INFECTION MONONUCLEOSIS COMPLICATED BY SPONTANEOUS RUP-
TURE OF THE SPLEEN AND CENTRAL NERVOUS SYSTEM
INVOLVEMENT

By Stuart L. Vaughan, M.D., J. Sutton Regan, M.D.,
and Kornel Terplan, M.D.

WHILE infectious mononucleosis is usually a benign disease, serious com-
plifications develop occasionally. Spontaneous rupture of the spleen has
been described in four well documented reports,1-4 and two other cases5, 6 in which
the evidence is not conclusive have been cited. Central nervous system involvement
has been described also, and the literature concerning this complication has been
reviewed recently.7-9

CASE REPORT

A married white male, aged 38, was admitted to the hospital November 3, 1944. About one month
previously he had complained of stiffness in the back of the neck. This symptom continued steadily and
one week before admission became exaggerated. At this time he developed an intractable headache which
was chiefly frontal in distribution, and felt feverish. Treatment at home brought no relief, and he was
admitted to the eye, ear, nose, and throat service for observation. After admission he noticed some
blurring of vision for the first time.

Past history revealed that the patient had been subject to frequent colds and sore throat. He had
undergone appendectomy in 1919, tonsillectomy in 1929, and hemorrhoidectomy in 1940. Otherwise, his
health had been good.

Physical examination on admission revealed that he did not have the appearance of serious illness,
although he was complaining of pains in the head and throat. The temperature was 100.3; the pulse
rate, 101; and the respiratory rate, 24. The conjunctivae were inflamed. The throat was red and inflamed.
Tonsils were missing. The lymph nodes were not enlarged, and no abnormal signs were found on examina-
tion of the heart, lungs, or abdomen. The appendectomy scar was noted. Reflexes were hyperactive. A
yellowish, maculo-papular circinate lesion the size of a ten cent piece was found on the inner surface
of the right thigh near the groin.

Routine blood counts showed the following. R.B.C., 5,100,000 per cu. mm.; Hb., 14.4 Gm. per
100 cc.; W.B.C., 13,000 per cu. mm.; Band form polymorphonuclears, 15 per cent; filaments, 3 per cent;
eosinophils, 1 per cent; basophils, 1 per cent; lymphocytes, 66 per cent; monocytes, 4 per cent.

The laboratory reported that many of the lymphocytes were large and deeply basophilic and charac-
teristic of types I and II "leukocytoid" lymphocytes as described by Downey.10

X-rays of the paranasal sinuses were negative.

No changes occurred in the clinical condition until the third day after admission (November 5th).
At noon the patient went to the lavatory feeling fairly well. He sat down to defecate but does not know
whether he had a movement or not. He stated that there was no undue straining. Then he seemed to
lose consciousness momentarily and came to with his head lying against the tank. He arose, went to the
nurses’ station and then to bed. He felt weak but otherwise did not feel badly. A short time later his
lunch was brought in. He ate only a little ice cream and felt very weak. Because of weakness and marked
perspiration, the nurse called a physician. The pulse rate was 140, and the blood pressure was 60 systolic,
0 diastolic. The abdomen was tender throughout, but most markedly so in the umbilical region. It was
not until several hours later that pain developed. Definite spasticity was noted, but this was by no
means "boardlike." The red count was 4,000,000 and the hemoglobin 10 grams.

One of us (J. S. R.) was called in surgical consultation during the evening. Spasm and rigidity were
marked in the upper abdomen and less so in the lower abdomen. Under observation the rigidity became
more marked. Faint peristalsis was present.

From the Buffalo General Hospital and the University of Buffalo.
Treatment for shock, including transfusion of blood, was instituted, and twelve hours after the onset laparotomy was performed. At operation the peritoneal cavity showed evidence of massive hemorrhage. The spleen was found enlarged to about four times its normal size and very soft. A large amount of clotted blood was found adherent to the lateral and diaphragmatic surfaces, and from beneath the clots fluid blood was observed to escape freely. With some difficulty, because of the softness and friability of the organ, the spleen was removed and the wound closed.

**PATHOLOGIC-ANATOMIC REPORT**

3287-1944 Gross Report. The spleen is moderately enlarged; weight 400 grams; measurements 18 x 9.5 x 3.5 cm. Within the diaphragmatic surface near the upper pole and close to the anterior margin there is a small irregular tear nearly 1 cm. in length. It is partially covered with clotted blood and appears to be about 1 cm. deep. On the cut surface the consistency of the spleen is considerably decreased. The markings are completely obscured, the malpighian follicles are not visible, and the entire splenic substance is in a state of uniform swelling and of grayish pink color. About the tear there are distinct hemorrhages within the pulp. Small localized hemorrhages from 1 to 4 mm. in diameter are seen in other parts of the spleen also, especially close to the capsule. The larger ones, including those about the tear, have an infarct-like appearance. (This latter feature grossly suggested the possibility of small embolic lesions as seen in bacterial endocarditis.)

