

Systemic lupus erythematosus and chronic myeloid leukemia: mere coexistence or association?

Rudrajit Paul, Jayanti Ray, Babulal Daulagajao, Rojina Choudhury, Sanjoy Bhattacharya

Department of Medicine, Medical College Kolkata, 88, College Street, Kolkata- 7000 73, India.

ARTICLE INFO

Article history:

Received on: 24/06/2014

Revised on: 11/08/2014

Accepted on: 09/10/2014

Available online: 27/11/2014

Key words:

SLE, CML, imatinib,
eosinophilia, myeloid
malignancy.

ABSTRACT

Systemic Lupus Erythematosus (SLE) is a multisystem connective tissue disorder associated with increased predisposition to haematological malignancies. Myeloid series malignancies are rarely associated with SLE. We here report a case of Philadelphia chromosome positive chronic myeloid leukemia (CML) associated with SLE in a 36 year old Indian housewife. This is probably the first such case to be reported from India and only a handful of such cases have been reported in World literature till now. The patient presented initially with leukopenia. She was treated with imatinib with good results.

INTRODUCTION

Systemic Lupus erythematosus (SLE) is a multi-system disease associated with a variety of clinical manifestations. Haematological manifestations are quite common in SLE and include anemia, leukopenia, thrombocytopenia or clotting disorders (Sasidharan *et al.*, 2012). In fact, in some studies, haematological manifestations have been found to be the commonest presenting symptom of SLE (Sasidharan *et al.*, 2012). Haematological malignancies are sometimes associated with SLE and malignancies of both myeloid and lymphoid lineage have been reported (Lu *et al.*, 2013). Among these, Chronic myeloid leukemia (CML) is very rarely associated with SLE. We here report a case of CML associated with SLE. As far as we searched, this is probably the first such case to be reported from India.

The case report

A 36 years old female housewife presented to the emergency with shortness of breath and pain in left upper abdomen for two weeks. Both the symptoms were gradually

progressive and at the time of presentation, she was severely dyspnic with inability to complete sentences. There was associated orthopnoea, but fever or chest pain was absent. Bipedal edema and pallor was also present. Abdominal examination revealed mild splenomegaly. After admission, analysis of past documents revealed that she was a diagnosed case of SLE for last two years. She had fulfilled six criteria of ACR guidelines. Renal biopsy done at that time had revealed stage IV SLE nephritis. However, after few months of treatment including two pulses of cyclophosphamide, she had stopped visiting the hospital and was not taking any treatment. Past blood records showed (figure 1) hemoglobin of 6.4 gm/dl with total leukocyte count of 1390/cmm (N60L36E2) and platelet count of 100 000/cmm. Urinary protein two years ago was 3.1 gm/24 hours. At present admission, blood reports revealed hemoglobin of 6.5 gm/dl with total leukocyte count (TLC) of 20 000/cmm (N76L12E12) and ESR of 71 mm in 1st hour. Platelet count was 190 000/cmm. She was presumed to have systemic infection and started on I.v. antibiotics. Other tests revealed serum LDH of 2229 IU/L and urea/creatinine of 51/1.7 mg/dl respectively. Chest X ray showed right sided pneumonitis and mild cardiomegaly. Ultrasonography of abdomen revealed splenomegaly (15.5 cm) with no other pathology. Serum C3 level was 101 ng/dl and anti dsDNA was positive at 1:40 titre (Cliff method). She was also started on i.v. torsemide.

* Corresponding Author

Rudrajit Paul, Medical College Kolkata, Kolkata, India.
Email: docr89@gmail.com

With use of these drugs, her dyspnea was abated and she discharged herself against medical advice after three days. One month later, the patient was again admitted with left sided abdominal pain.

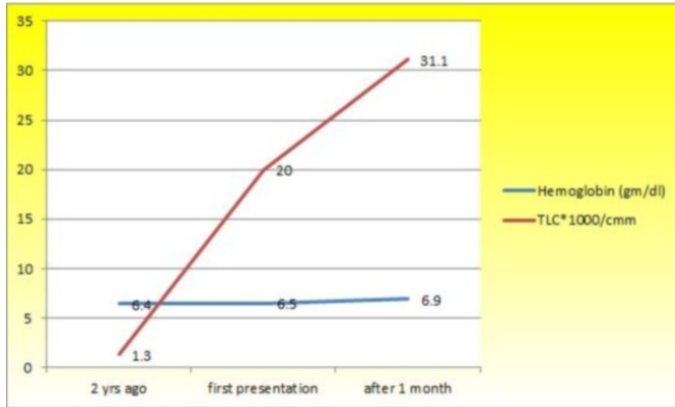


Fig. 1: Line graph showing the sequential blood reports of the patient.

