Int J Clin Exp Pathol 2010;3(7):718-722
www.ijcep.com /IJCEP1007007

Case Report

Isolated trisomy 10 in an infant with acute myeloid leukemia: a case report and review of literature

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Received July 17, 2010; accepted August 12, 2010; available online August 17, 2010

Abstract: Trisomy 10 as the sole cytogenetic abnormality in AML is rare, with an incidence rate of ≤ 0.5%. It tends to affect the elderly and is extremely rare in pediatric patients. We describe a case of an 8-month-old Caucasian baby who presented with prominence of left eye and fever without lymphadenopathy or hepatosplenomegaly. Bone survey showed diffuse periosteal reaction in the femur, pelvis, maxillary and orbital bones (with fracture). CBC revealed normal white blood cell count with increased blasts, mild anemia and moderate thrombocytopenia. Bone marrow biopsy showed increased myeloblasts with bilineage dysplasia and 3-4+ reticulin fibrosis. Flow cytometry revealed blasts positive for CD34, CD33, and MPO and negative for CD7, CD13, and HLA-DR. Trisomy 10 was demonstrated by chromosome analysis and fluorescence in-situ hybridization. The patient received induction chemotherapy and achieved complete clinical and hematologic remission at day 28. However, he relapsed after three cycles of chemotherapy. Compared to the two other reported pediatric cases, our patient has some unique features such as much younger age and additional findings such as bilineage dysplasia and bone marrow fibrosis. Both reported cases and our case were classified as AML-M2 indicating that this may be a common subtype in pediatric patients. Bone involvement was present in our patient and one other case and both had similar immunophenotype (CD33+, CD7-). These findings suggest that isolated trisomy 10 may be associated with distinct clinicopathologic features in pediatric AML. Studies on additional patients are needed to establish this association.

Keywords: Trisomy 10, acute myeloid leukemia, infant, review, CD7, CD13, CD33, CD34

Introduction

Trisomy 10 as a sole cytogenetic abnormality has been uncommonly described in a variety of hematopoietic malignancies including acute lymphoblastic leukemia (ALL), and myelodysplastic syndrome (MDS). However, it is extremely rare in acute myeloid leukemia (AML) particularly in the pediatric age group. The incidence ranges from 0.2% to 0.5% of AML, with only 22 cases having been reported thus far [1-4]. This cytogenetic abnormality has been reported in association with most French American British (FAB) subtypes except FAB-M3. Majority of reported cases were adults, ranging from 29 to 80 years of age with intermediate to poor prognosis. The two reported pediatric cases were a 2-year-old Japanese boy and a 7-year-old boy [5,6]. Here we report the third pediatric AML case with trisomy 10, including clinical and histological features in comparison to those reported in the literature.

