome such as noon and syndrome and neurofibromatosis type 1 is common. The diagnosis of LMMJ is made difficult by the heterogeneity of the irclinical-biological presentation however diagnostic criteria have been established to differentiate the LMMJ from other myeloproliferative syndromes. The prognosis for LMMJ is generally bleak and the only potentially curative treatment is bone marrow transplantation with high rate of relapse. Currently many research tracks are explored to propose more effective targeted therapies and to have a clearer vision for the future of these patients.

Keywords: Juvenile myelo Monocytic leukemia's, Neuro fibromatosis type 1, Child.

Introduction

Juvenile Myelomonocyte leukemia is a rare haemopathy that accounts for 2 to 3% of childhood leukemia. It affects mostly very young children, 75% of cases under 3 years of age The positive diagnosis of LMMJ is difficult but it sown biological characteristics such as Monocytic is associated with signs of dysplasia, the absence of the Philadelphia chromosome or protein BCR-ABL fusion, hyper gamma globulinemia and elevated fetal hemoglobin levels, differentiate it from chronic myeloid leukemia or chronic myelo Monocytic leukemia, which mainly affects the elderly [1]. We propose, through is case of LMMJ associated with a neurofibromatosis type 1 revealed late and the data of the literature, to study the different clinical, biological and therapeutic aspects of the LMMJ.

Observation

J. S, age 07, from a 1st degree consanguineous marriage, with a neurofibromatosis type 1 and having as antecedent a death of a brother and a sister at the age of 10 and 8 months in an imprecise context. The child presented 2 weeks before admission cut aneousmucosa anemia with abdominal distension evolving in a feverish context complicated by the appearance of a hemorrhagic syndrome made of hematomas is, existed is and melena of great abundance which required hospitalization in our training. The clinical examination found a child in poor general condition, malnourished, very pale, fever is that 39 ° C, gingival hypertrophy with givorragia. There were 19 'café au lait' stains on the trunk, the backs of different diameters, the smallest measuring 15 mm and the largest measuring 60 mm with lenities in the axillaryregion in favor of neurofibromatosis (Figure 1). Abdominal examination

found abdominal distention with collateral venous circulation, hepatomegaly (FH = 11 cm) and splenomegaly (FS = 11 cm). In addition, the cervical examination did not find lymphadenopathy. The blood count (NFS) on admission revealed anemia (hemoglobin level [Hb] = 3.9 g / dL), thrombocytopenia (platelets = 3000 / mm3) and leukocytes is (leukocytes = 61 000 / mm3). . The blood smear showed Monocytic is (46900 / mm3), 2% myelemia and the presence of 5% blasts. The myelo gram showed hyperplasia of the granular line with signs of dyserythropoiety and significant Monocytic is (Figure 2). Hyper gamma globulin anemia was also present. The karyo type did not reveal a cytogenetic abnormality and the search for the BCR-ABL gene was negative. The child was hyper hydrated with the worming, transfused into red blood cells and platelet. He received chemotherapy with aracytine and hydria. Two weeks later, the child developed febrileneutrop anemia with steps is and disseminated intravascular coagulation causing death.

Discussion

In 2008, the World Health Organization (WHO) ranked the LMMJ as a melody's plastic / myeloproliferative border syndrome (MDS / SMP). In 1998 Niemeyer and al developed diagnostic criteria for this entity, revised by the WHO in 2008 [2, 3]. 75% of cases occurring before the age of 3, However, some MMLD occur in old subjects such as the 3 observations reported by Azma et and this is also consistent with the age of our patient [1]. It is a pathology of the stem cell due to the deregulation of the signal in mediated by growth factors following the mutation of genes RAS (NRAS, KRAS), or regulators of RAS (PTPN11, NF1 or CBL). This results in hypersensitivity of myeloid progenitors to GM-CSF (granulo-macrophage growth factor), which causes excessive proliferation of Monocytic macrophages in the marrow and blood. This proliferation is the severity of the pathology since it can lead to massive Monocytic infiltration of all organs and death by multi organ failure. LMMJs are common in a context of pre dispose sing genetic syndrome such as Noonan's syndrome, neurofibromatosis type 1, which is linked to constitutional deregulation of the RAS pathway and is now grouped under the term "RAS apathies" [4]. The case were ported also presents with neurofibromatosis type 1, according to data from the literature, the association between neurofibromatosis type 1 and LMMJ was described in 1978 and the frequency of this association was 14% in the Niemeyer series and al [5, 6]. The main clinical manifestations in the case were ported were fever, pallor, hemorrhagic syndrome, hepatomegaly and splenomegaly. The same clinical signs have been reported in the literature [7]. Biologically, the leukocyte count in our case was 61,000 / mm3 with myelemia and circulating blastos is. Bisque and al. showed in their studies that most cases had a leukocyte is of less than 50 000 / mm3, and 8% had leukocytes is of> 100 000 / mm3 [8]. In the study by Niemeyer and al. Anemia was present in 83% of patients, of whom 16% had an Hblevel<7 g / dL and severe thrombocytopenia was present in 17% of patients, which is the case of our patient [2]. Most studies have reported dysmégacaryopoies is, dysgranulopoies is and dyserythropoiesis in the medullogram [1, 2, 7]. A polyclonal hyper gamma globulinemia is commonly observed. In the retrospective study of Niemeyer and al. The increase in IgG, IgM and IgA levels was observed in 65% of children [2]. The karyotype plays an important role in the prognosis since it makes it possible to classify patients in different risk groups. It is normal in most cases. Nevertheless, chromosomal aberrations such as 7q-, tri so my 8 and tri so my 21 have been detected in the LMMJ [7]. To date, the Philadelphia chromosome and the BCR-ABL fusion gene have never been reported in the LMMJ.

