Splenic Aspirations in Multiple Myeloma

By Henry D. Shapiro, M.D. and R. Janet Watson, M.D.

The technic of splenic aspiration has been used in over one hundred and fifty cases at Kings County Hospital during the past five years as an aid to the diagnosis and study of hematologic disorders. In 1951 the enlarged spleen of an undiagnosed patient was aspirated and found to have 27 per cent plasma-myeloma cells. The diagnosis of multiple myeloma was subsequently substantiated. The high incidence of extraosseous lesions in this disease reported in the literature has led some to speculate as to whether multiple myeloma is a generalized disease of the hematopoietic system analogous to leukemia. On the other hand, some have considered multiple myeloma to be a neoplastic disease of the skeletal system with occasional metastatic spread. It seemed to us that a study of splenic aspirations in several consecutive patients with multiple myeloma might throw some light on this controversial subject. Diffuse infiltration of the spleen with tumor cells in other types of neoplasia is much less common, and when it occurs, is usually in a localized form. In order to use consecutive patients, it was, of course, necessary to aspirate nonpalpable as well as palpable spleens. There were three advantages to this study:

1. Patients could be studied at any stage of their disease.
2. Random samples of the spleen could be obtained because only a minute fraction of the whole organ is studied in a nonselective manner.
3. Slide smears of splenic aspirations are morphologically similar to marrow and blood smears so that standard hematologic criteria could be used for identification. Autopsy material lacks the autolytic artefacts inherent in autopsy material. Also, because of shrinkage in fixed tissue, the morphologic criteria for distinguishing a normal plasma cell from the myeloma cell may be obscured. In fact, Churg and Gordon in their painstaking histologic study found it necessary to use such additional criteria for studies dealing with stilbamidine granules and Russell bodies.

Method

Ten patients with multiple myeloma were studied consecutively. In all cases, the diagnosis was based on the presence of plasma-myeloma cells in the bone marrow, skeletal X-ray lesions of the circumscribed lytic or the diffuse osteoporotic type, anemia, and a rapid sedimentation rate. The blood plasma globulin values ranged from 4.6 to 11.2 Gm. per cent. Splenic aspirations were performed with sterile technic in all cases, using a 20 cc. syringe and a 20 gauge needle. If the spleen was felt, it was aspirated at the midpoint of the palpable portion just below the costal margin. If not palpable, the aspiration was performed intercostally, the needle being plunged into the area of maximal percussion dullness with the patient lying on his back. Only a fraction of a cubic centimeter of material was aspirated. Slide smears were made from this aspirate and stained with Wright's stain in the usual manner. A two hundred cell differential count was done and compared with that of marrow.
and blood smears of the same patient. The plasma-myeloma cell was identified according to the following criteria: the presence of abundant bluish finely foamy cytoplasm, a perinuclear "holo" or halo, a nucleus with fine chromatin network, usually eccentrically placed and possessing a large nucleolus. The exact type of cell was morphologically unique for each patient, but was the same in different sites from the same person, and always had some degree of immaturity or lack of differentiation as compared with the normal plasma cell.

**Results**

An attempt was made to aspirate the spleen in eleven consecutive patients ill with multiple myeloma. However, since no splenic material could be obtained in one instance, the results are limited to ten patients, of whom only three had palpable spleens. The percentage of myeloma cells found in their spleen and marrow is listed in Table 1. The percentages in the peripheral blood are not listed because in no patient did they exceed 1 per cent. It is evident from the table that

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Spleen</th>
<th>Myeloma cells, marrow, %</th>
<th>Myeloma cells, spleen, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N.P.</td>
<td>76.5</td>
<td>68.5</td>
</tr>
<tr>
<td>2</td>
<td>N.P.</td>
<td>9.0</td>
<td>10.5</td>
</tr>
<tr>
<td>3</td>
<td>2 F.B.</td>
<td>37.0</td>
<td>45.5</td>
</tr>
<tr>
<td>4</td>
<td>N.P.</td>
<td>14.0</td>
<td>6.0</td>
</tr>
<tr>
<td>5</td>
<td>N.P.</td>
<td>13.5</td>
<td>0.5</td>
</tr>
<tr>
<td>6</td>
<td>3 F.B.</td>
<td>25.0</td>
<td>26.5</td>
</tr>
<tr>
<td>7</td>
<td>N.P.</td>
<td>31.0</td>
<td>25.0</td>
</tr>
<tr>
<td>8</td>
<td>2 F.B.</td>
<td>10.0</td>
<td>26.5</td>
</tr>
<tr>
<td>9</td>
<td>N.P.</td>
<td>18.5</td>
<td>31.5</td>
</tr>
<tr>
<td>10</td>
<td>N.P.</td>
<td>26.0</td>
<td>29.5</td>
</tr>
</tbody>
</table>

N.P. = not palpable.  
F.B. = fingerbreadths below costal margin.

in nine of the ten patients the number of myeloma cells in the spleen was of the same order of magnitude as in the bone marrow. In the one "negative" case, the percentage of myeloma cells in the splenic aspirate of two punches was not significantly increased.

