Pleural and pericardial effusions in chronic myeloid leukemia patients receiving low-dose dasatinib therapy

We read with interest the paper about pleural and pericardial effusion in chronic myeloid leukemia during low-dose dasatinib treatment by Krauth *et al.*[1] They reported 4 patients who developed effusions with 50 or 100 mg daily dasatinib out of a total number of 13 patients. Pleural and pericardial effusions were grade III/IV in 2 of the patients. There were no reports of pre-existing cardiac or pulmonary diseases for any of the 4 patients. In 3 cases, dasatinib had to be discontinued because of the persistence of the pleural fluids despite treatment with diuretics and glucocorticosteroids. In conclusion, Krauth *et al.* suggest that all patients should be examined for pre-existing comorbidities and risk factors before the initiation of dasatinib, and they should have repeated chest X-rays during the follow-up period because of the possibility of pleural or pericardial effusions even under low doses of dasatinib treatment.

We report our experience of chronic myeloid leukemia patients receiving low-dose dasatinib who had developed pleural and pericardial effusion. In our institute, a total number of 23 chronic phase chronic myeloid leukemia patients receive dasatinib (50-100 mg daily) due to resistance or intolerance to imatinib. Among these 23 patients, 10 of them (43%) had pleural and pericardial effusions (9 with pleural effusion and one with pericardial effusion).

Eight patients were males and 2 were females. Median age was 61.5 (range 44-69). Nine patients out of 10 were in late chronic phase who were switched to dasatinib because of imatinib resistance. Only one patient was in early chronic phase since she started receiving dasatinib due to intolerance of imatinib. The median duration of dasatinib use was 26 months (range 13-33). All of the patients had grade I/II effusions. In 7 patients dasatinib therapy was interrupted and furosemide plus glucocorticosteroids were initiated; effusions were totally resolved in 4 of the 7. Dasatinib was restarted in those 4 patients and effusions did not reoccur. The remaining 3 patients had just started receiving furosemide and glucocorticosteroids and are under follow up so we were unable to make a comment on the success of the treatment.

Dasatinib treatment was not stopped in one patient when he developed pleural effusion; we only added glucocorticosteroids and the effusion improved. No other intervention was made in the other 2 patients other than interrupting dasatinib treatment and the pleural effusions improved. After restarting dasatinib in those 2 patients, one of them developed pleural effusion which was then managed with furosemide and glucocorticosteroids, dasatinib was discontinued and he then fully recovered.

Pleural effusion is the most frequent non-hematologic adverse event in dasatinib-treated patients.[2] Although effusion formation may require some time and the risk of effusion formation is lower in patients treated with 100 mg dasatinib than patients receiving 140 mg dasatinib daily, patients treated with dasatinib at 100 mg daily dose may also develop pleural effusions.[3] The frequency of symptomatic pleural effusions was reported to be 13%, but grade III/IV pleural effusion is a rare entity. Krauth *et al.* examined 13 chronic myeloid leukemia patients receiving dasatinib at 50 or 100 mg daily, 4 of whom developed clinically relevant pleural or pericardial effusions; 2 of these 4 patients had grade III or IV effusions. In our cohort of 23 patients, 10 patients developed pleural or pericardial effusions, all grade I or II. None of our patients had grade III/IV effusions.

Pleural effusions occurring during dasatinib are managed by treatment interruption and supportive therapy.[4] Diuretics alone usually do not have a long-lasting effect, but glucocorticosteroid therapy is effective. Krauth *et al.* added low-dose steroids to the treatment of their patients and we also applied glucocorticosteroids during management of effusions in ours.

One important factor concerning the risk of effusion formation is the existing comorbidities, such as cardiac or pulmonary disorders. The 4 patients whom Krauth *et al.* had presented did not have any pre-existing comorbidities whereas one of our patients had chronic obstructive pulmonary disease. This patient had to be treated with dasatinib because nilotinib was not available on the market in Turkey at that time.

In conclusion, pleural and pericardial effusions occur during dasatinib therapy which can be managed by steroids and diuretics, as well as discontinuing or reducing the dose of dasatinib. These effusions are usually mild and easy to manage even when grade III/IV pericardial and/or pleural effusions are presented. We agree that pleural or pericardial effusions may occur with relatively lower doses of dasatinib and screening for any possible co-morbidities and potential risk factors before starting dasatinib is mandatory. All the patients should be followed up closely.

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