Spontaneous, Temporary Regression in a Lymphosarcoma: Can Procaine Produce This Effect?

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An unusual case of a large mediastinal mass and enlarged cervical lymph nodes proved to be lymphosarcoma, which disappeared within 24 hours following biopsy of one of the nodules. Gradual relapse occurred 12 days later and the disease progressed. No clear reason could be determined for the regression of the masses, but the question of procaine was raised.

Case History

A 16-year-old boy whose chief complaints were of bilateral, enlarged, cervical lymph nodes and difficulty in breathing, was admitted to the hospital. According to the patient, he had been well until three months prior to admission, when a single, firm painless nodule appeared on the right side of his neck. At that time an unknown drug, given by injection, was prescribed by a physician, but without any benefit. Since then, more cervical nodules were noticed and during the previous weeks they had become somewhat tender. At this time no fever was noted, but the patient began to experience difficulty in breathing and in swallowing solid foods. The patient's past and family history were unremarkable.

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Physical Examination: The patient was found to have bilateral, hypertrophied, hyperemic tonsils and there were several nodules, slightly tender on palpation. These nodules were bilateral, unattached to the skin and ranging in diameter from one to five cm. The heart and lungs were normal. Slight generalized tenderness was found in the abdomen. No masses were palpable, and there was no hepato-splenomegaly. Neurological examination and extremities were normal. Chest x-rays showed a large upper mediastinal mass (Figure 1).