Microscopic Report (Fixatives used: Zenker, Orth, Formaldehyde). In the low power magnification the structure of the spleen appears to be distinctly changed. While in some areas the malpighian follicles are still noticeable, in others they seem to blend with the hyperplastic red pulp; in the areas with hemorrhages they stand out more prominently. The trabecular system is indistinct, only the trabeculae containing larger blood vessels being clearly seen. So-called germinal centers cannot be recognized within the malpighian corpuscles.

With higher magnification the most outstanding feature is that the sinusoids are obscured; only close to the hemorrhagic areas a few of them can be recognized. The bulk of the cells composing the swollen pulp seems to stem from the reticulum of the spleen, gradually blending with the malpighian follicles. There is, apart from the hemorrhagic zones, but little blood between the reticulum meshes and in those sinusoids which still can be recognized. The following cells are most prominent: lymphoid elements with round nuclei and distinct though narrow rims of cytoplasm; slightly larger cells with round or oblong nuclei with indentations within the nuclear membrane and very distinct cytoplasm. These same cells frequently appear as the sinus endothelial cells. Leukocytes are comparatively few in number. Likewise only a few eosinophilic leukocytes and rare plasma cells are seen. Macrophages, free in the sinusoids, are also comparatively infrequent. Phagocytosis of erythrocytes is by no means prominent. The most outstanding feature is the rather regular cytoplasm in all the cells making up the bulk of this peculiar cellular hyperplasia.

There is a very rare follicle presenting enlargement of reticulum cells as seen in the germinal centers. However, there is a very marked degree of nuclear disintegration with many small chromatin particles within these cells, many of which have dark eosinophilic cytoplasm and blurred cellular borders. The arteries within the follicles show irregular hyaline degeneration in their walls. Some nuclear disintegration is also seen within the splenic trabeculae. The proliferation of the reticulum cells, finally, seems to extend through the trabeculae in some areas and to encroach upon the endothelial lining of the splenic veins. This is seen also within the walls of some arteries in the trabeculae. Sections stained for iron fail to show any granular hemosiderosis or diffuse imbibition.

In sections stained with methylene blue the larger lymphoid cells clearly show disintegration of nuclear substance into small fragments. Some of these fragments resemble bacterial inclusions of diplococcus form, while others are less homogenous and of various sizes. Gram stains give an entirely negative result. The bacteria-like structures seen in thin sections stained with methylene blue had to be interpreted as nuclear debris. They were seen also in some endothelial cells within packed sinusoids.

In comparing the histological picture with those reported by Warren,1 Ziegler,4 and Black,2 it is clear that our findings are very similar to theirs. In all of these reports it is stated that the sinusoids are less prominent than normal. The indistinct follicular architecture and also the absence of germinal centers are stressed by Ziegler and Black in particular. The large lymphocytes and reticulum cells mentioned by Ziegler and the larger lymphoid cells with characteristic nuclei and abundant cytoplasm in the...
Infectious Mononucleosis

Report of Black are apparently identical with those described in our report as small and large lymphoid cells which seemed to be in connection with the reticulum of the pulp and appearing frequently as endothelial cells wherever packed sinusoids can be made out.

Sinusoids nearly filled with young lymphocytes, monocytes, and an occasional polymorph appear also as the characteristic histological feature in the case of Davis, MacFee, Wright and Allyn. When we analyzed the histological picture we were impressed by the comparative absence of neutrophilic leukocytes and large endothelial cells with active erythrophagocytosis as seen frequently in acute swelling of the spleen reactive to various bacterial infections (meningococcus septicemia, typhoid fever, acute bacterial endocarditis). The absence of larger numbers of leukocytes, in particular, was surprising, as the soft consistency noticed in the gross specimen had directed our expectation toward an acute septicemic reaction.

The picture, then, that we found, is fully compatible with the hematological and serological diagnosis of infectious mononucleosis. Whether it is in itself sufficiently characteristic for the morphological diagnosis of this disease cannot be stated with any degree of certainty at the present time.

The immediate post-operative course was attended by moderate fever for eleven days. Sulfadiazine was administered until the third day, when it was discontinued because of the appearance of an erythematous eruption. On this day there was a chill. The urinary sediment was found to be crowded with red and white cells.

The patient complained of diplopia. Ophthalmological examination by Dr. Ivan Koenig showed paralysis of the left external rectus muscle. Both disks were fairly well defined, but the veins were slightly engorged. No definite edema, hemorrhages, or exudate were found. Pronounced bilateral ankle clonus was present.

The heterophile agglutination test done on November 13th was positive in a dilution of 1 to 1280. On November 15th a small incisional abscess was drained. Bacteriological examination of the exudate revealed anaerobic streptococci and small anaerobic Gram positive gas-producing bacilli. Penicillin was given for two days and the temperature returned to normal promptly. A test for cold agglutinins on November 17th was negative.

