CASE REPORT

Positron emission tomography – computed tomography as a monitoring response tool in pre-fibrotic myelofibrosis: A case report

Amna Qamar Uz Zaman[1], Shabbir Hussain[2], Ramsha Zaheer[3], Madiha Andleeb[4], Saba Raza[5], Tariq Siddiqui[6]

Abstract

Primary myelofibrosis is a haematopoietic stem cell neoplasm resulting in ineffective haematopoiesis and bone marrow fibrosis. We present a case of a 67-year-old male patient who came to the oncology/haematology department of Dr. Ziauddin Hospital, Karachi, in February 2020 with complaints of weight loss, gastroesophageal reflux and loss of appetite. Examination revealed splenomegaly and initial workup demonstrated bicytopenia on complete blood picture. Bone marrow biopsy was consistent with pre-fibrotic myelofibrosis (Janus kinase 2 (JAK-2) positive). He was categorized as intermediate-2 risk according to Dynamic International Prognostic Scoring System (DIPPS) with score of 3 and was advised to start JAK-1/JAK-2 inhibitors. Prior to therapy, he underwent positron emission tomography-computed tomography (PET/CT) scan which showed increased fluorodeoxyglucose (FDG) uptake in the spleen and bone marrow. Monitoring by the scan after initiating treatment demonstrated decreased FDG uptake in bone marrow and spleen, demonstrating that PET/CT is a non-invasive way to assess and monitor treatment response in pre-fibrotic myelofibrosis.

Keywords: Position-emission tomography, Pre-fibrotic myelofibrosis, Janus kinase 1, Janus kinase 2, Janus kinase inhibitor.

DOI: https://doi.org/10.47391/JPMA.4079

Introduction

Primary myelofibrosis is a chronic myeloproliferative disorder which comprises of cytopenias, visceromegaly, B symptoms, bone marrow fibrosis and extramedullary haematopoiesis. Anaemia with haemoglobin less than 10 g/dL is seen in approximately 50 percent of patients. The platelet and white blood cell (WBC) counts are variable. Primary myelofibrosis occurs mainly in middle aged and older adults.

[1,4]Department of Hematology, Dr. Ziauddin University and Hospital, Karachi, Pakistan; [2]Department of Oncology, Dr. Ziauddin University and Hospital, Karachi, Pakistan; [3]Dr. Ziauddin University and Hospital, Karachi, Pakistan; [5]Department of Chemical Pathology, Dr. Ziauddin University and Hospital, Karachi, Pakistan; [6]Department of Medical Oncology, Dr. Ziauddin University and Hospital, Karachi, Pakistan.

Correspondence: Amna Qamar Uz Zaman. e-mail: dramnadow@gmail.com

PET/CT is a non-invasive and a powerful method for estimating marrow activity in primary myelofibrosis, extramedullary haematopoiesis, evidence of transformations and monitoring of treatment response.[1] PET/CT can be helpful in assessing disease response to treatment. Few cases and analysis have been reported in this regard.[2]

We herein report a case where PET/CT scan was performed prior to initiation of treatment with JAK-2 inhibitors in a patient with pre-fibrotic myelofibrosis. PET/CT was repeated after the treatment to assess the response. Our case highlights the use of PET/CT in pre-fibrotic myelofibrosis.

Case Report

A 67-year-old male patient presented to the haematology/oncology outpatient clinic with complaints of weight loss of 6kg, loss of appetite and gastroesophageal reflux for 2 months. Other comorbid conditions included hypertension and ischaemic heart disease. He was a goldsmith by profession with an average socioeconomic status. The patient appeared to be a healthy looking male, however, abdominal examination, revealed a palpable spleen 8cm below the left costal margin. His weight was 59kg with the remaining examination to be unremarkable. Laboratory workup demonstrated haemoglobin of 10.4 g/dl (13.0-17.0gm/dl), total leucocyte counts of 17.0x10^9/L (4.0-10 x 109/L), and platelet count of 188 x 10^9/L (150-440x10^9/L). Peripheral film revealed normochromic, normocytic cells, anisopoikilocytosis, tear drop cells, and ovalocytes. Bone marrow biopsy was performed which was suggestive of trilineage haematopoiesis with 80-85% cellularity, distortion of bone marrow architecture, obscured cellular morphology due to background fibrosis (Grade 03), and increased megakaryocytic proliferation with characteristic atypia (Figure-1). JAK-2 mutation was noted to be positive on further workup.

