CASE REPORT

Synchronous Occurrence of Acute Myeloid Leukemia and Rhabdomyosarcoma

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Abstract Metachronous primary distinct tumors are frequently and increasingly encountered in oncology clinical practice of recent times, but synchronous tumours are still a rarity. We report an unusual case of a 2 year old male child who had synchronous occurrence of rhabdomyosarcoma of pelvis and acute myeloid leukemia. Our search of literature suggests that this may be the first reported case of simultaneous occurrence of these two malignancies.

Keywords Rhabdomyosarcoma · Acute myeloid leukemia · Synchronous tumors

Introduction

Multiple primary cancers are not an unusual phenomena in current oncology practice. These can be synchronous (within 2–6 months of diagnosis of first primary tumor) or metachronous (more than 6 months after first primary). The incidence of second primary synchronous or metachronous tumour is reported as high as 10 % [1]. There are many cancer predisposition syndromes in which sequential occurrence of different types of primary malignancies have been reported. However occurrence of synchronous double malignancies of different histological origin is rarer. Acute myeloid leukemia (AML) has been reported as a second malignancy in patients treated for rhabdomyosarcoma (RMS) [2]. This is perhaps the

first reported case of synchronous occurrence of RMS and AML.

We have obtained the consent of patient's guardian for the publication of this case report.

Case Report

A 2 year old male child presented with complaints of abdominal mass, constipation and urinary retention of 1 week duration. On clinical examination, he appeared pale and emaciated. He had dysmorphic features in the form of hypertelorism, anti mongoloid slant of eyes and bilateral ptosis. There were no bleeding manifestations, significant lymphadenopathy, neurocutaneous markers or hepatosplenomegaly. Abdomen was distended and a firm mass was palpable in the right iliac fossa arising from pelvis, extending up to right hypochondrium and crossing the midline. Other systems were unremarkable. Laboratory investigations revealed anemia (Hemoglobin—8 gm %). Total leukocyte count was 12,800/mm³ and platelet count was 3.2 lakhs/mm³. Serum LDH level was 895 U/l. Liver function tests and renal function tests were within normal levels. Serological tests for HIV, HbsAg and HCV were negative. CT scan of abdomen and pelvis revealed a well-defined mass lesion between urinary bladder and rectum, extending into the abdomen and encasing major blood vessels. The mass was seen compressing both ureters and causing hydronephrosis. Incision biopsy was done from the retroperitoneal mass which showed tumor cells in nests in fibrous stromal background. Individual cells were small with scanty cytoplasm and round to oval nucleus with fine chromatin (Fig. 1a). Immunohistochemistry showed positivity of tumor cells for myogenin and desmin (Fig. 1b, c). Other immunomarkers (Leukocyte common antigen, cytokeratin, synaptophysin, chromogranin, MIC 2) were negative.

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Fig. 1 **a** Nests of tumour cells with scanty cytoplasm and round nucleus with clumped chromatin in a fibrous stroma. (H & E $\times 400$). **b** Tumour cells are positive for myogenin (IHC $\times 400$). **c** Tumour cells are positive for desmin (IHC $\times 400$)

Thus morphology and immunohistochemistry findings were consistent with RMS. Bone marrow imprint and biopsy was done as part of the metastatic work-up for RMS. Bone marrow imprint smears were cellular. Myelogram showed erythroid series (30 %) with normoblastic maturation and megaloblastoid change. Myeloid series showed 22 % blasts with moderate amount of cytoplasm and round nucleus with immature chromatin and prominent nucleoli (Fig. 2a, b). Blasts were myeloperoxidase positive (Fig. 2c). Myeloid maturation (29 %) was present. Megakaryocytes were adequate and seen with normal and dysplastic forms. Bone marrow aspiration with flowcytometry was not done. Bone marrow biopsy also showed erythroid series with megaloblastoid change, myeloid series with clusters of blasts and megakaryocytes (Fig. 3a). Immunohistochemistry done showed positivity of blasts for CD 33 and myeloperoxidase (Fig. 3b, c) and negative for myogenin and desmin. Thus bone marrow study was consistent with AML with maturation. FISH studies for $t(8; 21)$, $t(15; 17)$ and $t(9; 22)$ were negative. Karyotyping done from peripheral blood showed 46 XY pattern. For stress cytogenetics, mitomycin was used as the clastogen. Stress cytogenetics did not show any significant spontaneous chromatid breaks and was hyposensitive to mutagen. There was no family history of malignancies. He was diagnosed to have synchronous double malignancies with RMS and AML with maturation. Patient was treated using a combination of vincristine, adriamycin and etoposide, since these agents are effective for both RMS and AML. We were able to induce remission of both malignancies with 6 months of chemotherapy. But 3 months later he developed recurrence of tumor in the pelvis and expired soon after.