On November 18th a clinical examination from the hematological standpoint was made by one of us (S. V.). (This examiner had confirmed the diagnosis of infectious mononucleosis from the laboratory standpoint previously.) The skin color was normal. No hemorrhagic signs were present. The cervical, axillary, epitrochlear, and inguinal lymph nodes were not enlarged. The only node palpable was a small one in the left side of the neck. Ocular movements were practically normal, and diplopia had disappeared. However, all tendon reflexes were greatly exaggerated. Ankle clonus was easily elicited bilaterally but was not sustained. Patellar clonus was absent. Plantar reflexes were normal, and no other abnormal neurological findings were noted.

Lumbar puncture done November 20th showed initial pressure of 175 mm. of water. With jugular

---

**Table 1.—Blood Changes**

<table>
<thead>
<tr>
<th></th>
<th>1944</th>
<th>1945</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (million)</td>
<td>5.10</td>
<td>3.96</td>
</tr>
<tr>
<td>Hemoglobin (grams)</td>
<td>14.4</td>
<td>10.0</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>13,000</td>
<td>17,000</td>
</tr>
<tr>
<td>Myelocytes (%)</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Young forms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Band forms</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Filament forms</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Basophils</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>66</td>
<td>41</td>
</tr>
<tr>
<td>Monocytes</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Normoblasts</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Heterophile titer</td>
<td>1280</td>
<td>320</td>
</tr>
</tbody>
</table>

* Percentage of nucleated cells.
compression the pressure rose to 220 mm. within 10 seconds and returned to 175 mm. within 10 seconds of releasing the compression. Respiratory and arterial pulsations were present. The fluid was clear and colorless. The cell count was 8 white blood cells per cu. mm. The Pandy test and nitric acid ring test were slightly positive. Copper reduction was prompt. The colloidal gold curve was 1111000000. Complete fixation tests were negative and cultures were sterile. Glucose was 131 mg. per cent and protein was 0.116 Gm. per cent.

On November 17th, after several days of progressive improvement, the patient complained of dull steady pain in the right flank accentuated by deep respiration. Temperature rose to 103.2, the pulse rate to 132, and respiratory rate to 40; otherwise physical signs were indefinite, and radiographic examination revealed no abnormality. However, within two days signs of fluid in the right pleural cavity were present; radiographic examination was confirmatory. On December 4th the fluid removed from the chest was faintly turbid. It contained 31,500 R.B.C. and 3,300 W.B.C. per cu. mm. Stained films of sediment showed no bacteria, and cultures, including special ones for tubercle bacilli, were sterile. Cytological examination showed the following: young forms of polymorphs, 2 per cent; bands, 7 per cent; filaments, 3 per cent; lymphocytes, 10 per cent; monocytes, 5 per cent; plasma cells with highly vacuolated cytoplasm, 22 per cent; mesothelial cells, 41 per cent.

The febrile reaction subsided within a few days, and the patient was discharged from the hospital on December 16th, 44 days after admission. At that time he was in good condition, and all abnormal signs had disappeared.

On February 23rd, June 5th, and November 14th, 1945, he was re-examined by one of us (S. V.). On each occasion he appeared to be in excellent health and had no complaints except that he tired more easily than before his illness. Lymph nodes were barely palpable in the neck and axilla. No abnormal ocular or neurological signs were present. The blood findings throughout the illness are shown in Table 1.

**DISCUSSION**

The clinical course in this patient was not typical of that seen in the majority of cases of infectious mononucleosis. Peripheral lymph node enlargement and ulcerative manifestations were not present at any time. Even after the diagnosis was known a careful examination failed to disclose these signs. The first evidence of the disease was disclosed by the laboratory technician in the routine blood count. However, before this evidence was evaluated and re-checked the acute crisis of splenic rupture had taken place.

The significance of the blood findings was not appreciated by the physicians in attendance up to this time and infectious mononucleosis was not considered in the preoperative differential diagnosis. In fact, it must be acknowledged that the signs did not seem to indicate splenic rupture, and this finding was disclosed only during the operation after an initial upper right rectus incision had been made.

Examination of the spleen in the tissue laboratory presented similar difficulties. The initial findings suggested an acute inflammatory process and a painstaking search for bacteria was instituted. It was only after this search failed to reveal any organisms and after the diagnosis of infectious mononucleosis became apparent from other evidence that the findings in the spleen were regarded as compatible with this diagnosis.

These difficulties in preoperative and pathological diagnosis are similar to those described by other authors. Preoperative diagnosis will only be improved by wider dissemination of the knowledge that spontaneous splenic rupture due to infectious mononucleosis is a possibility in surgical crises. As to the tissue diagnosis, this must await further descriptions of splenic changes in this condition and the organization of criteria so that it may become diagnostic.
It is to be noted that our case resembles that of King\(^1\) in that the onset of pain and shock was associated with defecation.

Finally, it was of some interest in our case that evidences of central nervous system involvement as a complication of infectious mononucleosis were present.

REFERENCES

INFECTION MONONUCLEOSIS COMPLICATED BY SPONTANEOUS RUPTURE OF THE SPLEEN AND CENTRAL NERVOUS SYSTEM INVOLVEMENT

STUART L. VAUGHAN, J. SUTTON REGAN and KORNEL TERPLAN