In fact, the absence of translocation t (9; 22) and BCR-ABL is now part of the diagnostic criteria according to the international group of LMMJ [9]. Intensive chemotherapy alone seldom reaches patients in remission and those who reach it have very short survival [7]. Indeed, the only cure is all organic stem cell transplantation that can cure approximately 50% of patients with risk of relapse [10], the European Blood and Marrow Transplantation Working Group (EMBT), has developed a study on 100 children and reported a survival rate of 64% after transplantation [11].

Conclusion

The LMMJ is a rare and serious blood disease, is the prerogative of the very young child. Diagnosis remains difficult despite well-established criteria. The prognosis to date is pejorative with high mortality rate. Only all organic stem cell transplantation increased the survival rate.

References

1. Azma RZ, Zarina AL, Hamidah A, et al. Juvenilemyelomonocyticleukaemia: a case series. Malaysian J Pathol 2009; 31:121–8.
2. Niemeyer CM, Fenu S, Hasle H, et al. Differentiatingjuvenilemyelomonocyticleukemiafromi nfectiousdisease. Blood 1998;91:365–6.
3. Vardiman JW, Brunning RD, Arber DA, et al. Introduction and overview of the classification of the myeloidneoplasms. In: Swerdlow SH, Campo E, Harris NL, et al., editors. WHO Classification of tumours of haematopoietic and lymphoid tissues. 4th ed., Lyon: IARC Press; 2008.
4. J. Lachenaud, M. Strullu, A. Baruchel, H. Cavé. Juvenilemyelomonocyticleukemias. Bulletin du cancer 10.1684/ bdc.2014.1908
5. Benessahraoui M, Aubin F, Paratte F, et al. Leucémie myélomonocytaire juvénile, xanthomes et neurofibromatose de type 1. ArchPediatr 2003; 10:891–4.
6. Bader JL, Miller RW. Neurofibromatosis and childhoodleukemia. J Pediatr 1978; 92:925–9.
7. I. Ghariani, N. Jmili-Braham, H. Regaieg, B. Achour, Y. Ben Youssef, H. Sendi, L. Bakir, M. Kortas. Juvenilemyelomonocyticleukemia: A three-case series. Archives de Pédiatrie 2016; 23:1264-1269
8. Busque L, Gilliland DG, Prchal JT, et al. Clonality in juvenilechronicmyelogenousleukaemia. Blood 1995; 85:21–30.
9. Chan RJ, Cooper T, Kratz CP, et al. Juvenilemyelomonocyticleukemia: a report from the 2nd International JMML Symposium. LeukemiaRes 2009; 33:355–62.
10. Emanuel PD. Juvenilemyelomonocyticleukemia. CurrHematolRep 2004; 3:203–9.
11. Locatelli F, Nollke P, Zecca M, et al. Hematopoietic stem cell transplantation (HSCT) in children with juvenile myelomonocytic leukemia (JMML): results of the EWOG-MDS/EBMT trial. Blood 2005 ;105:410–9.

Legends Figures

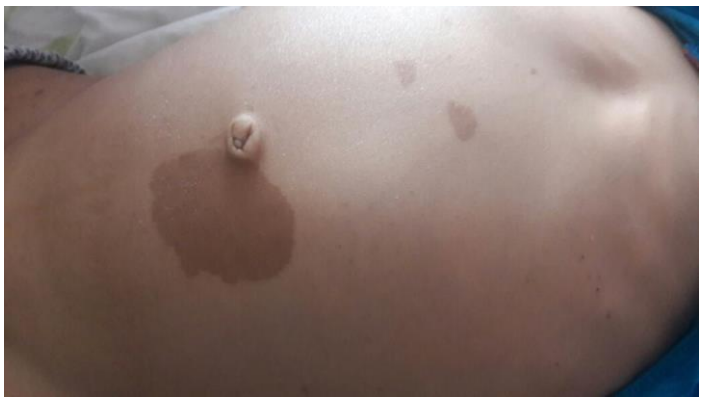

Figure 1: "café au lait" stains of different diameters

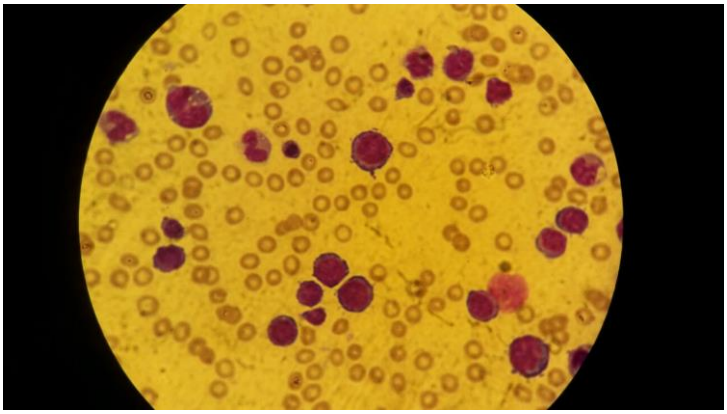

Figure 2: Myelogram of our patient showing hyperplasia of the granular line with signs of dyserythropoiesis and significant monocytosis