The percentage of myeloma cells in the spleens of nine patients varied from 6 to 68 per cent, while the marrow percentages varied from 14 to 75.5 per cent. These wide variations were from patient to patient and not from marrow to spleen in the same patient. Wide marrow variations are, of course, commonly seen in different patients. The similarity in the morphology of the myeloma cells from the marrow and spleen can be seen in three typical patients in figure 1 to 6.

The incidence of normal plasma cells in splenic aspirations in our series of one hundred and fifty patients with a variety of diseases did not exceed 3 per cent in any instance. Our findings are in accord with those of Moeschlin who reports the "normal" splenic differential count as: plasma cells 0 to 2.3 per cent, neutrophils 8 to 25 per cent, band forms 1 to 7 per cent, lymphocytes 38 to 94 per cent, monocytes 1.2 to 2.4 per cent, and eosinophils 0.2 to 1.5 per cent.
FIG. 1.—Myeloma cells in bone marrow of case 9.
FIG. 2.—Myeloma cells in spleen of case 9. (Note large nucleoli.)
FIG. 3.—Myeloma cells in bone marrow of case 10.
FIG. 4.—Myeloma cells in spleen of case 10.
FIG. 5.—Myeloma cells in bone marrow of case 6. (Note dumb-bell nucleus.)
FIG. 6.—Myeloma cells in spleen of case 6. (Note cytoplasmic vacuoles and abnormal nuclei. Normal lymphocyte is seen in the center of the field.)

DISCUSSION

From the time of Rustizsky in 1873, a continuing line of investigators (Lubarsch, Jackson, Bethea, and Parker, Patek and Castle, Rubinstein, and others) have felt that multiple myeloma was a disease of the hematopoietic system rather than a localized bone lesion from which metastases occur irregularly and infrequently. The discussion has been focussed at times upon the
validity of the differences between plasma cell leukemia and multiple myeloma, and upon whether all extraosseous lesions arise by direct extension from bony lesions. Perhaps the best exposition of the problem was made in 1931 by Patek and Castle*: "There are considerable gradations in plasma cell tumors analogous to lymphomata. There may be single and benign, multiple and malignant plasma-cell tumors. There may be diffuse cellular infiltration with or without outpouring in the peripheral blood... We wish to reassert the desirability of regarding this plasma-cell tumor as a pathological entity whose different forms are not distinct diseases but gradations in extent and activity of the same disease process."
(The italics are ours.)

One point of focus for this discussion has been the occurrence of extraosseous lesions. It is now generally accepted that such lesions are not produced merely by direct extension from bony lesions. Indeed, in the solitary form they occur extraosseously as often, or more often, than intraosseously. The increasing frequency with which these lesions have been found has been one of the strongest bits of evidence for the generalized nature of the disease.

Churg and Gordon in 1950 reviewed forty-four autopsies of multiple myeloma at Mt. Sinai Hospital in New York City. Working with fixed tissues they were able to demonstrate some involvement of the extraosseous hematopoietic system in 70 per cent of their cases. In some the involvement was obvious and grossly visible; in others this had to be established by "certain pathognomonic cellular details in the bone marrow or biopsy specimen which, in conjunction with the general criteria, permitted identification of cells in visceral locations."

Even more recently, Hayes, Bennett, and Heck* in 1952, in analyzing thirty-eight autopsies at the Mayo Clinic, obtained a figure of 71 per cent with extraosseous lesions, of which half were grossly detectable.

In nine of our ten patients with multiple myeloma the percentage of myeloma cells in the splenic material corresponded very well with the percentage in the marrow. If extraosseous lesions are produced by direct extension, metastasis, or hematogenous implantation there could be no such correlation of percentage of myeloma cells between spleen and bone marrow on random sampling. Some samples would have been too high in myeloma cells, others too low. The high degree of correlation militates against any such chance involvement. It suggests rather the autochthonous origin of a disease process arising approximately simultaneously in the marrow and the spleen. This provides strong evidence for multiple myeloma being a generalized disease of the hematopoietic system similar in its diffusion to the leukemias.

**SUMMARY**

1. Splenic aspirations were performed in ten consecutive patients with multiple myeloma, in only three of whom the spleen was palpable.
2. In nine of the ten patients there was an increase of the percentage of myeloma cells in the splenic aspirations comparable to that in the marrow.
3. It is postulated that these findings support the concept of multiple myeloma as a generalized hematopoietic disease comparable to the leukemias.
REFERENCES

1 Unpublished data.


4 Hellwig C. A.: Extramedullary plasma cell tumors as observed in various locations. Arch. Path. 35: 95, 1943.


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