

Lymphocytopenia with Lymph Extravasation from Abnormal Lymphatics: Its Occurrence with Chylous Ascites and Chylothorax

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Lymphocytopenia develops with severe lymph loss and depletion of lymphocyte bearing lymph. Cannulation and protracted drainage of the thoracic duct in laboratory animals and man are invariably associated with lymphocytopenia (1-6). Concurrently the lymphocytes become progressively immature and it is possible to confuse them with malignant lymphoma cells.

We have observed the clinical counterparts of these phenomena in patients with severe lymph depletion associated with recurrent chylous effusions. Four such patients are reported. Each had severe protracted recurrent chylous effusions associated with lymphocytopenia. The lymphocytopenia was attributed to the depletion of lymphocytes associated with persistent loss of lymph into the body cavities. In two patients actual leakage from the lymphatics was demonstrated by lymphography. In the other two, the presence of chylous effusions was direct evidence of lymph extravasation.

In two patients, as the lymph extravasation persisted the lymphocytes exhibited such increasing immaturity that the possibility of malignancy was raised. The explanation lay however, in the progressive immaturity of the lymphocytes which coincided with the protracted lymph effusions.

Case Reports

Pat. 1: M. N. was a 68 year old female with massive right chylothorax of at least 4½ months duration and chylous ascites of unknown duration. Physical examination gave no clue to the cause of her illness. There was no peripheral adenopathy. Lymphography demonstrated the lymph nodes up to the cysterna chyli to be exceedingly sparse in size and number. The nodes showed no evidence of lymphoblastic disease or other malignancy. The thoracic duct was visualized in its entirety. There was reflux filling of several lower thoracic lymphatics. Some of the contrast material lay free in the projections of the right pleural and peritoneal cavities, interpreted as indicating leakage from the lymphatics.

Pleural biopsy and bronchoscopy were negative. Thoracotomy revealed a "leak" from the lower thoracic duct, 1.8 cm. of which was ligated and resected, but no abnormality was found in the specimen. The patient did not improve. A sigmoid polyp was discovered and sigmoidectomy of an adenocarcinoma was performed. The contiguous lymph nodes showed no metastases and were otherwise unremarkable. It was felt that this tumor had not metastasized and that it had been removed entirely.

On admission, the lymphocyte count was 29% with an absolute count of 1663 cells/cc³ of blood (normal), but concurrently with the persistent recurrent chylous effusions a percentile and

absolute lymphocytopenia developed (Fig. 1). This was further compounded by repeated removal of large quantities of the effusions followed by rapid refilling and further lymph depletion.

The lymphocytopenia was attributed to the loss of lymphocytes in the lymph extravasated into the body cavities. Fluid from the chest and abdomen were examined repeatedly and found to contain many lymphocytes.

Initially the extravasated lymphocytes showed no abnormalities, but as the lymph extravasation persisted the lymphocytes began to assume an immature appearance and on the last two chest fluid specimens they were described as "consistent with lymphoma". However, it was decided that the progressively increasing immaturity of the lymphocytes from the chylous effusions

