ISSN No:-2456-2165

An Excellent Response to Chemotherapy in a Young Patient Diagnosed with Undifferentiated Pleomorphic Sarcoma: A Case Report and Review of Literature

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Abstract:- Undifferentiated pleomorphic sarcoma (UPS) was earlier termed as malignant fibrous histiocytoma (MFH). UPH mainly affects extremities and retroperitoneum with the age predisposition of 50+. We present a case of 16 year old boy with malignant UPS; primary in thigh with lung metastases showing an excellent response to multidisciplinary approach involving surgeryfollowed by systemic combination chemotherapy. The treatment of the patient with metastatic UPS/MFH was successfulutilizing a multidisciplinary approach; although, this type of sarcoma carries a poor prognosis and seen to be insensitive to both chemotherapy and radiotherapy.

Keywords:- *Undifferentiated pleomorphic sarcoma, Malignant fibrous histiocytoma, Chemo radiotherapy.*

I. INTRODUCTION

Soft tissue sarcomas, one of the mesenchymal tumours consists of connective tissue, which includes muscles, fats, deep skin tissues, blood vessels, nerves, bones and cartilages. Undifferentiated pleomorphic sarcoma(UPS) is a soft tissue sarcoma which was previously known as malignant fibrous histiocytoma- a high grade, aggressive sarcoma.(1)(2)The first case was reported by O'Brien et al. in 1964.(3)MFH, being the single largest in the category of soft tissue sarcomas still did not fit in any of the recognized sarcoma categories by the end of the 1980s. In 2013, World Health Organizationrelabeled MFH as "undifferentiated pleomorphic sarcoma".(4)

We experienced a young patient with metastatic UPS who achieved a complete metabolic response with surgery followed by chemotherapy with drugs Gemcitabine and Docetaxel followed by VAC-IE.

II. CASE REPORT

A 16 year old boy presented 2 years back with complaints of swelling over left thigh since 3-4 months along with pain which was acute in onset and progressive in nature, associated with fever and headache. The patient was on anti-tubercular therapy (ATT) at that time for pulmonary tuberculosis (9 months of ATT- completed treatment); anti-retroviral therapy (ART) for HIV which was diagnosed at the same time.

A MRI was done showing alarge multiloculated cold abscess of size 7.8*5.8*15 cms on left thigh for which incision and drainage was done followed by immunohistochemistry which ensued the findings of malignant mesenchymal cells in a background of hemorrhage and necrosis and came out positive for HMB 45, CD34, SMA, EMA and negative for CK & Desmin suggesting a high grade pleomorphic sarcoma.

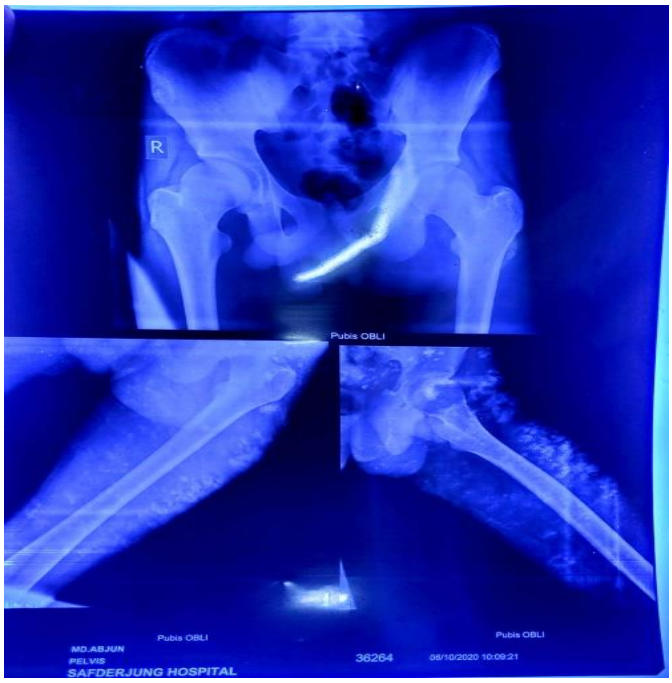
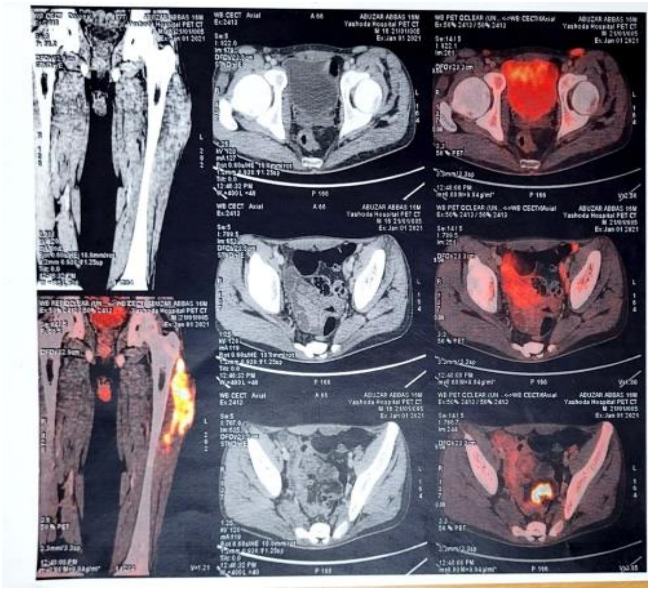


