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T-Lymphoblastic Lymphoma in Association with Lobster Syndrome (Split-Hand/Split-Foot *Syndrome)* – Is It A Coincidence?

Ponraj Madasamy[1], Jogamaya Pattnaik[2], Murali Paramanandhan[3], Biswajit Dubashi[4], Naresh Jadhav[5], Jagdeep Singh[6]

Senior Resident,[1,2,3,5,6] Additional Professor & Head of Department[4], Department of Medical Oncology, RCC, JIPMER, Pondicherry

Corresponding Author: Murali Paramanandhan, Department of Medical Oncology, RCC, JIPMER, Dhanvantri Nagar, Pondicherry 605 006, Email: josh.messi19@gmail.com

ABSTRACT: Split hand/foot syndrome (SHFS) also known as Lobster hand foot malformation, is defined as longitudinal deficiency of a digital ray of the hand or foot. In the following case report, we report a 15 year old male presenting with history of dyspnea, dysphagia, hoarseness of voice and facial puffiness for 15 days without any B symptoms, diagnosed as precursor lymphoblastic lymphoma, had associated features of lobster syndrome on presentation. The patient was treated with Multi- Centric protocol MCP-841, patient was under remission after induction. A thorough literature review was done, and this is the first reported association of lymphoblastic lymphoma with Lobster syndrome.

KEYWORDS: Lobster Syndrome, Split Hand/Foot Syndrome, Lymphoblastic Lymphoma, Acute Leukemia

INTRODUCTION:

Split hand/foot syndrome (SHFS) also known as Lobster hand foot malformation, is defined as longitudinal deficiency of a digital ray of the hand or foot. It can present either as syndromic or non-syndromic. The association between the hematological malignancies (lymphoma/leukemia) and SHFM is unknown. This is the first case report of a patient presenting with T cell lymphoblastic lymphoma and Split –hand/foot syndrome.

CASE REPORT

A 15 year old male presented with history of dyspnea, dysphagia, hoarseness of voice and facial puffiness for 15 days without any B symptoms. On examination patient had features of superior vena cava obstruction without lymphadenopathy and hepatosplenomegaly with normal testis. Patient had absence of 2nd and 3rd digit in bilateral foot and fusion of left thumb and index finger since birth. Family history of the patient revealed that he was born of second degree consanguineous marriage pre-maturely weighing1.5Kg .The patient's younger sister also was found to have similar hand/foot abnormalities. Chest radiograph showed mediastinal widening. Computed tomography (CT) chest and PET CT scan confirmed an anterior mediastinal mass of size 8.7 x 7.4 cm with SUV-5.8. Patient baseline haemogram, renal and liver function was normal. Tru-cut biopsy from mass reveals sheets of medium sized cells with high N/C ratio, one or two nucleoli along with interspersed mature lymphocytes. These cells were positive for Tdt, CD3, and negative for CD10, CD20, CK, and PLAP, Ki67-90%. Overall features are suggestive of precursor lymphoblastic lymphoma. Bone marrow showed no evidence of infiltration and CSF study was normal. After confirming the diagnosis patient was started MCP-841 ALL chemotherapy after initially treatment with steroids alone. Post induction chemotherapy there was significant reduction in mediastinal mass (2.5x2 cm) without metabolic activity.

DISCUSSION:

Split-hand/foot syndrome (SHFS) involves median clefts of the hands and feet with associated syndactyly, aplasia and/or hypoplasia of the phalanges, metacarpals and metatarsals. The reported incidence is approximately 1:90,000 babies with no sex predilection. [1] There are two expressions of SHFS, syndromic and non-syndromic. The non-syndromic variant is usually associated with only

isolated involvement of the limbs, whereas the syndromic variant is associated with other cranio-facial anomalies like cleft palate, low set ears, deafness, mental retardation, tibial aplasia etc. [2] The case in discussion is a non-syndromic variant of SHFS as there is no associated anomaly.

The SHFS is associated with five different genetic mutations. The type I is the most frequent variant. It is seen due to mutations on chromosome 7 in a region of DLX5 and DLX6 homeobox genes. [1] The genetic expression in syndromic form is variable. The pattern of inheritance in non-syndromic SHFS is autosomal dominancewith a high penetrance and is limited only to the hands and feet. [3] However, in our case, the probable inheritance pattern is autosomal recessive as only siblings and no other family member are affected. There have been isolated case reports in the literature of the autosomal recessive inheritance pattern of SHFMs of the non-syndromal type. Verma *et al*. described the pattern of inheritance to be autosomal recessive in his study. The siblings born of consanguineous marriage had split hand foot malformation. [4] In our case the patient and his younger sister have split hand foot malformation and are born of a second degree consanguineous marriage.

