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## Case Report

### A Dermatomyositis Patient Developing Chronic Myeloid Leukemia is able to Experience Improvement in the Quality of Daily Life, Following Treatment with Imatinib Mesylate

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## Abstract

A female patient was originally diagnosed with dermatomyositis in 1985 at the age of 56 because of the presence of interstitial pneumonia and skin lesions. Early in 2008, she experienced a high fever for one week, and essential thrombocytosis was suspected. However, G-banding analysis revealed reciprocal translocation between chromosomes 9 and 22 [t(9;22)(q34;q11.2)]. She was diagnosed with chronic myelogenous leukemia. Daily administration of 400mg of imatinib mesylate was started on April 1, 2008, and the patient's WBC and thrombocyte counts had dropped from 11,200/ $\mu$ l to 5,500/ $\mu$ l and from 1,491,000/ $\mu$ l to 168,000/ $\mu$ l, respectively, by the end of April. However, imatinib mesylate was reduced to a half dose, because of severe adverse effects such as facial and leg edema in January, 2009. Thereafter, she could walk slowly with a cane, but a compression fracture of her lower lumbar vertebra in April, 2009, rendered her bedridden. We discuss the rare association between dermatomyositis and chronic myelogenous leukemia and the effect of imatinib mesylate in improving activity of daily life with a mHAQ score of 0.875 in this particular dermatomyositis patient because imatinib mesylate may inhibit interleukin 6 and other cytokine production.

**Keywords:** Dermatomyositis (DM); Chronic Myeloid Leukemia (CML); Imatinib Mesylate (IM), Interleukin 6 (IL-6); modified Health Assessment Questionnaire (mHAQ); Essential Thrombocytosis (ET)

## Introduction

Imatinib mesylate (IM) is a computer designed drug which specifically blocks the tyrosine-kinase receptor formed by ABL-BCR protein [1]. Previously, we reported that a male rheumatoid arthritis (RA) patient, 75 years old at onset, subsequently developed chronic myelogenous leukemia (CML) at the age of 80. This patient was unique in that his condition became stable not only in relation to CML, but also with regard to rheumatoid arthritis following treatment with IM [2]. Actually, efficacy of IM was also proven in arthritic mice [3,4]. Recently, IM has been shown to be effective not only in treatment for CML but also several manifestations of rheumatic diseases [5]. In the present case, IM treatment was effective not only for CML but also for dermatomyositis (DM).

## Case Report

The patient was originally diagnosed with DM in 1985, at the age of 58, because she manifested severe interstitial pneumonia, skin lesions and proximal muscle weakness. She visited the Keigu Clinic when in her most severe condition in September 2003, and tests revealed the presence of anti-nuclear antibody at a 1:80 dilution by indirect immunofluorescence, and anti-Jo1 antibody at a 1:8 dilution by double immunodiffusion. She received 5mg of predonisolone daily for a few years and her modified Health Assessment Questionnaire (mHAQ) score dropped from 2.9 to 1.87. Early in 2008, the patient experienced a high fever for one week, and essential thrombocytosis (ET) was suspected on the basis of an elevated thrombocyte count of 978,000/ $\mu$ l. She was sent to the University Hospital whereupon tests revealed a WBC count of 11,200/ $\mu$ l accompanied by myelocytes at 2.5%, basophiles at 11.5%, and thrombocytes at 1,491,000/ $\mu$ l. The presence of the BCR-ABL1 fusion gene (Philadelphia chromosome, Ph) was confirmed in 59% of segmented and 10% of mononuclear cells by fluorescence in situ hybridization (FISH) [6]. The reciprocal translocation between chromosomes 9 and 22 [t(9;22)(q34;q11.2)] was observed in all 20 cells analyzed by G-banding. Daily administration of 400mg of imatinib mesylate (IM) was started on April 1, and the patient's WBC and thrombocyte counts had dropped to 5,500 and 168,000, respectively, by the end of April. Although the administered dosage of IM was reduced from 400mg to 200mg in January, 2009, because of severe facial and leg edema, she kept in good health (Figure 1a) with an mHAQ of 0.875. Unfortunately, she had difficulty in walking because of a lower vertebral compression fracture which appeared in April, 2011, bringing her mHAQ score up to 2.5. However, she has received IM and continued to be in good health maintaining an active daily life with reduced levels of AST (GOT) and KL-6 for the past 5 years (Figure 1b).

