Antinuclear antibodies positive patient with splenic infarct a diagnostic dilemma

**Sabina Langer, Ravi Daswani, Rahul Arora, Nitin Gupta,
Anil Arora, Jyoti Kotwal**

ABSTRACT

Introduction: Presence of autoimmune phenomenon along with splenic infarct made clinician relate the two considering the splenomegaly as a consequence of splenic vein thrombosis and autoimmune myelofibrosis as a cause of pallor and repeated blood transfusions. The presence of near normal counts masked the underlying myeloproliferative neoplasm which led to the patient wrongly being treated as autoimmune myelofibrosis. This case highlights the need to keep a high level of suspicion for chronic myeloproliferative neoplasms in all cases of splanchnic vein thrombosis. The autoimmune phenomenon including Antinuclear antibodies (ANA) positivity is incidentally found to coexist with the primary myelofibrosis.

Case Report: A 69-year-old male presented with splenic infarct and ANA positivity. The splenomegaly was initially attributed to the splenic vein thrombosis and autoimmune phenomenon like Raynaud's phenomenon and skin rash brought clinician's attention. The presence of splenic vein thrombosis, near normal counts with mainly pallor the patient was been treated on the lines of autoimmune myelofibrosis. The bone marrow done pointed towards the diagnosis of primary myelofibrosis which was confirmed by molecular studies positive for JAK-2 mutation.

Conclusion: Autoimmune phenomenon can coexist with the chronic myeloproliferative neoplasms like primary myelofibrosis. All patients presenting with splanchnic vein thrombosis should be investigated for underlying myeloproliferative neoplasms especially molecular studies like JAK-2 V617F mutations.

International Journal of Case Reports and Images (IJCRI)

International Journal of Case Reports and Images (IJCRI) is an international, peer reviewed, monthly, open access, online journal, publishing high-quality, articles in all areas of basic medical sciences and clinical specialties.

Aim of IJCRI is to encourage the publication of new information by providing a platform for reporting of unique, unusual and rare cases which enhance understanding of disease process, its diagnosis, management and clinico-pathologic correlations.

IJCRI publishes Review Articles, Case Series, Case Reports, Case in Images, Clinical Images and Letters to Editor.

Website: www.ijcasereportsandimages.com

CASE REPORT

PEER REVIEWED | OPEN ACCESS

Antinuclear antibodies positive patient with splenic infarct a diagnostic dilemma

Sabina Langer, Ravi Daswani, Rahul Arora, Nitin Gupta,
Anil Arora, Jyoti Kotwal

ABSTRACT

Introduction: Presence of autoimmune phenomenon along with splenic infarct made clinician relate the two considering the splenomegaly as a consequence of splenic vein thrombosis and autoimmune myelofibrosis as a cause of pallor and repeated blood transfusions. The presence of near normal counts masked the underlying myeloproliferative neoplasm which led to the patient wrongly being treated as autoimmune myelofibrosis. This case highlights the need to keep a high level of suspicion for chronic myeloproliferative neoplasms in all cases of splanchnic vein thrombosis. The autoimmune phenomenon including Antinuclear antibodies (ANA) positivity is incidentally found to coexist with the primary myelofibrosis. **Case Report:** A 69-year-old male presented with splenic infarct and ANA positivity. The splenomegaly was initially attributed to the splenic vein

thrombosis and autoimmune phenomenon like Raynaud's phenomenon and skin rash brought clinician's attention. The presence of splenic vein thrombosis, near normal counts with mainly pallor the patient was been treated on the lines of autoimmune myelofibrosis. The bone marrow done pointed towards the diagnosis of primary myelofibrosis which was confirmed by molecular studies positive for JAK-2 mutation. **Conclusion:** Autoimmune phenomenon can coexist with the chronic myeloproliferative neoplasms like primary myelofibrosis. All patients presenting with splanchnic vein thrombosis should be investigated for underlying myeloproliferative neoplasms especially molecular studies like JAK-2 V617F mutations.