Autosomal recessive split hand foot malformation has also been reported by Ray and Freire-Maia.[5,6] In a report by Klein, two siblings born of mating between a man and the daughter of his half-brother have ectrodactyly. [7] The alternative hypothesis that is being suggested is the two-locus model, wherein the dominant mutation causing the malformation is controlled by a gene at the other locus. A dominant mutation at the controlling locus leads to non-penetrance of the split hand/foot mutation and the appearance of normal carriers. [8]

The association of lymphoma with lobster syndrome has not been reported in literature. This the first case report on lymphoma with lobster syndrome. The case presented with features of dyspnoea, dysphagia, and puffiness of face since 15 days, these features where suggestive of superior vena caval obstruction. Chest radiograph showed mediastinal widening. CT chest and PET CT scan confirmed an anterior mediastinal mass of size 8.7x7.4 cm with SUV-5.8. Patient baseline haemogram, renal and liver function was normal. Trucut biopsy from mass shows sheet of medium sized cells with high N/C ratio, one or two nucleoli along with interspersed mature lymphocytes. These cells are positive for Tdt, CD3, and negative for CD10, CD20, CK, and PLAP, Ki67-90%. Overall features are suggestive of precursor lymphoblastic lymphoma. Bone marrow showed no evidence of infiltration and CSF study was normal. The age, sex, presentation and flow cytometry are in accordance with literature available for T-LBL.

After confirming the diagnosis patient was started MCP- 841 ALL chemotherapy. Post induction chemotherapy there was significant reduction in mediastinal mass (2.5 x 2 cm) without metabolic activity. Until recently, pre-T ALL/LBL had a poorer prognosis than B-lineage ALL/LBL; however, the use of intensive chemotherapy has led to remarkable improvement in rapid treatment outcomes, and recent studies have reported very high remission and overall survival rates. Still, patients with pre-T ALL/LBL are at high risk for induction failure, early relapse, and isolated central nervous system relapse. [3]

FIGURES:

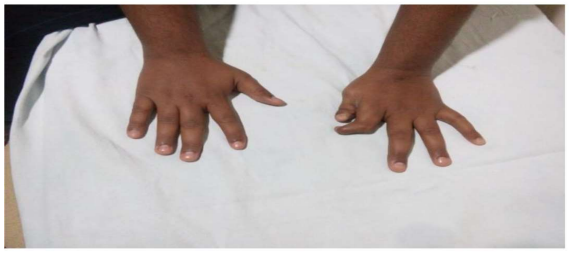

FIGURE: 1 PATIENT WITH FUSION OF LEFT INDEX AND LEFT THUMB

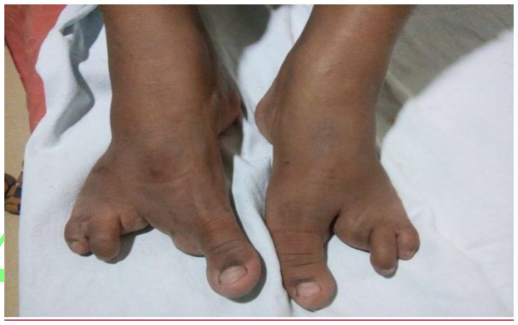

FIGURE 2: ABSENCE OF 2ND AND 3RD DIGIT IN BILATERAL FOOT

FIGURE 3: PATIENT SISTER- LEFT FOOT WITH FUSION OF 2ND TOE WITH FIRST AND 3RD WITH 4TH TOE. RIGHT FOOT WITH ABSENCE OF 2ND, 3RD, AND 4TH TOES.

CONCLUSION:

Lymphoblastic lymphoma is an aggressive variant of lymphomas, and it is associated with poor prognosis when compared to the other lymphomas. The association of LBL with SHFS has not been reported. The authors would like to conclude that there is a need to study such association in lymphoma and every such association should be reported.

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CONFLICT OF INTEREST: There is no conflict of interest

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