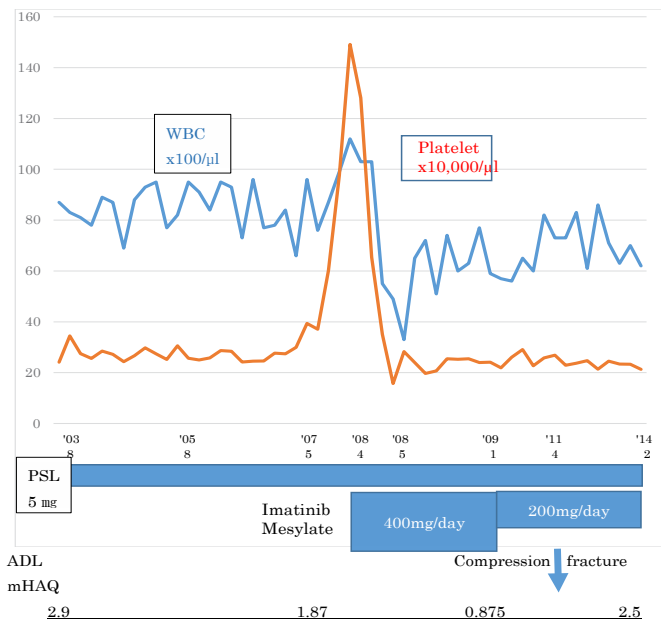


Figure 1a. Changes of WBC and Platelet counts before and after treatment of IM

mHAQ: modified Health Assessment Questionnaire (range 0-3)

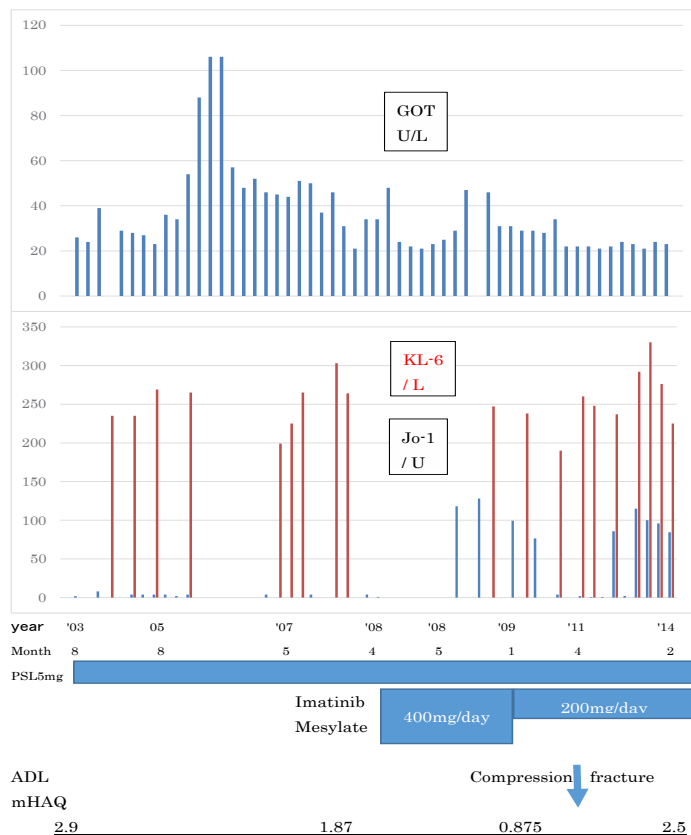
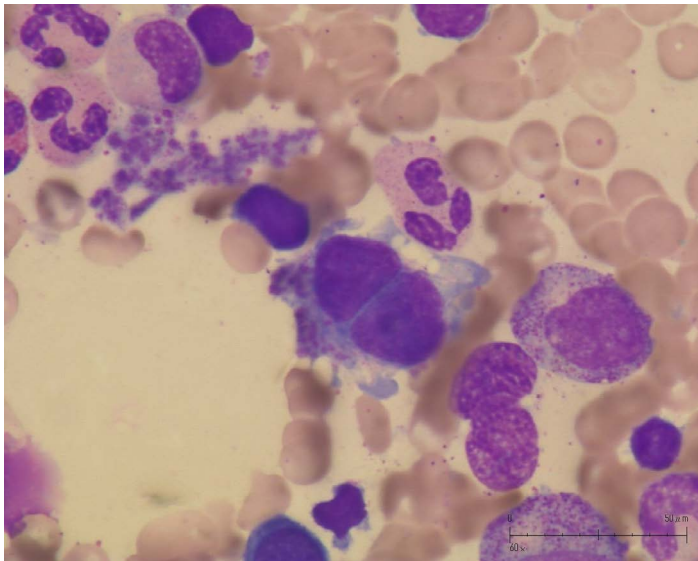