Fig. 1: X-ray of left thigh showing an abscess

For a metastatic work-up, a PET-CT scan was done which revealed an ill-defined necrotic mass lesion of size 5.8*5.6*17.3 cms involving inter and intra muscular planes at anterior compartment of left proximal thigh consistent with sarcoma along with bilateral pulmonary cavitatory and non-cavitatory nodular densities with increased FDG uptake, largest in right lower lobe measuring 2.7*2.1 cms (SUV max- 12.99) and in left lower lobe of size 1.2*1.0 cms (SUV max- 18.5). Few FDG avid lymph nodes were visualized along g right hilar, mesenteric, left common/ external iliac and inguinofemoral lymph nodes along with an ill-defined necrotic lesion of size 2.8*1.5 cms is seen involving right posterior chest musclesopposite to posterolateral aspect of right 6^{th} and 7^{th} ribs (SUV max- 18.42).

ISSN No:-2456-2165



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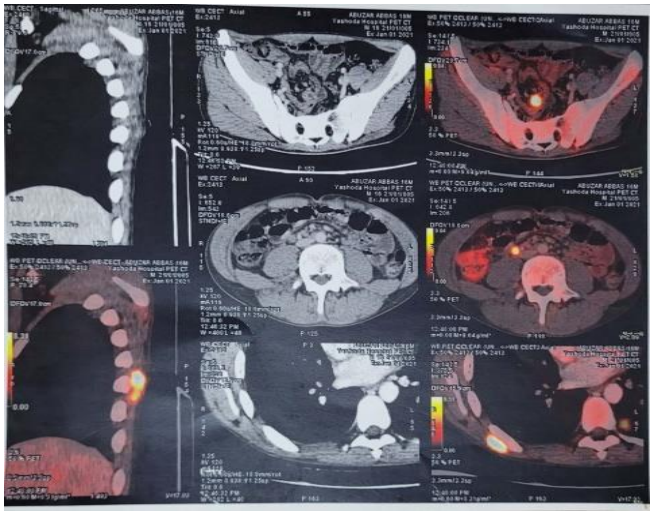