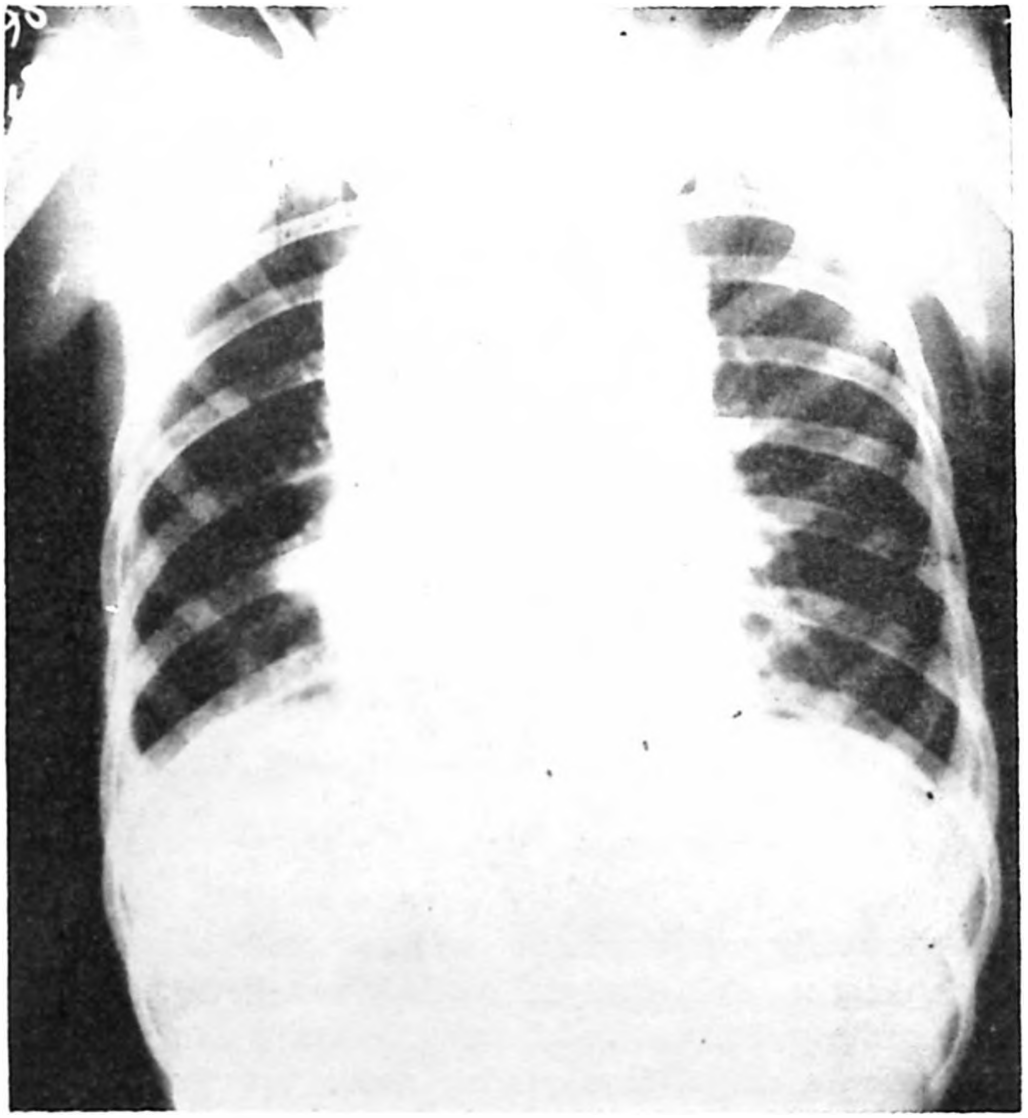

Figure 1. The upper mediastinal mass

Blood pressure was 105/70, pulse 80 regular, respiration 20 per minute and temperature 37.6°C. The urine was normal with 1030 specific gravity, and the sediment contained occasional white cells per high power field. Hb was 13.05 at first, decreasing to 10 gm ten days later. White cell count was 14.600 with 74 per cent neutrophils, 21 per cent lymphocytes, four per cent eosinophyls and one per cent monocytes. Platelets appeared

normal. Total proteins were 7 gm/100 ml, albumin 4.3/100 ml, globulin 2.7/100 ml; non-protein nitrogen (NPN) was 15.5 mg/100 ml, bilirubin 0.40 mg/100 ml, thymol was 1.4 units and blood sugar 84 mg/100 ml. Heterophil antibodies were twice found positive at 1/28. A sputum smear for Koch bacilli was negative and throat culture yielded alpha hemolytic streptococci and Neisseria. Bone marrow aspiration revealed a normal smear. In a 24 hour urine specimen the 17 ketosteroids were 4.1 mg and the 17 hydroxycorticoids 9.8 mg. On repetition these were found to be 3.1 mg and 9.7 mg respectively.

On the third day after hospitalization a biopsy of the left cervical nodules was done. On the fourth day the attending physician was surprised to see that the cervical nodules had very much decreased in size and number, and an immediate chest x-ray was taken (Figure 2), which showed that the mediastinal mass had also regressed. The chest x-ray was repeated