Figure 1b. Changes of GOT, KL-6 and Jo-1 levels before and after the treatment of IM

mHAQ : modified Health Assessment Questionnaire (range 0-3)

## Discussion

This patient was initially suspected of having ET, but was subsequently diagnosed with CML accompanied by marked thrombocytopenia. In particular, CML with marked thrombocytopenia, in contrast to ET, is characterized by the presence of smaller megakaryocytes having round hypolobulated nuclei [7]. Plasma cells were also found to be relatively abundant in her bone marrow specimen (Figure 2). Although we have had no opportunity to detect IL-6 levels, it was reported that serum IL-6 levels were higher in CML than myelofibrosis, ET and normal controls [8]. So far, thrombocytosis, persistent fever and abundant plasma cells in her bone marrow suggested to us that IL-6 might be mostly related to the clinical and laboratory manifestations between onset and the early stage of CML in this particular case.



**Figure 2.** Small megakaryocytes containing small vacuoles in the cytoplasm observed in bone marrow. Plasma cells were thought to be relatively increased as a result of dermatomyositis.

Worldwide, 20 or more patients with connective tissue disease (CTD) associated with CML have been reported (Table 1). Prior to 2002, 11 authors reported 12 cases documenting the association of CTD and CML. Four cases with CTD as a first diagnosis developed CML later, [9-12] however, 6 cases with CML as a first diagnosis developed CTD, mostly following INF therapy [13-18]. IM therapy has been available for the treatment of CML since 2002. Eight cases with first diagnosis of CTD developed CML [2, 19-23] however only 2 CML cases developed CTD, following INF and or Hydroxyurea (HDU) therapy [19]. Probably, regarding CML therapy, IM is more useful and prevalent for CML than INF or HDU. On the other hand, prior to 2002, immune mediated complications occurred in connection with CML, during the treatment with INF or HDU [24].

On the other hand, DM is more closely associated with malignancy

including ovarian tumor, lung and gastric cancer than polymyositis [25]. In our particular case, such a malignant disease was not found by CT examination.

Year	First diagnosis	Age/Sex	Therapy	Second diagnosis	Time between diag.	
1	1985	RA/Sjogren	ND	NA	CML	ND
2	1985	CML	30/M	HDU/MPL	DM	2
3	1985	SSc	33/F	NA	CML	ND
4	1994	SSc	44/F	HDU/IFN	CML	2.5
5	1994	CML	53/M	HDU/IFN	DM	3
6	1995	CML	ND	IFN	RA	ND
7	1999	CML	ND	IFN	RA	ND
8	1998	SSc	ND	NA	CML	3
9	1998	CML	ND	BMT	SJS	ND
10	2002	CML	ND	IFN	SSc	2
11	2003	RA	72/M	GST/NSAID	CML	8
12	2006	Behcet	23/F	Col/S	CML	6
13	2006	CML	24/F	IFN/HDU	Spondyloarthritis	8
14	2006	RA	58/F	MTX/LEF/S/HCCQ	CML	12
15	2006	CML	65/F	HDU	dcSSc	0.5
16	2006	CREST	ND	D-penicillamine	CML	3
17	2008	RA	ND	HCCQ/SASP/MTX	CML	ND
18	2009	AOSD	25/M	ND	CML	2
19	2009	RPC	ND	ND	CML	ND
20	2015	DM	56/F	S	CML	24

ND: not determined      S: Steroid      MLP: melphalan  
 BM: bone marrow transplant      LFM: leflunomid      CSP: cyclosporin  
 AOSD: adult onset still's disease  
 RPC: relapsing polychondritis

**Table 1.** A review literature of association between CTD and CML.

Here, we have described a female DM patient 56 years old at the onset of the disease, who subsequently developed CML at age 80. This was an interesting case in that treatment with IM not only put CML in remission, but also appeared to have a positive effect on DM as well. Recent studies on IM have revealed several therapeutic effects owing to its function as a tyrosine kinase inhibitor not only on platelet derived growth factor receptors on the surface of synovial cells in RA, but also on transforming growth factor- $\beta$  on the skin in systemic sclerosis [26]. Moreover, it was recently reported that IM treatment inhibits IL-6, IL-8, nuclear factor-kappa B (NF-kB) and activator protein 1 (AP-1) production and modulate intracellular calcium in CML patients, [27] therefore clinically stable manifestations of DM will also be caused by administration of IM.

**Conflict of Interest:** None

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