Abstract

We report an 18-months old boy with trisomy 21 who initially presented with myelodysplastic syndrome MDS, and later transformed into acute megakaryoblastic leukaemia AML. At presentation he was found to have some unusual findings namely multiple soft tissue masses over scalp, left elbow and over the knee joints as well as hard mass felt in left hip. Biopsy of soft tissue of scalp revealed granulocytic sarcoma. Generally granulocytic sarcoma is seen with AML-M2 and its association with AML-M7, to our belief has rarely been reported previously.

Keywords:
Down syndrome, Megakaryoblastic leukemia, granulocytic sarcoma

Introduction

Acute myeloid leukaemia (AML) represents a heterogeneous group of hematologic malignancies arising from the transformation and expansion of early myeloid stem cells. During the mid-1970s the French/American/British (FAB) classification system was developed and defined the categories of AML as M1 through M7. Granulocytic sarcoma is mostly associated with M2. Acute megakaryoblastic leukaemia (M7) is associated with GATA1 mutation and risks are increased in individuals with Down’s syndrome. Here we report a case in which granulocytic sarcoma is seen in association with acute megakaryoblastic leukaemia in DS (Down syndrome) which to our belief is not reported before in literature. We have also observed that this case had extensive bony disease with extensive periosteal reaction and osteolytic lesions which is also rarely seen.

Case Report

This Kuwaiti boy was a product of consanguineous marriage delivered prematurely at 7 months of gestation with a birth weight of 1.2 kg by caesarean section in view of fetal distress and oligohydramnios. Patient was mechanically ventilated for 8 days and received one dose of surfactant. In addition to intrauterine growth retardation IUGR, he had transient myeloproliferative disorder (TMD), jaundice for which he received phototherapy, and congenital heart disease (ASD and PDA) which closed spontaneously. He was also hypothyroid and maintained on eltroxin.

This child was initially followed at general paediatric ward, but later in view of anaemia and thrombocytopenia was referred to our department NBK children’s cancer hospital in May 2012. On examination he was pale, hypotonic and showed the characteristic clinical features of trisomy 21. Spleen was felt up to 2cms below costal margin. CBC at that time showed Hb 62gm/l, WBC 7.9x10⁹/l, Polymorphs 30%, Lymphocytes 61%, Monocytes 9%, and Platelet 39x10⁹/l. Bone marrow examination was as follows: hypo cellular bone marrow with decrease in all hematopoietic cell lines. There were 3% blast cells. Erythroid lineage shows dyserythropoietic changes. Immunophenotyping demonstrated normal values. Based on the clinical data and result of investigation he was diagnosed as myelodysplastic syndrome. He was admitted on several occasions for blood and platelet...
transfusion. In August 2012 he developed left temporal painless firm scalp swelling size 2.5cm x 2cm (Figure 1). CT head showed multiple bony erosions with the largest one in left temporal and left parasellar region. Hence a biopsy of temporal swelling was taken and histopathology revealed extra medullary myeloid cell tumour “granulocytic sarcoma”. Bone marrow examination was repeated in September 2012 which revealed acute megakaryoblastic leukaemia M7 with extensive myelofibrosis. Cytogenetic study showed 47XY,+21c.

Child was admitted for chemotherapy. At the time of admission he had the following new findings: firm scalp swelling in left temporal area, left elbow (Figure 2), and above both knee joints. There was a hard mass felt in left hip without signs of inflammation. Spleen was 3cm and liver 4cm below their respective costal margin. X-ray study of these swellings in elbow and lower limbs revealed multiple lytic lesions with leukemic infiltrates (Figures 3, 4). He received induction chemotherapy as per UK- AML-17 Great Ormond Street GOSH protocol. Following chemotherapy the size of the swellings were decreased up to 60 to 70%. Unfortunately post chemotherapy bone marrow suppression was complicated by prolonged diarrhoea, paralytic ileus, typhilitis, sepsis, hypocalcaemia, hypoglycaemia and finally died on 23/10/12 despite best possible management.

**Discussion**

Individuals with Down Syndrome (DS) display higher incidence of leukaemia up to 10–20 fold (1). Even more strikingly young children less than 4 years of age with DS have a 500 fold increased incidence of acute megakaryoblastic
leukaemia AMKL (2). The natural history of leukaemia in children with DS suggests that trisomy 21 directly contributes to the malignant transformation of hematopoietic cells. In addition, somatic mutations of the GATA1 gene have been detected in nearly all DS AMKL cases and are notably absent in non-DS.

There is a well-recognized preceding transient myeloproliferative disorder (TMD) occurring in the neonatal period in 10% of infants with DS(3,4,5). TMD is a clonal pre-leukaemia characterized by an accumulation of immature megakaryoblasts in the fetal liver and peripheral blood (5). The incidence of TMD may be underestimated as not all cases come to medical attention. Usually TMD present early in neonatal life in DS (6,7,8). The clinical presentation of neonates with TMD ranges from a healthy appearance to bruising, respiratory distress, fulminant hepatic failure, hydrops fetalis. Overall, the majority of cases resolve spontaneously with normal blood counts at a mean of 84 days (9). After a latency period of 1–4 years, a subset of these children (20–30%), develop acute megakaryoblastic leukaemia (10). Patients with AMKL develop anaemia, thrombocytopenia, myelofibrosis, organomegaly, extensive skeletal lesions (12,13), and leucocytosis (14, 15). CNS involvement is unusual (11).

Down syndrome with AML shows heightened sensitivity to high dose cytarabine and anthracycline based therapy compared to non DS AML (16), however intensive induction showed unacceptable toxicity and increased mortality in DS AML (14). Myeloid leukaemia DS has been treated on protocols involving either conventional dose of cytosine arabinoside (Ara-C) 100–300mg/m² (16) or high dose 3g/m2 with reported 3 year overall survival of more than 80%. However significant toxicity has been reported with the high dose Ara-C (11,14,17).

Granulocytic sarcoma is a solid tumour composed of immature white blood cells (18). It is an extra medullary manifestation of acute myeloid leukaemia; i.e. it is a solid collection of leukemic cells occurring outside of the bone marrow. Granulocytic sarcoma may be somewhat more common in patients with the following disease features (18):

- French-American-British (FAB) classification class M2
- Cytogenetic abnormalities t(8;21) or inv(16)
- Expression of T-cell surface markers, CD13, or CD14
- High peripheral white blood cell counts

Extra medullary AML may occur in virtually any organ or tissue. The most common areas of involvement are the skin also known as leukaemia cutis and the gums. Other tissues which can be involved include lymph nodes, the small intestine, the mediastinum, the lung, epidural sites, the uterus, the ovaries, and the orbit of the eye. Definitive diagnosis of a granulocytic sarcoma usually requires a biopsy of the lesion in question, and should always be considered as a manifestation of systemic disease, rather than an isolated local phenomenon, and treated as such. In a patient with newly diagnosed leukaemia and an associated granulocytic sarcoma, systemic chemotherapy against the leukaemia is typically used as the first-line treatment, unless an indication for local treatment of the granulocytic sarcoma (e.g. compromise of the spinal cord) emerges. Granulocytic sarcoma is typically quite sensitive to standard antileukemic chemotherapy.

**Conclusion**

Granulocytic sarcoma which is an extra medullary manifestation of acute myeloid leukaemia is seen generally with AML-M2 and its association with myeloid leukaemia in Down syndrome to our belief has rarely been reported in literature before.
References