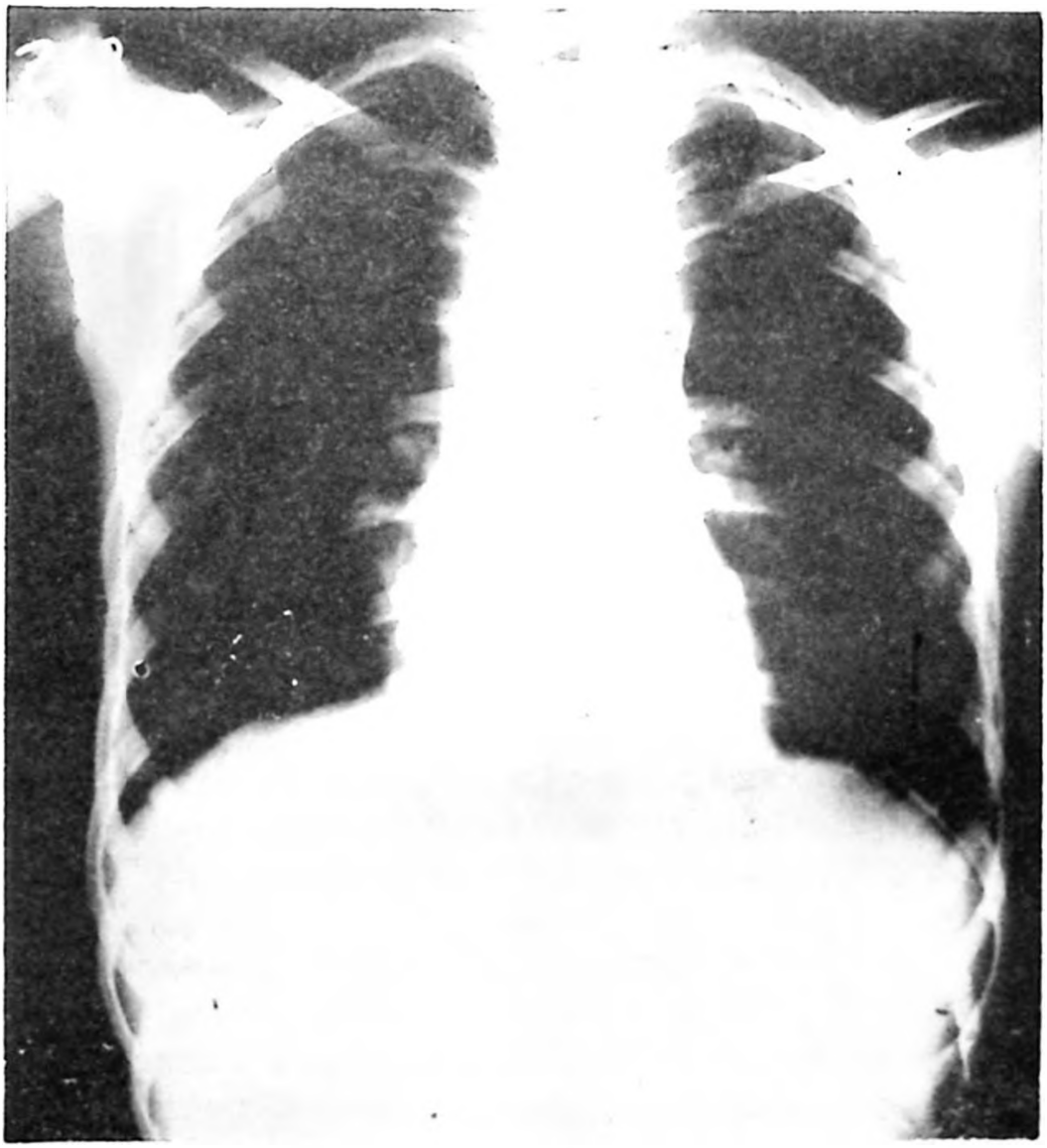

Figure 2. The regression of the mass (within 24 hours of biopsy)

the same day to verify this finding. That day mild diarrhea was also noted. The patient received no medication, except for the second day when 800.000 units of penicillin procaine daily was started.

Biopsy revealed lymphosarcoma type lymphoma (Figure 3). Until the tenth day after admission the cervical nodules remained the same, but thereafter there was a gradual increase in size. On the twelfth day chest

