Use of leucocyte alkaline phosphatase (LAP) score in differentiating malignant from benign paraproteinaemias

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Abstract
The leucocyte alkaline phosphatase (LAP) score of peripheral blood neutrophils was examined in 20 patients with multiple myeloma and compared with the score in 18 patients with monoclonal gammopathy of undetermined significance (MGUS). The mean (95% confidence limit) LAP score in those with multiple myeloma was 186 (169–218) compared with 92 (64–120) in the MGUS group. In the multiple myeloma group all but one patient had a high LAP score, irrespective of disease. No cause for raised LAP, such as infection, was present in any of the patients with multiple myeloma. In the MGUS group six patients had a raised LAP score; in two of them another cause for such a rise was present (autoimmune haemolytic anaemia and primary thrombocytopenia). In neither group did the LAP score correlate with duration of the disease, bone marrow plasma cell count, paraprotein concentration, haemoglobin, total white cell or neutrophil count.

It is concluded that a normal LAP count in patients with paraproteinaemia suggests a benign condition, but a raised count does not indicate a malignant condition.

Monoclonal gammopathy is a common disorder, especially in the elderly, but only a small percentage of these patients have overt multiple myeloma or related conditions at the time of diagnosis. The rest are diagnosed as having MGUS and usually followed up for an indefinite period as a significant proportion of them progress to multiple myeloma and related malignant disorders. Several tests have been proposed for differentiating malignant from benign paraproteinaemia but none has been found to be fully reliable. The LAP score has been recommended as a useful test for such differentiation. We examined the LAP score in patients with multiple myeloma and MGUS to assess the value of this test in differentiating malignant from benign paraproteinaemias.

Methods
Twenty patients (11 men, nine women, mean age 67 years) with multiple myeloma diagnosed by the standard criteria were included in this study. Four were newly diagnosed, 11 were in the plateau phase and five were in relapse. The MGUS group comprised 18 patients (10 men, eight women, mean age 63 years) with paraproteinaemia who did not fulfil the diagnostic criteria for multiple myeloma and were followed up for at least 24 months without any change in disease course. None in either group had a raised white cell count at the time of the present investigation. Blood films were made at the time of routine follow up and were stained for LAP by using a commercial kit (Diagnostica Merck). Scoring...
was done blind by a standard method with individual cells being scored from 0–4. One hundred neutrophils were examined consecutively in each film. The normal range for the LAP score in this laboratory is 20–100. Eight patients with multiple myeloma and seven with MGUS were scored on two different occasions at a mean interval of 27 (range 23–32) weeks.

Results
The LAP scores of all the patients are shown in the figure. The mean LAP score for the group with multiple myeloma was 186 (95% confidence limit 169–218). The score was not different in newly diagnosed (177, 144–211), plateau phase (192, 163–221) and relapsed (209, 134–285) patients. Those eight patients who were scored twice showed very similar results on each occasion (182, 149–216 and 178, 151–205). In this group all but one patient had a raised LAP score. In the MGUS group the mean score was 92 (64–120) which was significantly lower than the multiple myeloma group (p < 0.01). Six patients in this group had a raised LAP score. Two of these six had an associated disease which could explain the raised score (one with autoimmune haemolytic anaemia and the other with primary thrombocytopenia). These two patients were excluded from further analysis. Among the remaining 16 patients with MGUS, four had a raised LAP score and the difference with the multiple myeloma group was significant (χ² 30.4, p < 0.001). Those seven patients who were scored twice showed similar results on each occasion (96, 54–138 and 92, 63–122). In neither group did the LAP score show any correlation with age, duration of illness, haemoglobin concentration, white cell count, neutrophil count, paraprotein concentration or bone marrow plasma cell count.

Discussion
The only previous report comparing LAP score in patients with multiple myeloma and MGUS showed a difference between the two groups similar to that of the present study. In that study nearly half of the myeloma patients, including all treated patients, had a LAP score within the normal range. In our study we found that all but one patient with myeloma had a raised LAP score, irrespective of the disease course. None of the patients with multiple myeloma had any known cause for a raised LAP score. These results are similar to those published by Brook and Dreisbach, who found a raised LAP score in 60 out of 62 myeloma patients, irrespective of the disease course. Similar results were also published by Mukibi and Kyobe. Johansen and Jensen found a positive correlation between paraprotein concentration and LAP score both in myeloma and MGUS patients. No such correlation was found in our study. Repeat tests in a section of the patients in either group showed consistent results.

The cause of a raised LAP score in myeloma is unknown. The malignant clone may induce high LAP activity in the neutrophils. Results of Johansen and Jensen support this view but we found no positive correlation between the disease activity as reflected by the bone marrow plasma cell count and paraprotein concentration with the LAP score.

LAP scoring is a simple test routinely performed in most of the laboratories. One advantage of LAP scoring over some other tests is that it is performed on peripheral blood film, thus avoiding invasive procedures like bone marrow aspiration. Its value in differentiating malignant from benign paraproteinaemia, however, seems to be limited. A normal LAP score is suggestive of a benign condition but a high score does not have a clear diagnostic value. Whether the patients with MGUS with a high LAP score will eventually develop multiple myeloma can only be determined by long term follow up.

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J Clin Pathol 1991 44: 606-607
doi: 10.1136/jcp.44.7.606

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