Keywords: Primary myelofibrosis, Splenic infarct, Thrombosis

How to cite this article

Langer S, Daswani R, Arora R, Gupta N, Arora A, Kotwal J. Antinuclear antibodies positive patient with splenic infarct a diagnostic dilemma. Int J Case Rep Imag 2016;7(4):245–248.

Article ID: Z01201604CR10630SL

doi:10.5348/ijcri-201642-CR-10630

INTRODUCTION

Splanchnic vein thrombosis with near normal white blood counts can mask an underlying myeloproliferative

Sabina Langer¹, Ravi Daswani², Rahul Arora³, Nitin Gupta⁴, Anil Arora⁵, Jyoti Kotwal⁶

Affiliations: ¹Consultant, Department of Haematology, SirGangaram Hospital, New Delhi, Delhi, India; ²DNB Fellow, Department of Gastroenterology, Sir Gangaram Hospital, New Delhi, Delhi, India; ³DNB Fellow, Departement of Haematology, Sir ganga Ram Hospital, New Delhi, India; ⁴Consultant, Clinical Haematology, Department of Haematology, Sir Gangaram Hospital, New Delhi, Delhi, India; ⁵Senior, Consultant, Department of Institute of Liver Gastroenterology & Pancreatico-Biliary Sciences, Sir Gangaram Hospital, New Delhi, Delhi, India; ⁶Senior, Consultant & Head, Department of Haematology, Sir Gangaram Hospital, New Delhi, Delhi, India.

Corresponding Author: Dr. Sabina Langer, Consultant, Department of Hematology, Sir ganga Ram Hospital, New Delhi, 110005; Email: sabinapost@yahoo.com

Received: 03 October 2015

Accepted: 29 December 2015

Published: 01 April 2016

disorder which needs to be investigated and is confirmed by molecular studies [1]. We present here a case of splenic vein thrombosis leading to splenic infarct with autoimmune phenomenon like skin pigmentation, Raynaud's phenomenon and ANA positivity. This had created confusion in the minds of clinician attributing splenomegaly to thrombosis and both as the consequence of autoimmune condition. The patient was therefore wrongly treated for three months. However, on bone marrow examination and molecular studies this turned out to be a case of primary myelofibrosis. The autoimmune process is an incidental finding in this case which is reported in literature to be associated with primary myelofibrosis [2]. It is important to diagnose correctly as both conditions have distinct prognosis and course of disease [3].

CASE REPORT

A 69-year-old male, presented to gastroenterology department with hyperpigmentation, pallor, history of itching and hematemesis. He was transfused five units of packed red cells and was on azathioprine and prednisolone since last three months. On examination there was pallor, spleen 10 cm below costal margin and ascites. There was no lymphadenopathy and no icterus. On investigation he had hemoglobin 9.0 g/dl, white blood cell count 12,100/ μ l, platelet 2,16,000/ μ l and serum creatinine 1.6 mg/dl. His liver function test was near normal. The β 2 GPI-IgM and anticardiolipin antibodies were negative. Ultrasound abdomen had shown splenomegaly with infarct and splenic vein thrombosis and left kidney atrophy with right normal kidney. Upper gastrointestinal endoscopy showed mild linear fundal varices and fibroscan was 13.4. The patient had Raynaud's phenomenon while admitted in hospital along with history of darkening of skin of the abdomen and lower limbs. Antinuclear antibody (ANA) done by immunofluorescence which was strongly positive, ANA profile revealed JO1 and centromere positivity. The splenomegaly was attributed to splenic vein thrombosis this together with significant autoimmune phenomenon like skin rash, Raynaud's phenomenon and joint pains. The clinician considered autoimmune myelofibrosis as the diagnosis, bone marrow was done to confirm this. The patient was investigated for inherited thrombophilia disorders all the tests were found to be negative.