Examination revealed a firm slightly tender splenomegaly. She was pale and there was mild fever. Blood tests revealed hemoglobin of 6.9 gm/dl with TLC of 31130/cmm. Differential count revealed Neutrophil 66%, myelocyte 10%, metamyelocyte 11% and eosinophil of 5%. Platelet count was 120000/cmm. Reticulocyte count was 3.6% and direct Coomb's test was negative. Liver function test was normal. Bone marrow examination revealed (figure 2) features of myeloproliferation with occasional foci of fibrosis.

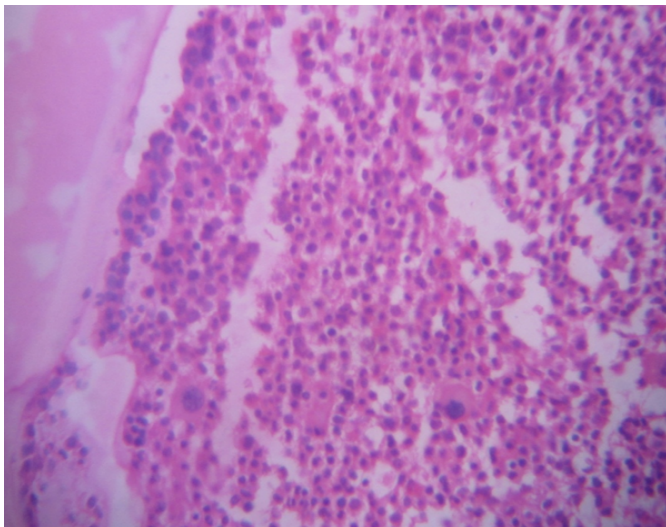


Fig. 2: microscopic picture of bone marrow aspiration study of the patient.

Chromosomal analysis of cells from bone marrow aspirate showed presence of Philadelphia chromosome (figure 3) in 69% of the cells. This was thus diagnosed as a case of chronic myeloid leukemia (CML). Meanwhile, the patient started to develop hyperviscosity symptoms like headache and visual dimness. Retinoscopy showed engorgement of retinal veins. She was started on oral imatinib and hydroxyurea along with

hydration. Slowly, her TLC came down to 21000/cmm and hemoglobin also improved to 8.1 gm/dl. The patient is now under follow up. She has not shown any new manifestations of SLE.

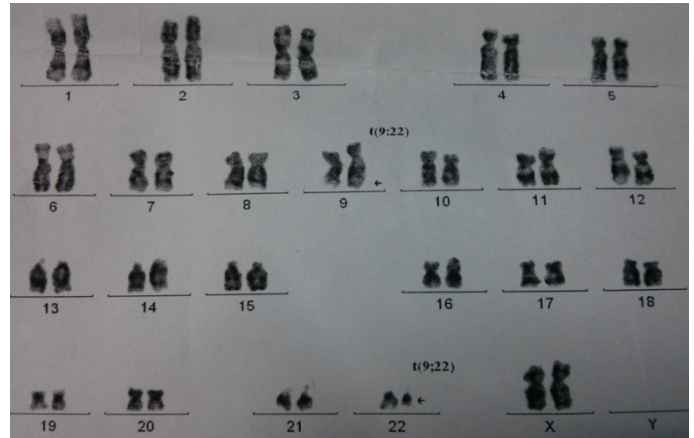


Fig. 3: Karyotype study showing Ph chromosome.

DISCUSSION

SLE is associated with increased risk of some malignancies. Rarer cancers like those of female genital tract and hepatobiliary cancers are increased in SLE patients compared to the general population (Bernatsky *et al.*, 2009). However, the main increased risk is in haematological malignancies, especially non-Hodgkin's lymphoma (NHL) (Bernatsky *et al.*, 2009). The exact link between SLE and cancers is unknown; besides the disease process itself, use of drugs like cyclophosphamide is also said to be responsible for the development of malignancies (Bernatsky *et al.*, 2009).