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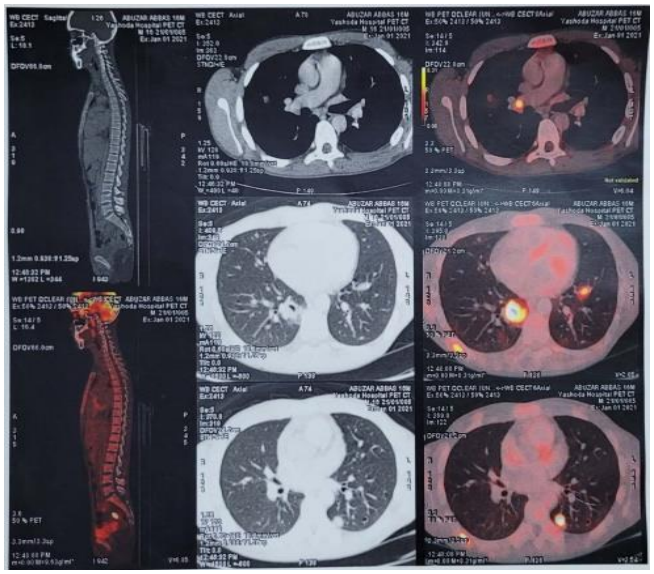
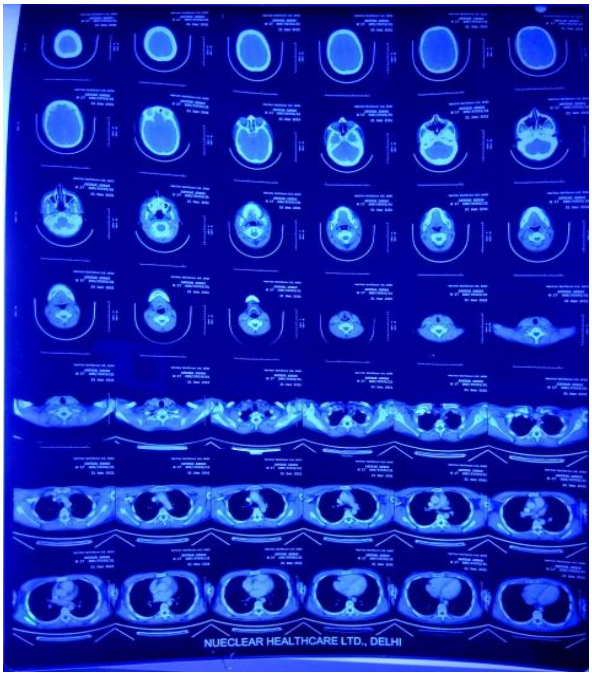


c)

Fig. 2 (a,b,c): PET-CT scan revealing a primary mass in left proximal thigh with bilateral lung metastasis along with involvement of 6th and 7th ribs

Thereafter, the patient was given 9 cycles of chemotherapy consisting of Gemcitabine 1.3g and Docetaxel 120mg with a gap of 3 weeks in between each with a gradual improvement in symptoms. Following which, a PET-CT scan was done which showed a significant decrease in size and metabolic activity of soft tissue lesion involving primary disease in left proximal thigh(1.2*2.3*2.8 cms, SUV max- 7.04) with a complete metabolic and near total morphological regression of mesenteric and left common iliac nodes (SUV max- 2.8).Complete regression of previously seen multiple cavitatory and non-cavitatory bilateral lung nodules was also seen along with of soft tissue lesion in the posterolateral aspect of right 6th and 7th rib.



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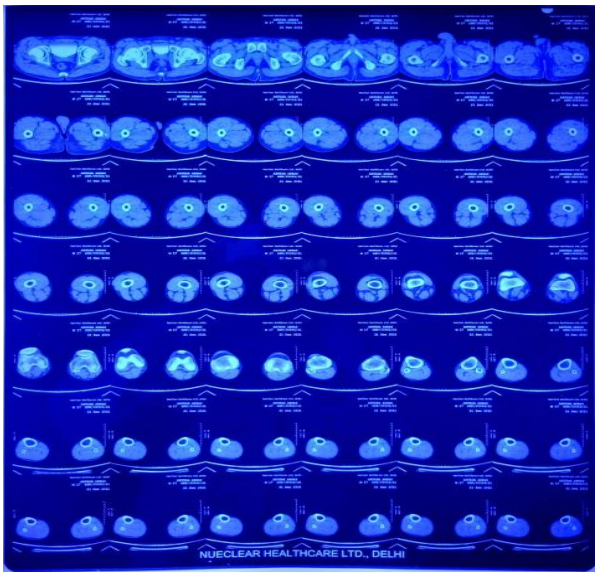