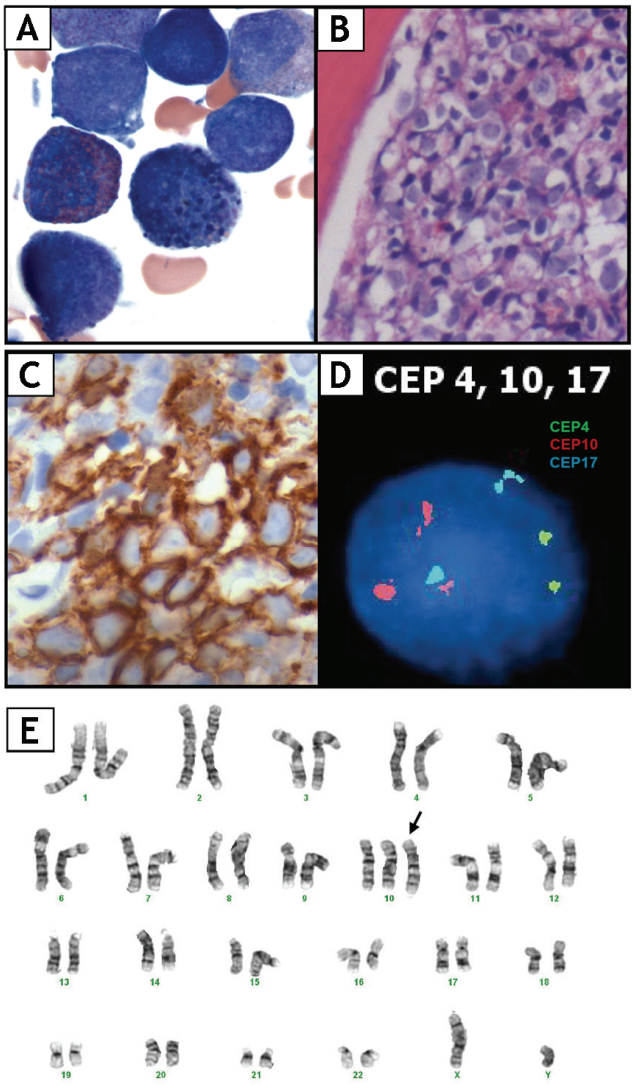
Case report

An 8-month-old Caucasian boy presented with a prominence of the left eye, episodes of fever, and a delay in motor development. On physical examination, there were no skin rashes, lymphadenopathy or hepatosplenomegaly. X-ray, bone survey and CT scan showed diffuse periosteal reaction in the femur, pelvis, maxillary and orbital bones (with fracture). Biochemical studies showed markedly elevated levels of C-reactive protein 15,900 mg/dL (normal 0-0.74 mg/dL), and lactate dehydrogenase 1,015 u/L (normal 120-246 u/L).

The initial CBC (**Table 1**) did not show increased blasts or thrombocytopenia. A week later, CBC

Table 1. Complete Blood Count (CBC) count and WBC differential

CBC	First CBC	Second CBC	Reference range
Hgb (g/dl)	8.8	9.6	
MCV (fl)	80.8	84.1	
Platelet (k/mm^3)	216	87	150-450
WBC (k/mm^3)	12.0	11.7	6-14
Blasts (%)	0	8	0
Myelocytes (%)	0	2	0
Bands (%)	2	7	
Neutrophils (%)	69	24	
Lymphocytes (%)	22	46	
Monocytes (%)	4	9	
Eosinophils (%)	3	4	
Basophils (%)	0	0	



revealed a normal white blood cell count of 11.7 k/mm^3 with 8% blasts (**Table 1**). Moderate normocytic anemia and thrombocytopenia were present. Tear drop red blood cells, hypogranular and hyposegmented neutrophils were present in the peripheral blood smear.

The patient underwent biopsies of bone marrow (BM) biopsy and the left femoral lesion. BM biopsy was 100% cellular with increased myeloblasts (25%) and mild eosinophilia (**Figure 1B**). Blasts were type II myeloblasts characterized by presence of increased N/C ratio, fine cytoplasmic granules and open chromatin. No Auer rods were seen. Mild dyserythropoiesis characterized by nuclear hyperlobation and multinucleation. Dysplastic eosinophilic precursors containing coarse basophilic granules were also noted (**Figure 1A**). In addition, 3-4+ reticulin fibrosis was observed. Flow cytometry analysis of BM demonstrated a population of blasts (25%) expressing CD33, CD34, weak CD117, and MPO, but was negative for HLA-DR, CD7, CD13, and TdT. CD34 (**Figure 1C**), CD117 and

Figure 1. (A) Bone marrow aspirate showing type II myeloblasts and a dysplastic eosinophilic precursor with coarse basophilic granules. (B) Bone marrow biopsy revealing sheets of blasts. (C) Blasts demonstrating CD34 positivity by IHC. (D) FISH using CEP10 on cultured bone marrow cells showing three copies of chromosome 10 (red signal). (E) Karyotype of bone marrow cells showing trisomy of chromosome 10.