In the post-transfusion peripheral blood smear (PBS) (Figure 1) there were normocytic normochromic to microcytic hypochromic red cells with a fair number of tear drop cells, polychromasia and presence of nRBCs (25/100 WBCs). The differential count on the PBS was neutrophils 80%, lymphocytes 11%, myelocytes 3%, metamyelocytes 3% and eosinophils 3%. The bone marrow aspirates were hemodilute, with a leukoerythroblastic blood picture. Due to the presence of tear drop cells in parent cells and marked splenomegaly the possibility of myeloproliferative neoplasm/myelofibrosis as primary

etiology to splenomegaly were suggested and need to be ruled out on bone marrow biopsy. The bone marrow biopsy (Figure 2) was adequate with 50% of marrow spaces showing severe fibrosis and others showing mild fibrosis. It showed panmyelosis with myeloid preponderance, increase in number of megakaryocytes with clustering showing nuclear atypia, cloud like and hyperchromatic nuclei. Micromegakaryocytes were also seen with focal areas of clustering. In many areas, new bone formation was also seen. The special stains of reticulin and Masson's trichrome (Figure 3) revealed grade 3 fibrosis which commensurate with findings on bone marrow biopsy. Together with bone marrow morphology, significant splenomegaly the final impression of primary myelofibrosis was given. The splanchnic vein thrombosis is also reported in many cases of underlying Philadelphia negative chronic myeloproliferative neoplasms. The molecular studies for bcr-abl, and JAK-2 V617 F mutations were done, which showed JAK-2 positive and bcr-abl negative hence commensurate with the diagnosis of primary myelofibrosis. This patient was later started on lenalinomide, steroids and acenocoumarol (3 mg). He responded well to treatment and his hemoglobin was improved

Figure 1: Peripheral blood picture showing, nucleated red cells and tear drop cell.

Figure 2: Bone marrow biopsy showing marrow fibrosis and megakaryocytes showing nuclear atypia and clustering.

Figure 3: Masson's trichrome showing blue bundle of collagen.

DISCUSSION

As this patient had presented with skin hyperpigmentation, Raynaud's phenomenon and joint pains and pallor, therefore, he was investigated for autoimmune condition and was found to have strong ANA positivity. Computed tomography scan had revealed splenic vein thrombosis, despite the presence of normal counts. The clinician attributed the presence of splenomegaly to splenic vein thrombosis and autoimmune etiology.

The hematopathologists on examining bone marrow aspiration and biopsy correlated with marked splenomegaly and refuted the diagnosis of autoimmune myelofibrosis considering the diagnosis of primary myelofibrosis. The splenic vein thrombosis leading to splenic infarct is found in cases of chronic myeloproliferative neoplasms. The ANA positivity is reported as coexisting finding in some cases of primary myelofibrosis. These cases can also have underlying inherited thrombophilias like protein C, protein S deficiency or factor V Leiden mutations. However, in this case these investigations turned out to be negative.

Primary autoimmune myelofibrosis is now defined as a distinct steroid-responsive clinicopathologic entity with excellent prognosis [3]. The neoplastic cause of primary myelofibrosis can sometimes have overlapping features with non-neoplastic causes like autoimmune myelofibrosis, secondary to SLE or primary autoimmune myelofibrosis. The features of primary autoimmune myelofibrosis have been well elucidated by Pullarkat et al. include

- (i) grade 3 or 4 reticulin fibrosis of the bone marrow;
- (ii) lack of clustered or atypical megakaryocytes;
- (iii) lack of myeloid or erythroid dysplasia, eosinophilia, or basophilia;
- (iv) lymphocyte infiltration of the bone marrow;
- (v) lack of osteosclerosis;
- (vi) absent or mild splenomegaly;

- (vii) presence of autoantibodies; and
- (viii) absence of a disorder known to cause MF

In our patient, only 3 out of 8 criteria were present. The features favoring primary myelofibrosis over autoimmune myelofibrosis (AIMF) were presence of significant splenomegaly and leukoerythroblastic blood picture with several tear drop cells, presence of osteosclerosis, presence of megakaryocyte clustering.