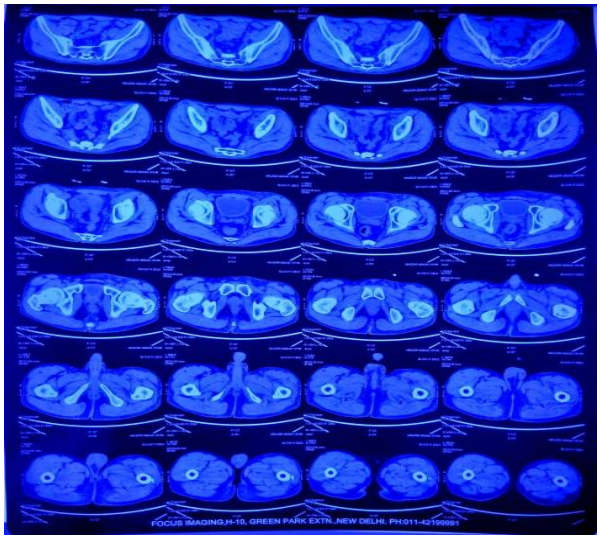
b)

Fig. 3 (a,b): PET-CT scan showing a decrease in size of primary lesion with complete regression in metastatic sites.

ISSN No:-2456-2165

Following this, palliative radiotherapy was given to the primary site with a dose of 30Gy in 10# which was tolerated well. Thereafter, the patient was considered for radical dose to left thigh accounting for 2Gy/1# in a total on 9#. Additionally, the patient was irradiated at the site of left pelvis and left inguinal region with a dose of 50Gy/25# for the nodal site mets with 3D collapsed code photon modality.

A PET-CT was done after 3 months to see the disease response to RT which found minimal FDG avid heterogeneous enhancement in anterolateral left thigh (SUV max-1.92) and non FDG avid partially calcified nodule in right upper lobe along fissure & few relatively small nodules randomly distributed in bilateral lungs with near complete resolution in pelvic and inguinal lymph node suggesting a positive response to chemo radiotherapy. The newer findings were FDG avid sclerotic changes in spinous process of right scapula (SUV max- 5.1)with hypermetabolic mediastinal lymph nodes; hereby, ensuing a progressive disease.



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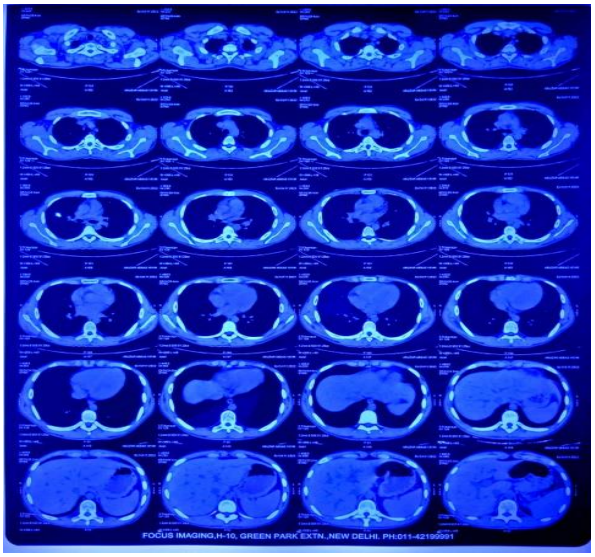

b)

Fig. 4 (a,b): PET-CT scan showing complete metabolic response with new lesions in right scapula

In the view of progression, a 2nd line chemotherapy was started this year taking into consideration the CD4 count (chemotherapy given when CD4 more than 400). The treatment for HIV continued (Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate tablets) alongside the chemotherapy VAC-IE regimen - vincristine 2mg, doxorubicin 120mg and cyclophosphamide 1900mg given followed by Ifosfamide 2900mg (under the cover of mesna) and Etoposide 160mg post 3 weeks of VAC. In total, 2 cycles of VAC-IE were given and response was evaluated by PET-CT scan which revealed no definite evidence of any hypermetabolic lesion in previous associated including spinous process of right scapula. Although, new sclerotic foci was delineated in right ala of sacrum with no tracer uptake. The patient is now put on further courses of chemotherapy as VAC-IE also showed a near complete metabolic response and advised to regular follow-up.