Table 2. Clinico-hematological and cytogenetic findings of trisomy 10 in AML

Case	Race	Age/sex	Presentation	Dx	WBC (10^9/L)	Blast [a] (%)	Positive Surface marker	Trisomy 10[b]	Survival (month)	Ref.
Pediatric cases										
1	Japanese	2/M	Fever, petechiae, LA, HSM, bone lesions	M2	61.6	91.6	CD13/15/33	NA	14	[6]
2	NA	7/M	Fever, photophobia, headache, double vision	M2	3.7	52	CD7/13/15/33/34/38/56	NA	12+	[5]
3	Caucasian	8 mos	Fever, bone lesions	M2	11.7	25%	CD33/34/117/MPO	3/20	3+	current case
Adult cases										
4	Japanese	66/M	Hepatomegaly, LA	M0	7.8	31	CD7/33/HLA-DR	NA	2	[4]
5	NA	78/F	Dehydration, fatigue, LA, HSM	M0	51.3	38 (PB)	CD5/7/13/33/34	11/19	NA	[11]
6	Japanese	80/F	Anemia, LA	M0	4.9	94	CD7/33	8/8	4	[1]
7	Chinese	29/M	Gum bleeding	M1	3.5	88	NA	3/13	60+	[12]
8	Japanese	43/M	NA	M1	11.0	77	CD7/10/13/HLA-DR	NA	54+	[4]
9	Japanese	48/M	NA	M1	7.1	86	CD13/33/HLA-DR	NA	38	[4]
10	Chinese	51/F	NA	M1	260	87	CD7, HLA-DR	NA	14+	[13]
11	Chinese	37/F	NA	M2	21.8	9	CD7/13/33, HLA-DR	NA	NA	[13]
12	Caucasian	45/M	Anemia	M2	NA	NA	CD7/13/33/34/HLA-DR	17/20	10+	[14]
13	Japanese	57/M	Weight loss, loss of appetite, cough	M2	4.5	64	CD7/13/33/34/38/HLA-DR	3/19	16+	[1]
14	Spanish	65/M	Asymptomatic	M2	6.1	50	CD7/13/33/34/HLA-DR	33/35	33	[3]
15	Italian	72/M	NA	M2	NA	47	CD13/33/34/45/HLA-DR	NA	NA	[2]
16	Italian	75/M	NA	M2	NA	NA	CD33	NA	NA	[15]
17	NA	69/F	Fever	M4	5.2	50	NA	10/24	34	[16]
18	NA	63/M	Exposed to organic solvents	M5	NA	NA	NA	12/12	NA	[17]
19	Chinese	60/F	NA	M6	3.8	32	NG	2/10	6	[8]
20	NA	68/F	Gastrointestinal hemorrhage, bruising, fatigue	M6, dysplasia, fribrosis	9.7	85	CD7/11c/13/33/Glycophorin A	15/15	1	[7]
21	NA	72/M	LA	M7	9.3	85	NA	32/32	8	[16]
22	Caucasian	43/M	Joint pain, lethargy, SOB, weight loss	NA, fibrosis	NA	NA	CD13/15/33	13/18	5	[14]
23	Chinese	59/M	NA	NA	68	36 (PB)	NA	2/4	122	[8]

a: percentage of blasts in BM; b: proportion of trisomy 10 in karyotyped metaphases; Dx: diagnosis; HSM: hepatosplenomegaly; LA: lymphoadenopathy; NA: not available; PB: peripheral blood; SOB: shortness of breath

MPO positivity were further confirmed by immunohistochemistry. BM aspirate and biopsy findings were consistent with AML-M2. The patient received induction chemotherapy consisting of cytosine arabinoside (intravenous and intrathecal), etoposide and daunorubicin and achieved complete clinical and hematologic remission at day 28. However, he relapsed in 3 months after three cycles of chemotherapy.

Cytogenetic and fluorescence in situ hybridization analysis

Chromosome analysis and fluorescence in situ hybridization (FISH) were preformed at diagnosis on cultured bone marrow cells. Twenty metaphases were analyzed by the conventional trypsin-Giemsa (G-) banding technique and three showed 47,XY,+10 (**Figure 1E**), which was further confirmed by *centromeric* enumeration *probe* (CEP) for chromosome 10 by FISH (**Figure 1D**). No other clonal abnormalities were identified by FISH using probes specific for rearrangement at *MLL* locus, PML-*RARA* fusion or recurrent abnormalities in MDS (ETO/AML1 fusion, monosomy5/deletion5q, monosomy7/deletion7q, deletion13q, inv(16), del(20q), CBFB, 20q12).