Discussion

Multiple primary cancers in children can be synchronous or metachronous. The occurrence of metachronous tumors is increasing because of the prolonged survival following aggressive treatment of the first cancer. But the occurrence of synchronous tumours is still a rarity. Billroth first reported multiple primary tumors of different histology, in different organs, at different time interval in same individuals in 1860 [3]. Perilongo et al. reported a case of a child manifesting five different tumor types simultaneously [4]. These multiple primary cancers are known to occur with greater frequency in certain familial cancer predisposition syndromes like Li Fraumeni syndrome [5]. Certain dysmorphism syndromes like Noonan syndrome are also known to be associated with higher chance of malignancies arising from different tissues [6]. Our patient also had dysmorphic features like hypertelorism and antimongoloid slant of the eyes suggestive of a Noonan syndrome phenotype, but further mutational analysis for confirmation could not be done due to limited resources. Whole genome analysis of such cases may help in detecting the underlying mutation, which may otherwise be missed by conventional cytogenetics.

Acute myeloid leukemia has been reported as a second malignancy in children treated for RMS, possibly related to therapy with cyclophosphamide and etoposide [2]. But simultaneous occurrence of AML and RMS has not been previously reported in literature. Synchronous occurrence of these cancers points to an underlying genetic event affecting two entirely different lineages. Review of

Fig. 2 **a** Bone marrow aspirate showing several blasts (Giemsa, $\times 400$). **b** Blasts show scanty cytoplasm and round nucleus with immature chromatin and distinct nucleoli (Giemsa, $\times 1000$). **c** Blasts are peroxidase positive ($\times 1000$)

Fig. 3 **a** Bone marrow biopsy showing cluster of blasts (H&E $\times 400$). **b** Blasts are positive for myeloperoxidase (IHC $\times 400$). **c** Blasts are positive for CD 33 (IHC $\times 400$)

literature revealed study comparing the expression profiles of Precursor T cell lymphoblastic leukemia and RMS cell lines and identified common oncogenic driving forces which were responsible for the progression of cancer cells [7]. Both muscle and hematopoietic stem cells arise from the embryonal mesoderm. Further differentiation enables the two cell types to possess different functions and roles by differential gene regulation [7]. An early mutation occurring during embryonal development may predispose the individual for double malignancies involving the tissue

types which develop from the mesoderm. There are case reports of RMS presenting as leukemia without evidence of primary tumour [8]. This supports the stem cell theory of cancer origin that stem cells of cancer maintain the capacity to differentiate, migrate and develop into a new malignant tumour with completely new traits. Syndromes associated with increased risk of RMS like Li–Fraumeni syndrome, Type I Neurofibromatosis, noonan syndrome have also reported occurrence of AML although not as synchronous occurrence [4–6].

The therapeutic dilemma raised by such cases is the simultaneous management of two cancers which may have quite different treatment strategies. Some suggest that the treatment should be directed towards the malignancy that is more advanced at presentation. But when both the malignancies are aggressive and advanced at presentation the treatment option would be to use a combination of chemotherapeutic agents that are likely to be effective against both. In general outcome in these cases with synchronous malignancies is likely to be poor and new options need to evolve.

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