THE FREQUENCY OF MEGAKARYOCYTES IN AUTOPSY SECTIONS

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The presence of megakaryocytes in tissue sections has been frequently reported as a significant finding. According to Petri, who reviewed the literature, Muller was the first to note the occurrence of megakaryocytes in organs. Aschoff often observed them in the lungs in infectious diseases, and less frequently in the kidneys, liver and myocardium. Bunting, in a study of bone marrow and lung sections in 11 cases of Hodgkin's disease, found megakaryocyte nuclei in the lung capillaries of all cases; in 4 of these he thought megakaryocytes were more numerous than to be expected in cases with marked leukocytosis. There was an increase in the number of marrow megakaryocytes in 3 of the 5 cases studied.

In cases of active tuberculosis, Medlar and Sasano noted numerous megakaryocytes in the lungs. Orbison reported a case of lobar pneumonia with widespread distribution of megakaryocytes in the lungs and many other organs. Goroncy found megakaryocytes in the lesser circulation (lungs) in 61 per cent of his series of autopsies; in 13 per cent they were observed also in one or more of the organs supplied by the greater circulation; in only 3 of these necropsies were they found in the lungs, spleen, liver and kidneys of the same case. Petri also lists their presence in the bone marrow capillaries and sinusoids of the lymphoid tissue. Downey and Nordland, in a case of myeloid leukemia, observed megakaryocytes in the cortex of the adrenals and the surrounding fatty tissue, as well as in other organs.

Most investigators feel that megakaryocytes appear in the organs in conditions associated with increased hematopoietic activity, a viewpoint first expressed by Aschoff. Hewer, in a case of osteosclerotic anemia, observed many megakaryocytes in the spleen. Because of their absence in the lung sections, he concluded that in this case they were formed in the spleen. Downey, Palmer and Powell found megakaryocytes in liver and spleen biopsies in a case of atypical myelosis, and thought they were produced in situ. Klemperer, in his report of cavernomatous transformation of the portal vein, noted numerous megakaryocytes in the spleen. He was undecided as to whether or not they were 'carried to the spleen by the blood stream, because even when present in great numbers in the venous sinuses they were not found in the arteries.' Howell and Donahue maintained that megakaryocytes developed in the lungs from 'myeloblastic cells in the same manner as they do in the liver, spleen and bone marrow.' However, Jordan did not agree with this conclusion.

There have been several reports of the unusual finding of intact or fragmented megakaryocytes in the smears of peripheral blood. Minot stated that they were present in the peripheral blood smears in cases of myelogenous leukemia, polycythemia, and rarely in 'simple leukocytosis,' lobar pneumonia, Hodgkin's

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disease and sepsis. He believed that it was indicative of "intense bone marrow strain." Downey\(^5\) stated that megakaryocytes appeared after splenectomy in the peripheral blood smears from a case of myelogenous leukemia.

This problem was pursued at the suggestion of Dr. William Antopol and Dr. Lester Goldman, who had observed the frequency of megakaryocytes in paraffin sections and felt that they were partially filtered out in the lungs and that the spleen had a special affinity for actively arresting and fixing them therein. It was decided to study megakaryocyte occurrence in the tissues of 50 autopsy cases.

**METHODS AND MATERIAL**

The first 27 cases chosen for study were cases such as bacterial endocarditis, pneumonia or metastatic carcinoma, in which megakaryocytes were expected to be found. Then 7 autopsies were selected with no history of infection, neoplasm or blood dyscrasia, in which tissue megakaryocytes were not expected to be found. To round out the number an additional 16 random cases were studied.

The diagnoses in the 50 cases were as follows: 9 cases of neoplasm with metastases including bone; 7 of pneumonia; 7 of rheumatic heart disease; 3 of acute bacterial endocarditis; 3 of subacute bacterial endocarditis; 3 of pulmonary tuberculosis; 3 of cardiovascular-renal disease; 2 of Hodgkin's disease; 2 of leukemia; and one each of periarteritis nodosa, Libman-Sacks disease, chronic glomerulo-nephritis, granulomatous ulcer of the buttock, hypoglycemic shock, methyl alcohol poisoning, syphilis of the central nervous system, Landry's paralysis, traumatic death, primary amyloidosis, and a postoperative death.

Studied, but not included in this group of 50, were an additional 4 cases which showed extramedullary hematopoiesis.

With routine hematoxylin and eosin stain, the appearance of the megakaryocyte in the peripheral capillaries differs somewhat from that in the bone marrow. In the latter site the megakaryocyte is round; it possesses an abundant, homogeneous pink cytoplasm, the edge of which may or may not be irregular; the nucleus is large, vesicular or pyknotic, and may have few or many lobules. In the tissue capillaries, the megakaryocytes assume various shapes, being distorted by the channels in which they lie; their cytoplasm is often not discernible and the nucleus may appear naked (fig. 1). To a great extent, identification of megakaryocytes depends on their intravascular location and their enormous size, and especially on the large multilobulated nucleus which is most often pyknotic. Megakaryocytes with abundant cytoplasm are occasionally present, particularly in the wider channels (fig. 2).

In the lungs, the megakaryocytes are most frequently found in the capillaries of the alveolar septa. The glomerular tufts are their usual site in the kidneys; however, they are also seen in the interstitial capillaries. In the liver and spleen sections they are usually found in the blood sinuses. In heart sections they appear in the capillaries between the muscle fibers.