At the time of relapse, trisomy 10 was identified in 4 of 800 cells by FISH. However, cytogenetic analysis of cultured bone marrow cells did not demonstrate any clonal chromosome abnormality in any of the 20 metaphase cells analyzed.

Discussion

AML with trisomy 10 as the sole cytogenetic abnormality is rare with an incidence rate of ≤ 0.5%. Though AML with trisomy 10 can occur at all ages it tends to affect adults with mean age of 54. The male to female ratio is about 2:1. Half of the cases have been seen in patients of Asian descent, including one reported pediatric case. The clinical presentation is variable. Review of published cases of trisomy 10 (**Table 2**) showed the most common FAB subtypes were M0, M1, and M2. In adults, 7 of 11 (78%) CD7 positive cases also co-expressed CD33, which is likely a common immunophenotype in this group of patients. Survival data were available in 18 cases (**Table 2**) with median follow-up time of 11 months. The prognosis seems to be intermediate to poor in these patients, with the median survival of 33 months.

The two reported pediatric cases and our patient share several common features. All three were males (case #1, 2 & 3, **Table 2**) and morphologically were all consistent with FAB AML-M2. The clinical presentation of all three cases was atypical in that one presented with meningitis and other two presented with bone lesions [5,6]. Our case and patient #1 (**Table 2**) shared many similar findings include presentation with bone lesions. Both cases had type II myeloblasts with fine granules in the cytoplasm, but no characteristic morphological features have been described in patients with trisomy 10 in the literature. In both patients the blasts were negative for CD7 but positive for CD33.

On the other hand, our case also had some unique features. The patient was much younger (8-months *vs*. 7- and 2-years) and there was morphologic evidence of myelodysplasia. The presence of bilineage dysplasia and BM fibrosis suggests that this AML may have arisen from underlying MDS, though FISH was negative for recurrent clonal abnormalities in MDS. Only one other case (#20) revealed both trilineage dysplasia and fibrosis of in an adult patient with AML M6, who died 26 days after admission [7]. Two adults cases of MDS with trisomy 10, have been reported, but survival data was not available for these cases [8,9]. One pediatric patient (case #2) had allogeneic stem cell transplantation after high-dose intravenous and intrathecal chemotherapy. He was alive a year after diagnosis at the time of report [5]. The other pediatric patient with bone lesions (case #1) exhibited an unfavorable prognosis: the patient relapsed in 6 months and expired 14 months after initial diagnosis [6]. Though our patient initially responded well to induction chemotherapy, he relapsed in 3 months and had several adverse prognostic indicators including associated dysplasia, fibrosis and extremely young age.

The impact of trisomy 10 on prognosis in the reported cases is variable. Pedersen et al observed that in AML and ALL patients, trisomy 10 clonal size directly correlated with peripheral blood leukocyte count in that small clones tended to be associated with few to no circulating blasts and vice versa. [8]. The authors hypothesized that trisomy 10 cells are highly malignant and that clinical progression from premalignant to malignant conditions is associated with clonal expansion. However, there was no

difference in survival in patients with small clones versus those with large clones, which did not lend support to their initial hypothesis. Review of all AML with trisomy 10 cases, clone size data, WBC, and percentage of blasts were available in 11 cases (**Table** 2). Analysis of these cases revealed no correlation between the clone size with WBC or with percentages of blasts (r=0.257, p=0.435, and r=0.576, p=0.066, respectively, Spearman's rank correlation coefficient method). Interestingly, Sakai et al found the trisomy 10 disappeared at relapse in a pediatric patient [6], whereas another report showed addition of trisomy 10 at relapse [10]. In light of these variable reports and few cases in the literature, the role of trisomy 10 in disease progression and overall prognosis remains unclear.

In summary, trisomy 10 is a rare isolated numerical chromosomal abnormality in AML. The clinical and hematological features in adults are broad and variable. It is interesting that the two pediatric patients who presented with bone lesions had similar histology and immunophenotype (CD7-/CD33+). Review of additional cases is necessary to determine if trisomy 10 is in fact associated with unique immunomorphological features and an adverse prognostic indicator in the pediatric age group.

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