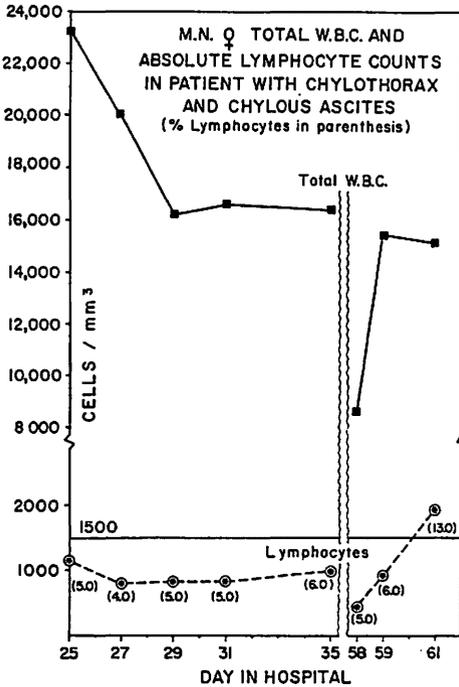


Fig. 1

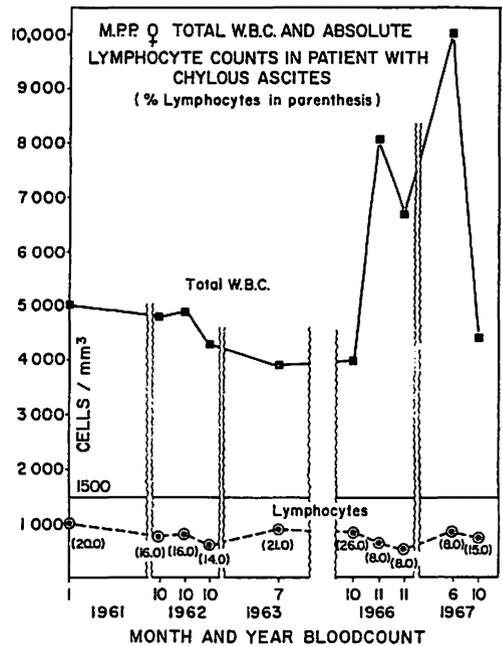


Fig. 2

Fig. 1 Lymphocytopenia in a patient with massive persistent chylothorax and chylous ascites. Lymph leakage noted by lymphography. Lymph depletion worsened by repeated thoracenteses and paracenteses.

Fig. 2 Lymphocytopenia with prolonged massive chylous ascites in a patient with lymphosarcoma. Lymph leakage was noted by lymphography.

coincided with the usual patterns seen with protracted lymph depletion rather than lymphoma. (A laboratory exercise was conducted by the pathologist who initially believed that these cells might be lymphomatous. The thoracic duct of a rat was cannulated, the lymph permitted to drain and sequential lymph smears were examined by the pathologist who then agreed that the progressively immature lymphocytes which appeared might be confused with lymphoma cells). Additional evidence against the presence of lymphoblastic disease was the absence of palpable lymph nodes, the normal nodes found in the sigmoidectomy specimen, and the absence of malignant nodes in the lymphography in the presence of severe lymphatic abnormality as evidenced by the chylous effusions.

The patient died of pneumonia on the 61st hospital day. The lymphocytopenia and the appearance of immature lymphocytes were attributed to the severe lymph depletion, a clinical example confirming the experimental results noted with lymph depletion.

Pat. 2: M. P. was a 67 year old female with massive abdominal swelling due to chylous ascites of 4 to 5 months duration. Lymph node biopsy revealed giant follicular hyperplasia with probable lymphosarcoma. She survived for 6 years and 10 months and died of lymphosarcoma. Except for the last few months of her life she suffered from massive recurrent chylous ascites. Numerous paracentesis fluid studies confirmed the presence of large numbers of lymphocytes which had leaked into the body cavities with the chylous effusions. She had an absolute and relative lymphocytopenia (Fig. 2).

Lymphography was done during the third year of her illness and abnormal lymphatics were noted with reflux into mesenteric lymphatics. Contrast material was found lying free in the peritoneal cavity, direct evidence of leakage of the contrast material and lymph from the damaged lymphatics.

The lymphocytopenia was attributed to the persistent lymph loss associated with the intractable chylous ascites. The patient did receive small doses of cobalt therapy, not in amounts usually associated with lymphocytopenia. She was variously treated with chlorambucil, nitrogen mustard and diuretics but no causal relationship to the chronic lymphocytopenia could be established. The disease itself caused no obvious failure of her immune mechanism, the patient surviving almost seven years in spite of her ascites. It appeared unlikely that the disease was directly responsible for the lymphocytopenia. The lymphocytopenia was constantly and concomitantly related to the lymph depletion associated with the chylous ascites. Lymph leakage was confirmed by lymphography, and perpetuated by the persistent recurrent chylous ascites. Large numbers of lymphocytes, as expected, were always found on examining the paracentesis fluid. The findings were therefore, accepted as another example of lymphocytopenia attributable to lymph loss.