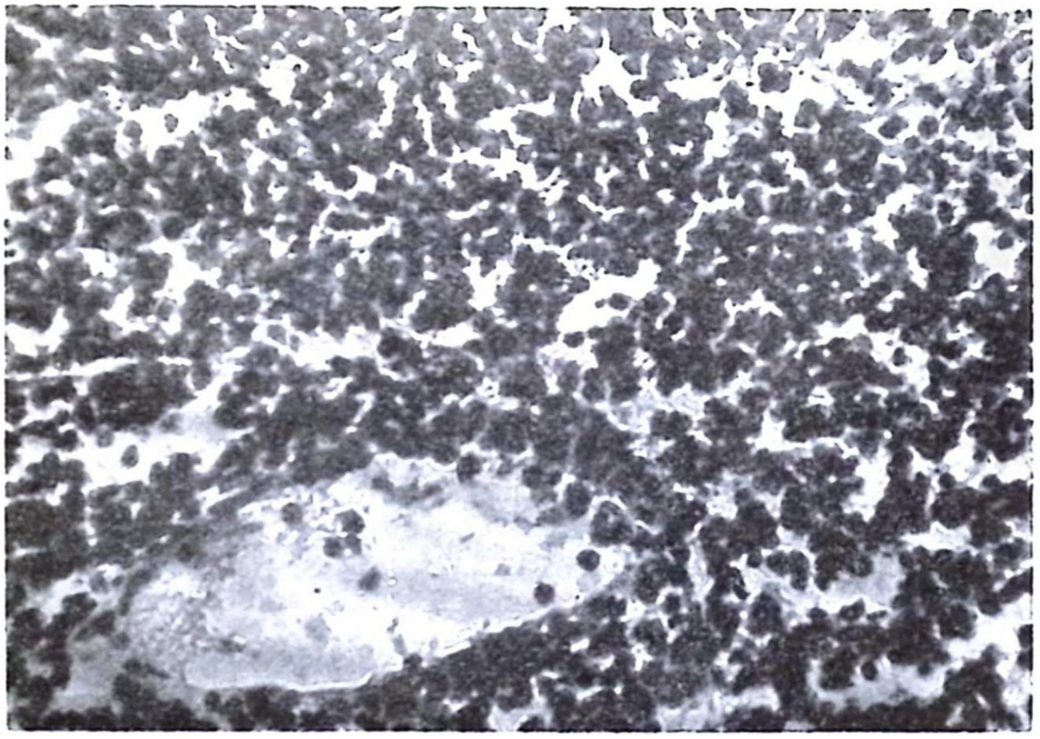

Figure 3. Lymph node showing lymphosarcoma.

x-ray showed the same upper mediastinal mass (Figure 4). On the 17th day a repeated biopsy revealed chronic lymphocytic leukemia due to invasion of the vascular structure (Figure 5). Later GI tests were performed. There were several filling defects all of different size in the ileum and colon. The mucosal pattern was distorted in some places, and from those findings the radiologist suggested lymphoma as a possible diagnosis (Figure 6). In the meantime, repeated white cell counts were between 9,400 and 6,600 with normal differentials. There was no lymphopenia, and eosinophilia was one to five per cent. At all times the platelets appeared normal.

Comments

Prolonged, spontaneous or induced remissions of leukemia have been reported, [1] [2] and partial or complete remissions following streptococcal sore throat, varicella and hemolytic staphylococcal septicemia have also been noted. [3] However, spontaneous and almost complete, though