Myeloid malignancies have been reported in SLE patients (Löfström *et al.*, 2009). In a recent study, eight cases of SLE with myeloid leukemia were reported (Löfström *et al.*, 2009). Similar other cases have been rarely reported from elsewhere. Leukopenia in SLE was found to be a risk factor for later development of myeloid leukemia (Löfström *et al.*, 2009). In our case too, the initial TLC was 1390/cmm. Thus, sudden normalisation of erstwhile low TLC in SLE may be an indication of incipient leukemia in these patients. In addition, like in our case, some patients may show unusual haematological features like eosinophilia. Sometimes, these patients are initially diagnosed as myelodysplasia (MDS) and only subsequent follow up can diagnose the leukemic transformation. The use of cytotoxic drugs like cyclophosphamide or azathioprine is not consistently associated with development of leukemia. In the aforementioned case series, out of the eight myeloid leukemia cases, only two were CML (Löfström *et al.*, 2009). Both the patients were aged 60 and above and survival after diagnosis of CML was 6–9 months. In contrast, our patient was diagnosed at 36 years of age and she has lived for ten months after the diagnosis of CML till now.

Some studies have found that myeloid malignancies are increased in patients with autoimmune conditions (Anderson *et al.*, 2009). Specifically, they found acute myeloid leukemia and MDS

to be associated with autoimmune conditions like rheumatoid arthritis and SLE (Anderson *et al.*, 2009). The exact cause of this association is unknown but it is postulated to be due to common genetic predispositions. Also, it is said that direct damage to the myeloid precursors by the underlying disease may be responsible for the malignant transformation (Anderson *et al.*, 2009). A case of CML in rheumatoid arthritis was reported from Morocco in 2012 (Mansouri *et al.*, 2013). However, that case presented with blast crisis and was Philadelphia chromosome (PH) negative. By contrast, our patient was PH positive and is still in stable phase.

CML has only rarely been reported in SLE. No such case has been reported from India till now. A report from Delhi described a case where interferon treatment for CML led to the development of SLE nephritis (Goyal *et al.*, 2005). But in our case, the SLE developed earlier. In another case report from Italy, bone marrow transplant for CML in blast crisis led to cure of the SLE too (Meloni *et al.*, 1997). However, there is no guideline on proper management of SLE with CML. Since our patient was PH positive, she was given imatinib with good results. Interferon should probably be avoided in these cases.

CONCLUSION

Autoimmune diseases like SLE are sometimes associated with haematological malignancies. Regular follow up is needed to diagnose the disease at an early stage. Treatment needs to be individualized and multidisciplinary approach is needed for proper management.

REFERENCES

- Anderson LA, Pfeiffer RM, Landgren O, Gadalla S, Berndt SI, Engels EA. Risks of myeloid malignancies in patients with autoimmune conditions. *British Journal of Cancer* 2009; 100: 822-8
- Bernatsky S, Ramsey-Goldman R, Clarke AE. Malignancy in systemic lupus erythematosus: what have we learned? *Best Pract Res Clin Rheumatol.* 2009;23:539-47
- Goyal H, Wadhwa J, Arora B, Dawar R, Agarwal SK, Singh D. Interferon-induced lupus nephritis in a patient with chronic myeloid leukemia. *Leukemia and Lymphoma* 2005;46: 481-2
- Löfström B, Backlin C, Sundström C, Hellström-Lindberg E, Ekblom A, Lundberg IE. Myeloid leukaemia in systemic lupus erythematosus-- a nested case-control study based on Swedish registers. *Rheumatology (Oxford).* 2009;48:1222-6
- Lu M, Bernatsky S, Ramsey-Goldman R, Petri M, Manzi S, Urowitz MB et al. Non-lymphoma hematological malignancies in systemic lupus erythematosus. *Oncology.* 2013;85:235-40
- Mansouri S, Tahiri L, Elmezouar I, Cherqui N, Khammar Z, Berradi R et al. A case of rheumatoid arthritis complicated by a chronic myeloid leukemia associated with pyodermagangrenosum. *The Egyptian rheumatologist* 2013; 35 :1-4
- Meloni G, Capria S, Vignetti M, Mandelli F, Modena V. Blast crisis of chronic myelogenous leukemia in long-lasting systemic lupus erythematosus: regression of both diseases after autologous bone marrow transplantation. *Blood.* 1997 15;89:4659
- Sasidharan PK, Bindya M, Sajeeth Kumar KG. Hematological Manifestations of SLE at Initial Presentation: Is It Underestimated? *ISRN Hematol.* 2012; 2012: 961872

How to cite this article:

Rudrajit Paul, Jayanti Ray, Babulal Daulagajao, Rojina Choudhury, Sanjoy Bhattacharya. Systemic lupus erythematosus and chronic myeloid leukemia: mere coexistence or association? *J App Pharm Sci*, 2014; 4 (11): 098-100.