Pat. 3: M. M. was a 57 year old male who previously received surgery and radiation therapy to the left supraclavicular area; dates, amounts and diagnosis unknown. With the present illness a left chylothorax was discovered and biopsy of cervical lymph nodes revealed Hodgkin's disease. There was an absolute and percentile lymphocytopenia in the amount of 672 (12%). The patient was given radiation to the left supraclavicular and anterior mediastinal areas in dosages not usually associated with lymphocytopenia. The fluid began to absorb almost immediately and within 5 months no free fluid could be detected but the lymphocytopenia persisted. This long delay in recovery from the lymphocytopenia after the chylothorax had absorbed is not completely explained but may have its counterpart in experiments in which there is a long delay in lymphocyte recovery even after lymph depletion has been terminated.

Fifteen months after radiation the blood count returned to normal. There were 1767 lymphocytes/mm³ (38%). Shortly afterwards the chylothorax recurred and simultaneously with the lymph loss, lymphocytopenia recurred (Fig. 3). There was no chemotherapy administered during this period. Lymphography was not done.

Since lymphocytopenia may occur as a parameter of Hodgkin's disease, without demonstrable lymph loss or extravasation, it is not possible to state that the lymphocytopenia was due only to the chylothorax. It should be noted, however, that after the normal count had been reestablished, when there was a recurrence of the chylothorax the lymphocytopenia recurred, strongly suggesting a casual relationship.

Pat. 4: H. W. was a 24 year old female with chylous ascites and chylothorax of several months duration, etiology undetermined. Lymphography, done once, did not demonstrate extravasation of the contrast material into the pleural or peritoneal cavities, although there was persistently recurrent effusion. Numerous lymphocytes were present in the chylous effusions and after repeated tapings followed by reaccumulations, the lymphocytes began to show increasing variations in size, enough to raise a suspicion of malignant lymphoma, but this was attributed to the appearance of immature lymphocytes, a parameter of chronic lymph loss.

The protein content of the fluid was high and this was accompanied by a reversal of the patient's serum albumin/globulin ratio with persistent hypoproteinemia. The serum cholesterol and calcium were somewhat below normal. There was an absolute and percentile lymphocytopenia (Fig. 4).

Biopsy of a juxtaaortic lymph node showed it to be hyperplastic. A jejunal biopsy revealed lymphatic dilatation and a small intestinal mesentery biopsy demonstrated chylous lymph stasis. Acute serosal inflammation was present as was granulomatous inflammation of the mesentery, but these were judged in the light of the numerous prior abdominoparacenteses. A lymph node taken from the chest showed hyperplasia.