When megakaryocytes were found in the organs, a rough estimate of their number was recorded as being one to three plus. When only two or three megakaryocytes were found in the examination of a whole paraffin section, about 1 cm.
Frequency of Megakaryocytes

square, a one plus was recorded. Those cases with large numbers of megakaryocytes, averaging 1 or more per low power field (16 mm. objective and 10 X ocular), were considered three plus. Two plus represented the intermediate group. No attempt
was made to use absolute numbers: first, because of the difference in anatomical blood supply in the different organs; secondly, because of the varying pathologic changes in the same organ in different cases.

Results

In all of the 50 cases studied, megakaryocytes were demonstrated in the lungs. Their presence in smaller percentages was noted in the spleen, kidney, liver and heart (table 1). Megakaryocytes were noted in the adrenals in two cases, and in the pancreas and stomach in one instance each, but these are not included in the table.

Table 1.—Incidence of Megakaryocytes in Various Organs

<table>
<thead>
<tr>
<th>Organs examined</th>
<th>No. of cases examined</th>
<th>No. with meg.s present</th>
<th>Percentage incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Spleen</td>
<td>45</td>
<td>28</td>
<td>62</td>
</tr>
<tr>
<td>Kidney</td>
<td>47</td>
<td>17</td>
<td>36</td>
</tr>
<tr>
<td>Liver</td>
<td>47</td>
<td>16</td>
<td>34</td>
</tr>
<tr>
<td>Heart</td>
<td>45</td>
<td>6</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 2.—Simultaneous Incidence of Megakaryocytes in the Organs in Forty Cases

<table>
<thead>
<tr>
<th>Lungs</th>
<th>Spleen</th>
<th>Kidney</th>
<th>Liver</th>
<th>Heart</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>16</td>
</tr>
<tr>
<td>P</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>6</td>
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<tr>
<td>P</td>
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<td>O</td>
<td>3</td>
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<tr>
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<td>O</td>
<td>P</td>
<td>O</td>
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<td>P</td>
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<td>P</td>
<td>O</td>
<td>2</td>
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<td>P</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>1</td>
</tr>
</tbody>
</table>

P: megakaryocytes present
O: megakaryocytes not found

Sections of all the five organs mentioned in table 1 were available for study in only 40 of the 50 cases. The simultaneous occurrence of megakaryocytes in one or more of these five organs of each of these 40 cases is listed in table 2. It will be noted that megakaryocytes were found in the lungs alone in 16 cases; and in the lungs and spleen in 6. There were 12 cases with megakaryocytes present in the lungs, spleen, kidney and liver, and in 5 of these, megakaryocytes were also seen in the heart. Smaller numbers of other combinations are listed in table 2.

There appeared to be some correlation between the concentration of megakaryocytes in the lung capillaries and their occurrence in other organs (fig. 3). Seventeen cases demonstrated a one plus megakaryocyte concentration in the lungs: no megakaryocytes were found in the other organs in 11 of these cases; in the other 6 cases, they were found only in the spleen or in the spleen and one other organ.

Eleven cases showed a two plus megakaryocyte concentration in the lungs.
FREQUENCY OF MEGAKARYOCYTES

Five of these had no megakaryocytes in the other organs. In 4 more, they were demonstrated only in the spleen or the spleen and one more organ. In the 2 cases with involvement of all five organs, the megakaryocytes were numerous in the lungs, but not sufficiently numerous to fall into the three plus category.

All 12 cases with a three plus concentration in the lungs had megakaryocytes also in other organs. In 3 cases all five organs were involved, and in 7 more, megakaryocytes were demonstrable in all but the heart.

![Graphs showing frequency of megakaryocyte concentration in the lungs and number of other organs involved.]

One interesting finding was the constant presence of megakaryocytes in the spleen, whenever there was involvement of organs besides the lungs (table 2).

The diagnoses in the 12 cases (table 2) with involvement of four or five organs were pneumonia, acute or subacute bacterial endocarditis and carcinoma with metastases.

In the 4 cases with extramedullary hematopoiesis, it was possible to show, in one or another of the organs, a megakaryocyte concentration roughly as great as, or greater than that in the lungs.

DISCUSSION

The greatest incidence of extramedullary megakaryocytes appears to be in the lungs. This fact suggests, in agreement with earlier investigators, that their...
presence is dependent upon their delivery into the peripheral blood from the bone marrow and their subsequent filtration by the pulmonary capillary bed. From the data presented one might conclude that with more megakaryocytes entering the blood stream from the marrow, more will reach the lungs; and in turn, the more that filter through the pulmonary capillary bed, the more will be carried to other organs.

One might also conclude that under normal conditions variable numbers of megakaryocytes enter the blood stream from the bone marrow and can be demonstrated in the lung capillaries. The number of these is frequently increased in disease processes. Those megakaryocytes passing the pulmonary capillary bed are most frequently demonstrated in the spleen.

**SUMMARY**

1. Megakaryocytes can be demonstrated with great frequency in the viscera.
2. Megakaryocytes were present in the lungs in all of 50 autopsies studied.
3. They were next most frequently found in the spleen.
4. The simultaneous occurrence in the various organs, in the absence of extramedullary hematopoiesis, is roughly related to the concentration in the lungs.
5. Under normal conditions megakaryocytes in small numbers circulate in the blood stream.

**REFERENCES**

7. **Gordony**: As quoted by Petri.
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