PET/CT dated 15th February 2020 showed diffuse marrow uptake in skeletal system (standardized uptake value (SUV) max upto 5.11) and an enlarged spleen of 18.3cm with increased fluorodeoxyglucose (FDG) uptake and SUV of 3.9 (Figure-2). An ultrasound scan done on 22nd June 2020 demonstrated the size of the spleen to be 21cm.

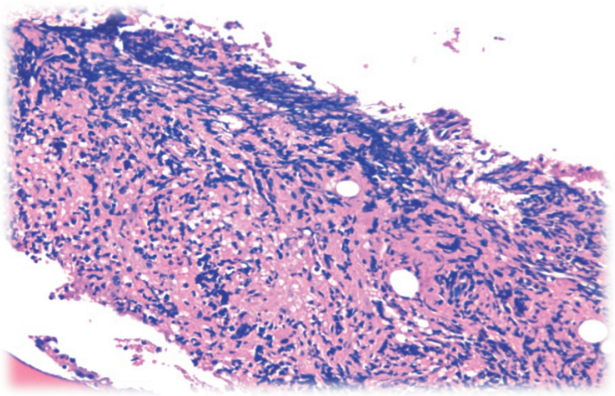

Figure-1: Bone marrow trephine biopsy exhibiting fibrosis and megakaryocytic atypical features.

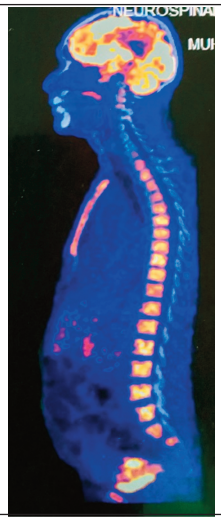

Figure-2: Positron emission tomography-computed tomography (PET/CT) scan showed diffuse marrow uptake in skeletal system (standardized uptake value (SUV) max upto 5.11).

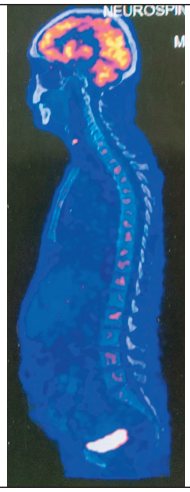

Figure-3: Positron emission tomography-computed tomography (PET/CT) in December 2020 demonstrated reduction in standardized uptake value (SUV) of bone marrow from 5.11 previously to 2.42.

His Dynamic International Prognostic Scoring System (DIPSS) score was calculated to be 03 (intermediate-2), based on age>65 years, WBC <25 x 10^9/l, haemoglobin >10g/dl, blasts >1 in peripheral blood and presence of constitutional symptoms. On the basis of history, examination, laboratory investigations, bone marrow biopsy, JAK-2 positivity and intermediate-2 scoring (DIPSS), he was advised JAK-2 inhibitor, ruxolitinib, which offers effective treatment and has capacity to diminish constitutional symptoms.

A PET/CT repeated in December 2020 demonstrated reduction in SUV of bone marrow from 5.11 previously to 2.42 (Figure-3). SUV also decrease in spleen size from 3.90 previously to 3.61. Ultrasound (26th Jan 2021) showed spleen size of 18.4 cm.

The patient is currently on follow-up with reasonable tolerance to the drug. His abdominal discomfort and peripheral blood cytopenias are under control.

Discussion

Apart from allogenic haematopoietic stem cells transplantation, which is the only curative option for primary myelofibrosis, treatment for primary myelofibrosis remains conservative and symptomatic. However, JAK-1/JAK-2 inhibitor, such as ruxolitinib, has remarkable outcomes when it comes to reduction of spleen size and improvement of B symptoms. Although there have been reports of post-transplant monitoring of myelofibrosis, not much has been discussed on evaluation of disease with the help of PET/CT before and after initiation of JAK-1/JAK-2 inhibitors. Our case therefore provides a clue where PET/CT, a non-invasive tool, can be initialized with convenience to monitor response to the treatment. Moreover, it aids in judging the severity of bone marrow fibrosis.