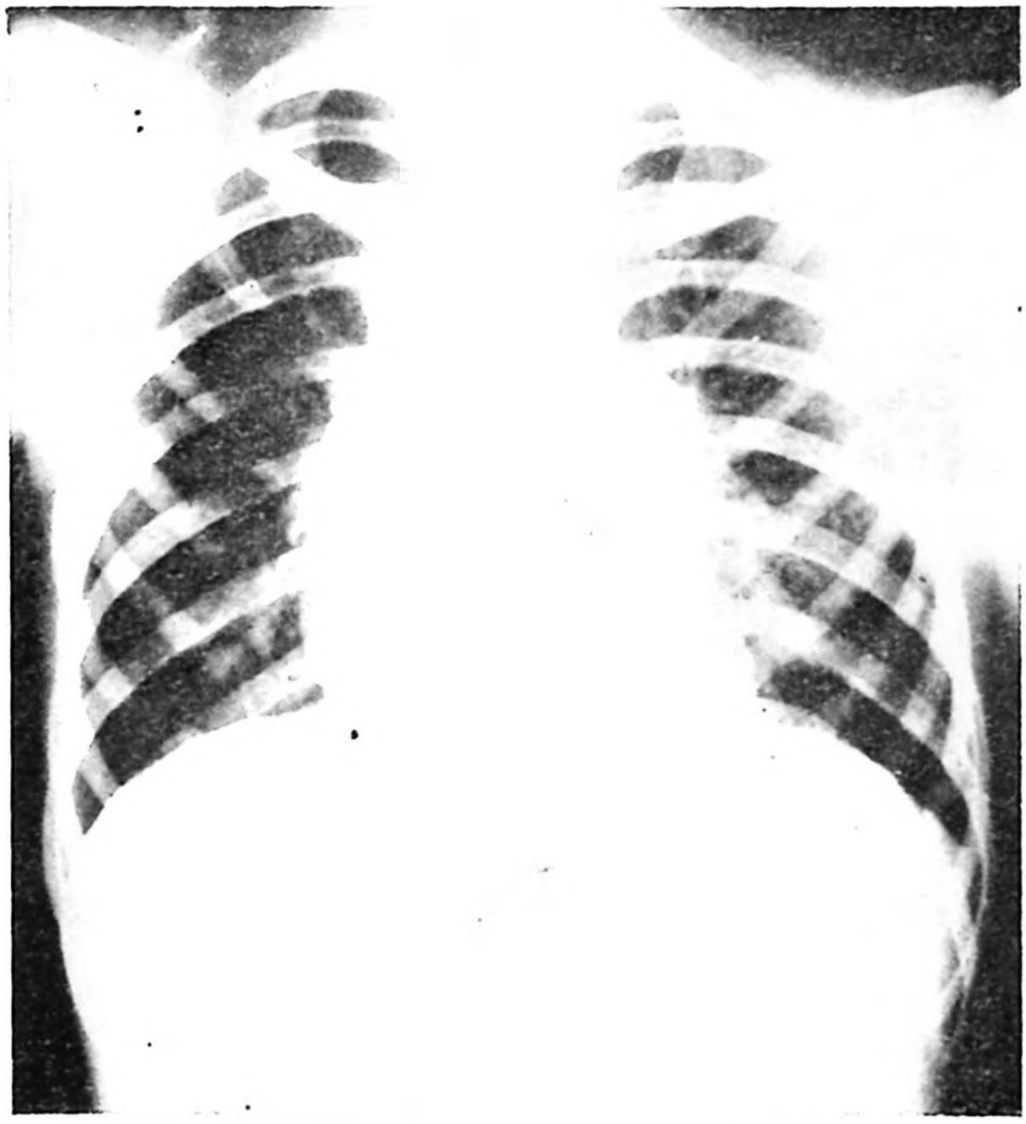

Figure 4. Gradual enlargement of the upper mediastinal mass 12 days after biopsy

temporary, disappearance of large mediastinal and cervical lymphoid tumors in a very short time, such as 24 hours, have not been reported as far as we can find.

Isaacs[4] reports two cases, the first of lymphosarcoma cell leukemia with enlarged cervical and axillary lymph nodes, with cough ing and pleural effusion, which apparently showed spontaneous retraction of the glands during the third month of pregnancy. The patient gave birth to a perfectly normal child, but nine months later gradual relapse occurred. The second case was of reticulum cell leukemia. Eighteen months after diagnosis the patient developed a perirectal abcess which was drained and the patient received penicillin. After this there was a gradual improvement in the blood picture and an apparent remission occurred, following which the patient remained well for the next 14 years.