The molecular reports confirmed this case to be philadelphia negative and JAK-2 mutation positive. The review of literature showed that ANA positivity is also reported in some sporadic cases of primary myelofibrosis (PMF), such cases were also shown to respond well to steroids [2]. Thus this case demonstrates the difficulty posed due to overlapping features of AIMF and PMF creates possibly indicating an associated etiology. It is pertinent to be able to distinguish between the two as they have differences in therapy, also whereas PMF has limited survival other causes including AIMF have a favorable clinical outcome.

The neoplastic cause of primary myelofibrosis can sometimes have overlapping features with non-neoplastic causes like autoimmune myelofibrosis, secondary to SLE or primary autoimmune myelofibrosis. The portal vein thrombosis (PVT) or splanchnic vein thrombosis can be the sole or chief presenting symptom of an underlying myeloproliferative neoplasms (MPN) with normal or near normal peripheral blood cell counts due to hemodilution, iron deficiency or splenomegaly. The JAK2V617F mutation contributes to detection of MPNs as it is present in ~95% polycythemia vera close to 50% of the cases with essential thrombocythemia or primary myelofibrosis therefore is an important part of the work-up of patients presenting with PVT in the absence of cirrhosis or hepatobiliary malignancies. However a bone marrow biopsy is often required as absence of the JAK2 mutation does not exclude the presence of MPN. The presence of portal vein thrombosis with underlying MPN is associated with high rate of recurrence and frequent extension of thrombosis into the splenic vein or superior mesenteric vein they require anticoagulation or antiplatelet therapy [4].

CONCLUSION

This case has highlights the need to have high level of suspicion of underlying myeloproliferative neoplasms in cases of splanchnic vein thrombosis. These cases should be systematically investigated including bone marrow examination and molecular studies to confirm. It should be kept in mind that Antinuclear antibodies (ANA) positivity and autoimmune features can superimpose or coexist with myeloproliferative neoplasms.

Author Contributions

Sabina Langer – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Ravi Daswani – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Rahul Arora – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Nitin Gupta – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Anil Arora – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Jyoti Kotwal – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2016 Sabina Langer et al. This article is distributed under the terms of Creative Commons Attribution

License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

REFERENCES

1. Kiladjian JJ, Cervantes F, Leebeek FW, et al. The impact of JAK2 and MPL mutations on diagnosis and prognosis of splanchnic vein thrombosis: a report on 241 cases. *Blood* 2008 May 15;111(10):4922–9.
2. Wang JC, Sindhu H, Chen C, et al. Immune derangements in patients with myelofibrosis: the role of Treg, Th17, and sIL2Ra. *PLoS One* 2015 Mar 20;10(3):e0116723.
3. Pullarkat V, Bass RD, Gong JZ, Feinstein DI, Brynes RK. Primary autoimmune myelofibrosis: definition of a distinct clinicopathologic syndrome. *Am J Hematol* 2003 Jan;72(1):8–12.
4. Hoekstra J, Bresser EL, Smalberg JH, Spaander MC, Leebeek FW, Janssen HL. Long-term follow-up of patients with portal vein thrombosis and myeloproliferative neoplasms. *J Thromb Haemost* 2011 Nov;9(11):2208–14.
5. Bass RD, Pullarkat V, Feinstein DI, Kaul A, Winberg CD, Brynes RK. Pathology of autoimmune myelofibrosis. A report of three cases and a review of the literature. *Am J Clin Pathol* 2001 Aug;116(2):211–6.

Access full text article on
other devices

Access PDF of article on
other devices

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.

Most Favored Author program

Join this program and publish any number of articles free of charge for one to five years.

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US