In comparison with the best available therapies, continuation of ruxolitinib has better improvements in overall quality of life. High and intermediate-2 risk patients should be considered for disease-modifying therapies, such as JAK inhibitors.[3] In COMFORT-II trials, individuals with primary myelofibrosis who received ruxolitinib had achieved spleen volume reduction of more than 35% at 48 weeks.[3] Bone marrow SUV in our case shows reduction after initiation of JAK-1/2 inhibitors which will be monitored closely along with spleen size in serial PET/CT scans. Cytopenias need to be dealt immediately in order to have enhanced and optimal response to ruxolitinib.[4]

Taking advantages of imaging quantification abilities, [18F]-fluoro-3'-deoxy-3'-L: -fluorothymidine ([18F]FLT) PET can be pertinent in assessing efficacy of JAK-1/JAK-2 inhibitors, as bone marrow exhibits a diffuse uptake pattern of FDG with PET/CT with an increased uptake in spleen, liver and central skeleton. Increasing fibrosis may be a consequence of longstanding bone marrow inflammation in myelofibrosis.[5] However, owing to fibrosis and osteosclerosis bone marrow intensity decreases later.[2,6,7] The most commonly used prognostic indicator in primary myelofibrosis is spleen size which is also a decent marker to evaluate response to ruxolitinib.[8] Our patient also showed a reduction in SUV in spleen on follow-up. Further studies are recommended to investigate the role of PET/CT to monitor response to JAK inhibitors in pre-fibrotic myelofibrosis.

Conclusions

This case report points to the role of PET/CT as a reliable and a feasible approach to assess the response of JAK-1 / JAK-2 inhibitors in patients with pre-fibrotic myelofibrosis. It can aid in diagnosis concerning FDG uptake in spleen and bone marrow, and is a useful tool to assess treatment response.

Disclaimers: None.

Conflict of Interest: None.

Funding Source: None.

References

1. Yassin MA, Nehmeh SA, Nashwan AJ, Kohla SA, Mohamed SF, Ismail OM, et al. A study of 18F-FLT positron emission tomography/ computed tomography imaging in cases of prefibrotic/early primary myelofibrosis and essential thrombocythemia. Medicine (Baltimore). 2020; 99:e23088.
2. Vercellino L, Ouvrier MJ, Barré E, Cassinat B, de Beco V, Dosquet C, et al. Assessing bone marrow activity in patients with myelofibrosis: results of a pilot study of 18F-FLT PET. J Nucl Med. 2017; 58:1603-8.
3. Harrison C, Kiladjian JJ, Al-Ali HK, Gisslinger H, Waltzman R, Stalbovskaya V, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med. 2012; 366:787-98.
4. Ho PJ, Marlton P, Tam C, Stevenson W, Ritchie D, Bird R, et al. Practical management of myelofibrosis with ruxolitinib. Intern Med J. 2015; 45:1221-30.
5. Hasselbalch HC. Chronic inflammation as a promotor of mutagenesis in essential thrombocythemia, polycythemia Vera and myelofibrosis. A human inflammation model for cancer development? Leuk Res. 2013; 37:214-20.
6. Van Son PM, Evers D, Aarntzen EHJG. The value of FDG-PET CT scans to evaluate bone marrow in haemato-oncological conditions. Neth J Med. 2019; 77:234-42.
7. Derlin T, Büsche G, Kröger N. Diagnostic value of 18F-FDG-PET/CT for monitoring myelofibrosis after allogeneic stem cell transplantation. Nucl Med Rev Cent East Eur. 2015; 18:35-6.
8. Krauth MT, Burgstaller S, Buxhofer-Ausch V, Gastl G, Geissler K, Keil F, et al. Ruxolitinib therapy for myelofibrosis in Austria: Consensus on therapy management. Wien KlinWochenschr. 2018; 130:495-504.