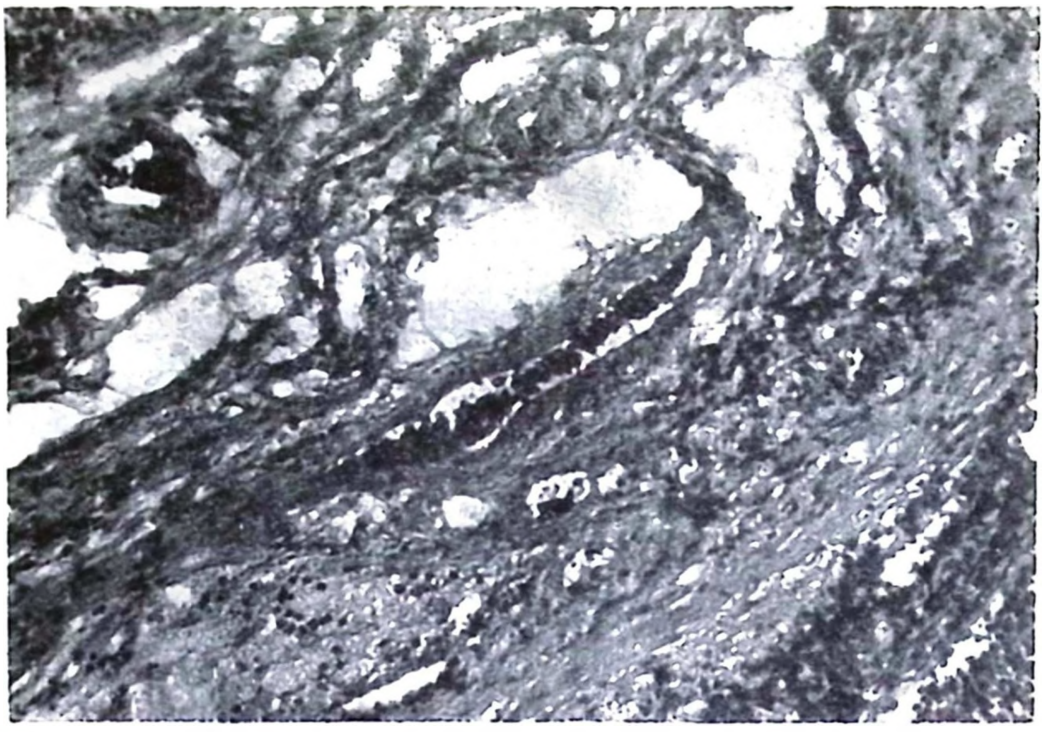

Figure 5. Second lymph node biopsy. because of lymphocytic vascular invasion reported to be leukemia.

Another interesting observation is the occasional instances of apparent lymphosarcoma cures which have been reported in patients after surgical excision of a primary extranodal lesion, i.e. in the small intestine.[5] In addition to this, Black,[6] in discussing a case at Massachusetts General Hospital's weekly CPC, mentions cases of Burkitt's lymphomas being cured with biopsies.

It is interesting to note whether or not the reported cases of spontaneous regressions followed a biopsy or minor surgical explorations. In our case the clinical course was altered rather suddenly, though temporarily, after biopsy.

There can, of course, be many opinions regarding spontaneous regression of lymphoid tumors, but one in particular seems worth mentioning. Could this effect be produced by procaine? The action of procaine is similar to that of other local anesthetics, but it does have certain unique functions and properties. Following systemic administration, procaine can produce a mild degree of general anesthesia. The mechanism of this anelgesic action is not clear, but can be attributed to the central action of the drug, or possibly to that of one of its properties such as hydrolysin or dethylaminoethanol. Besides this, procaine has another effect - sulfonamide antagonism.[7]

As for the use of novocain, it is known to dermatologists that procaine may be used specificially for granuloma annulare. The simple infiltration