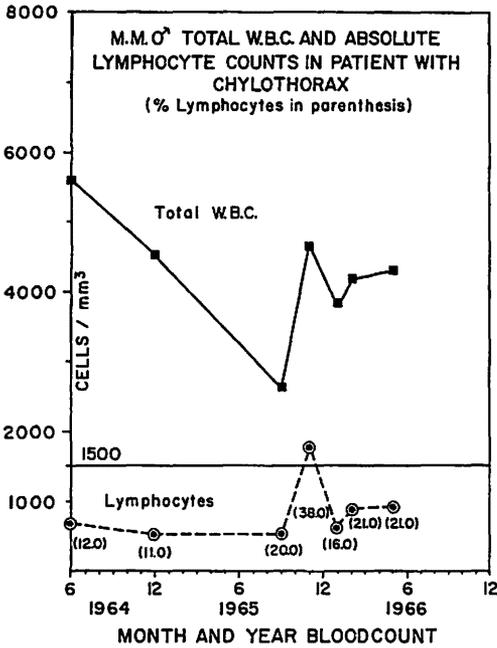


Fig. 3

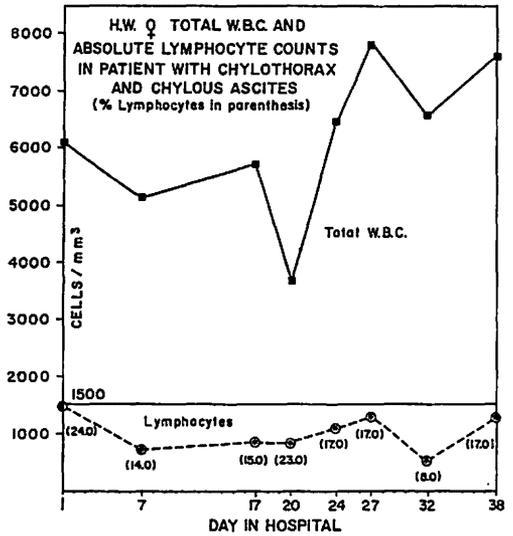


Fig. 4

Fig. 3 Lymphocytopenia with Hodgkin's disease and chylothorax. Since lymphocytopenia may be present in Hodgkin's it is not possible to state that the lymphocyte deficit was due to the chylothorax alone. However, at year end, 1965, the lymphocyte count peaked to normal and there was no longer any chylothorax. Shortly afterward, the chylothorax recurred and there was recurrent lymphocytopenia.

Fig. 4 Lymphocytopenia in a patient with massive persistent chylothorax and chylous ascites, etiology undertermined.

The patient was treated medically with correction of her serum protein depletion and improvement in her general status, but no definitive diagnosis was made other than serious lymphatic abnormality with lymph leakage into the pleural and abdominal cavities associated with reflux and dilatation of lymphatic channels. Each of the effusion specimens showed abundant lymphocytes and the lymphocytopenia was attributed to the lymph depletion associated with the chylous effusions. Some lymphocytes were probably lost by seepage through the distended intestinal lymphatics but the major loss was into the chylous effusions.

Summary

Four examples of severe chylous lymph effusions into serous cavities are reported. In each case there was an associated lymphocytopenia. This resembled and confirmed the findings noted in experimental lymph drainage from cannulated thoracic ducts in which the subject invariably develops lymphocytopenia as the lymph is permitted to drain. Each of these patients had communications between the lymph structures and the serous cavities. In two instances actual leakage of the lymphography contrast material was demonstrated. The performance of repeated thoracenteses and paracenteses in the presence of communications between the lymph structures and serous cavities added to the effect of converting the situation to one similar to thoracic duct drainage. The progressive immaturity of the lymphocytes which was noted in two patients lead to the problem of differentiating them from malignant cells. The explanation lay in the known progressive immaturity of lymphocytes which appear when lymph drainage persists.

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References

- 1 Beebe, D. S., C. A. Hubay, L. Persky: Thoracic duct ureteral shunt: A method for decreasing circulating lymphocytes. *Surg. Forum* 18 (1967), 541-543
- 2 Gesner, B. M., J. L. Gowans: The output of lymphocytes from the thoracic duct of unanesthetized mice. *Brit. J. Exp. Path.* 43 (1962), 424-430
- 3 Gowans, J. L.: The effect of the continuous re-infusion of lymph and lymphocytes on the output of lymphocytes from the thoracic duct of unanesthetized rats. *Brit. J. Exp. Path.* 38 (1957), 67-78
- 4 Iverson, J. G.: Phytohemagglutinin response of recirculating and nonrecirculating rat lymphocytes. *Exp. Cell Res.* 56 (1969), 219-223
- 5 Tilney, N. L., J. E. Murray: Chronic thoracic duct fistula: operative technic and physiologic effects in man. *Ann. Surg.* 167 (1968), 1-8
- 6 Yoffey, J.M.: The Lymphocyte. *Ann. Rev. Med.* 15 (1964), 125-148

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The Superficial Lymphatic System of the Cat

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Abstract

The superficial lymphatic system of fifty-four domestic cats was studied after the subcutaneous injection of India ink. The drainage areas of the lymph nodes are as follows: The lymph vessels of the head and neck drain into the parotid, mandibular, and superficial cervical lymph nodes. The vessels of the lateral surface of the forelimb and shoulder drain into the superficial cervical lymph node. The vessels of the medial aspect of the forelimb and shoulder course to the axillary and accessory axillary lymph nodes. The accessory axillary and internal lymph nodes receive the afferent vessels from the dorsum. The superficial inguinal lymph node drains the ventral portions of the abdominal and pelvic regions, the male external genitalia and flank. The mammary glands