III. DISCUSSION

UPS/MFH is an aggressive type of soft tissue sarcoma arising from mesenchymal cells. It accounts for 5–10% of sarcomas in adults.(5) UPS/MFH can occur anywhere in the body but the most common in the extremities - 16% (lower limb > upper limb) and retroperitoneum -68% [2] (4).Undifferentiated pleomorphic sarcoma (UPS) predominantly occurs in males in comparison to females (2:1), common in the age group of 50 to 70 years (commonly affected age group).(6)In our case, the patient belongs to adolescent age group, a rare occurrence with the primary in lower extremity. Metastasis occurs commonly via haematogenous route with the most common site being lung.(7) , which is true in our case report.

A panel of immune histochemical markers plays a crucial role in confirmation of diagnosis of UPS.(8) These include keratins, smooth muscle actin (SMA), S100 protein and desmin. All of these markers are expressed in metastatic sarcomatoid carcinoma, melanoma, and pleomorphic myogenic sarcomas, respectively. Histologically under the microscope, the cells are spindle shaped and highly pleomorphic with a storiform arrangement. Therefore, a histological grade (G) is devised for soft tissue sarcomas which consist of three parameters with a score: Differentiation (1 to 3), Mitotic index (1 to 3), and Tumor necrosis (0 to 2). A total sum of these numbers result in grading as GX, G1 (2 to 3), G2 (4 to 5), and G3 (6 to 8). The American Cancer Society (ACS) has accepted a TNM staging based on the location of tumour.(9)

The mainstay treatment for UPS of any site is en bloc surgical excision with microscopically negative margins, only performed for stage I tumors. Though, a few cases may pose trouble considering the involvement of neurovascular structures; but it is achieved by a locally wide excision with 2 cm margins of normal tissue. Various indications of postoperative radiotherapy are margins being close to the tumor (< 1 cm), positive under microscopic view, involvement of bone or major blood vessels or nerves.(10)(11) Effective RT should cover a 5 cm margin and can be administered through external beam RT

ISSN No:-2456-2165

(EBRT) (50 Gy), intraoperative RT (IORT) (10-16 Gy), low-dose brachytherapy (LDR) (45 Gy), or its high-dose equivalent (HDR).(10)(12)

For higher stages, chemotherapy is indicated with anthracyclines (16% to 27% response) may be given alongside of ifosfamide. Doxorubicin is usually preferable in palliative cases.(13) In a comparative study done on 286 patients, the observations were histotype-tailored neoadjuvant chemotherapy (gemcitabine plus docetaxel) was not superior to standard chemotherapy (epirubicin plus ifosfamide).The survival rates were better in UPS-affected subjects who got treated with the standard chemotherapy than those received histotype-specific regime (14)Another randomized controlled trial based study which included 435 soft tissue sarcoma patients from four countries, revealed that anthracycline plus ifosfamide must remain the preferred choice of treatment. (15)

UPS patients usually have poor prognosis, peculiarly when accompanied along with metastasis, it is further poorer. (7)Almost 50% of patients presents with recurrence, commonly within the first 2 years of treatment. Numerous factors are associated with recurrence, namely, more than 5 cm size, high-grade histology, deep seated tumour, poor resection during surgery.(16)To delineate the local recurrence or metastasis, follow-up visits are of principal value. Physical examination of stage I tumors should be performed at 3 to 6 month intervals for the first two years and then annually. Stage II to IV disease must be followed every 2 to 6 months for 2 to 3 years, then every 6 months for 2 years, and annually thereafter.(10) Further research is necessary to prevent recurrence and distant metastasis with regular follow-up.

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