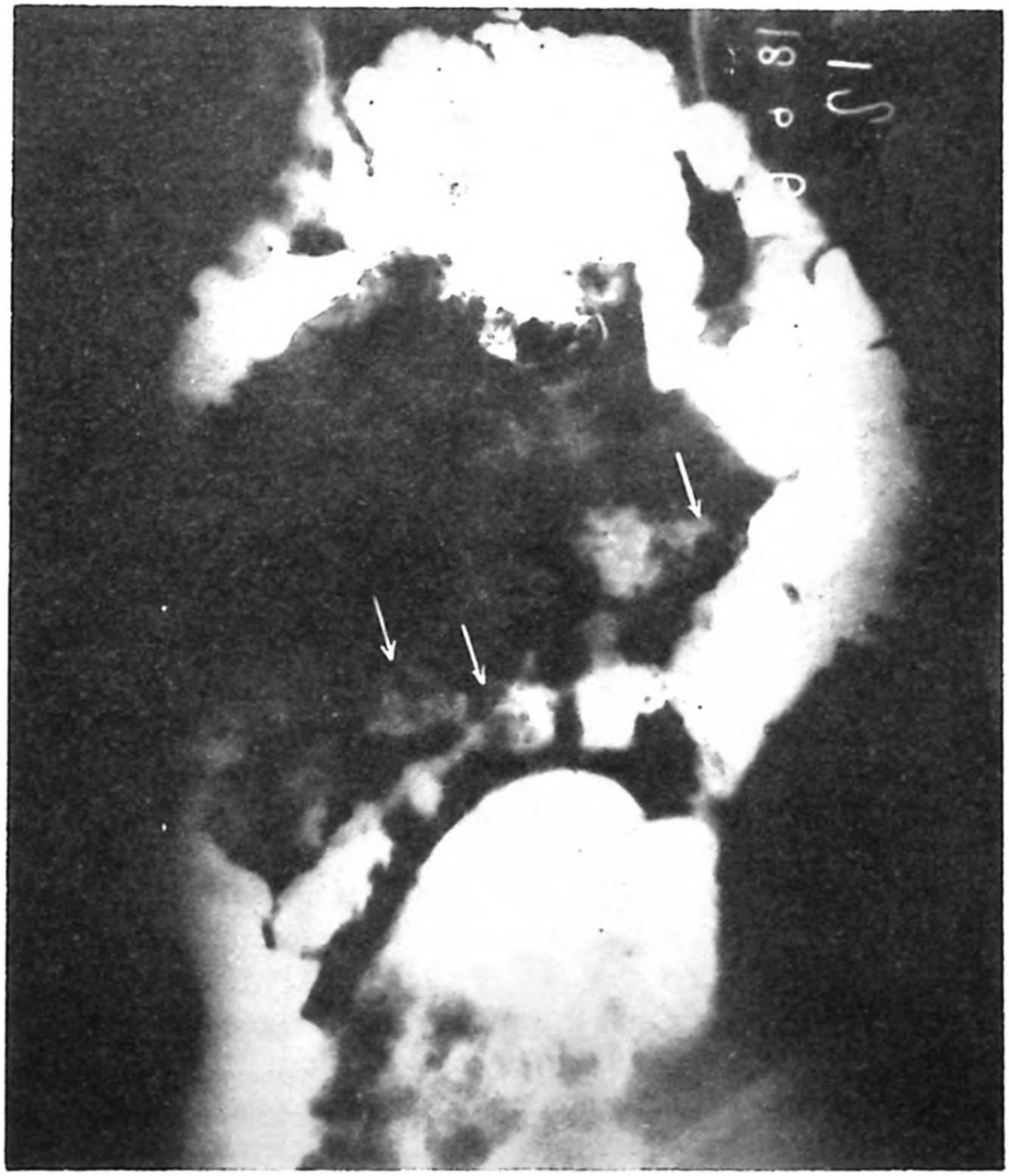

Figure 6. G. 1 series showing several filling defects (arrows)

of the area with procaine, or incision of the lesion, may at times be followed by complete and rapid involution. The etiology of the condition is unknown.[8]

Procaine was also used intravenously by State and Wangensteen[9] in the treatment of delayed serum sickness and urticaria of specific and non-specific origin. The results were favorable in a significant number of cases. In our case not only the local lymph nodes, but also the mediastinal mass regressed after biopsy. Any mechanism involved should have a systemic rather than a local effect to produce this result.

At this point the role of the thymus gland on the lymphocytes and the lymphoid tissues should be mentioned. Goldstein, Slater and White[10]

isolated a peptide with low molecular weight which they called thymosin. This has a powerful effect on lymphoid tissues, and when injected into thymectomized mice causes enormous lymphoid hypertrophy. Keeping this in mind, one wonders about the possible interplay between the thymic hormone and substances containing procaine. Could it be that procaine, or its products, suddenly depresses or blocks the hormone or its activity, which might be increased in a diseased state, thus suddenly causing the regression of lymphoid tumors?

It is true that at times the disappearance of enlarged lymph nodes, and their subsequent reappearance, without any specific treatment have been seen. It is also true that in cases of lymphoid tumors lymph node biopsies are regularly performed, and that usually a local anesthetic is used, of which procaine is one of the most universal. We believe that the occurrence of regression after biopsies of the lymphoid tumors should be surveyed, and that the effect of procaine or its hydrolysed products upon the thymus, the lymphoid tissues and the lymphocytes should also be investigated.

Besides the temporary regression of this tumor, the susbequent history of our patient should also be considered. The second lymph node biopsy was reported as chronic lymphocytic leukemia. It is well known that the relation of lymphomas to leukemia has been firmly established. Even Gall and Mallory[11] attempted to predict the presence or absence of clinical leukemia on the basis of nodal morphology, but found that nodes with apparent blood vessel invasion, or even large invasive tumors, were accompanied by leukocytosis. However, the relationship between leukemia and lymph node tumors was particularly noticeable among cases classed by lymph node examination as lymphocytic or lymphoblastic lymphoma. It has also been stated that the histologic pattern of lymphosarcoma is indistinguishable from that of chronic lymphocytic leukemia[12] and that leukemic transformation occurs in lymphosarcoma.[13]

The above statements proved valid in our case too. After his first admission the patient left the hospital without any change, but returned about a month later. On his second admission the lymph node enlargement remained as before, but in addition to this the blood smear and bone marrow smear displayed lymphoblastic leukemia.

Acknowledgement

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