

## Lymphographic Diagnosis of Malignant Lymphoma in the Course of Sjögren's Syndrome

M. Wiljasalo, K. Tallroth, O. Korhola, M. Valle, P. Vuopio

First Department of Radiology and  
Third Department of Medicine, University Central Hospital, Helsinki, Finland

### Summary

Three patients with Sjögren's syndrome complicated by malignant lymphoma are presented. During the benign stage, two showed non-specific hyperplastic lymph node patterns on lymphography. When the disease had become malignant, all cases revealed generalized involvement of the retroperitoneal lymph nodes. The lymphographic pattern was that of a malignant lymphoma: enlarged nodes, with a foamy, linear or reticular appearance but mostly preserved marginal sinuses. On lymphographic follow-up, the node alterations were consistent with the histological findings and the clinical status, including the therapeutic response.

Sjögren's syndrome (SS) is characterized by polyarthritis, dry mouth, and dry eyes. It is a systemic disease of unknown aetiology, occurring predominantly in women. Radiological examination usually shows destructive bone and joint lesions which simulate rheumatoid or psoriatic arthritis, and ectasia of the salivary gland ducts. Reticular and nodular lung infiltrates are seen in about one third of cases (5), and non-specific deep abdominal lymphadenopathy may be revealed by lymphography (6).

The combination of SS with lymph node abnormalities was first described by *De Graciansky* et al. (1) and later investigated by *Talal* and *Bunim* (3). In 1967 *Talal* et al. (4) pointed out that SS predisposes to the development of extrasalivary lymphoid abnormalities including pseudolymphoma, macroglobulinaemia and reticulum cell sarcoma.

Only one case has been reported in which the lymphographic findings in SS complicated by a malignant lymphoma have been described (2). In this communication we present three additional cases in which lymphography was performed to elucidate the state of retroperitoneal nodes.

### Case reports

**Case 1.** This 49 year old woman had had rheumatoid arthritis for 6 years before the onset of dryness of the mouth, decreased tear secretion, and swelling of the salivary glands led to the diagnosis of SS. The diagnosis was confirmed by  $^{99m}\text{Tc}$  scanning (7) and biopsy of the parotid glands. Sialography revealed typically narrowed ducts and ectasia. The spleen was enlarged and an excised cervical lymph node suggested a reticulum cell sarcoma. Lymphography disclosed pathological nodes in the parailiac and paraortic regions as well as in the groins, where they also were palpable. Multiple drug chemotherapy (nitrogen mustard-vincristine-prednisone) had a good result and was successfully continued for 3 years, at what time the patient died of an intestinal perforation. At autopsy the malignant lymphoma was confirmed by histological examination of mesenteric and retroperitoneal lymph nodes.

**Lymphography:** The initial lymphogram revealed very large lymph nodes in which the irregular structure and varied filling defects suggested a malignant lymphoma (Fig. 1a). Diminution of the nodes was noted after one month of cytostatic treatment, but the node architecture remained unchanged (Fig. 1b).

**Comment:** This patient had had rheumatoid arthritis for 6 years prior to the appearance of documented SS. Later, when she developed a malignant lymphoma there was a typical lymphoma node pattern on lymphography. A partial response to the therapy was shown in follow-up films.

**Case 2.** This 38 years old woman had a 2 year history of dry mouth, burning and itching of the eyes, and pains in the wrists,

Permission granted for single print for individual use.

Reproduction not permitted without permission of Journal LYMPHOLOGY.

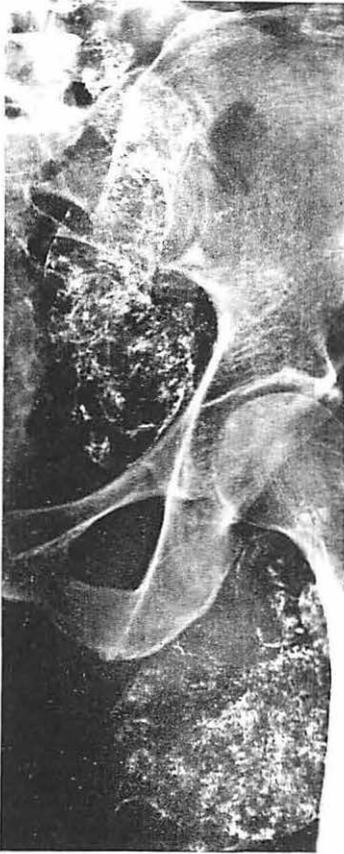


Fig. 1a: Case 1. Markedly enlarged and rounded lymph nodes with irregular structure and defects indicating a malignant lymphoma.

←

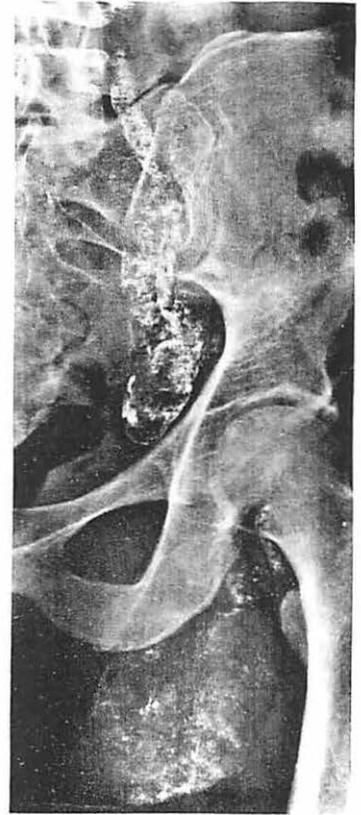


Fig. 1b: After one month of cytostatic treatment the lymph nodes are reduced in size.

ankles and back. When the symptoms increased, and large lymph nodes appeared in the neck and groins, she was admitted to hospital for investigation. Her general condition was good, although the spleen was enlarged.

Sialography was performed which disclosed changes typical of SS. A positive Schirmer test, i.e. decreased tear production, supported the diagnosis of SS. Diagnosis of pseudolymphoma was made on the basis of a lymph node biopsy, a positive PHA stimulation test and lymphography. With small doses of cyclophosphamide (50–100 mg. per day) a remission was achieved. One year later she relapsed and the nature of the disease changed into a malignant lymphoma, which was confirmed histologically. To cope with this, larger doses of cytostatics were needed. Since then, the patient has been in remission for three and a half years.

*Lymphography:* The lymphogram showed enlarged lymph nodes, whose structure suggested a non-specific hyperplasia rather than malignant lymphoma (Fig. 2a). The nodes diminished after 4 months of cytostatic therapy (Fig. 2b). About one year later, when the disease had turned clinically malignant, repeat lymphography revealed lymph node enlargement with a transverse linear structure typical of malignant lymphoma, especially in the enlarged lumbar nodes (Fig. 2c). After intensive cytostatic therapy, regression was lymphographically demonstrable.

*Comment:* This patient had had polyarthritis, dry conjunctivae and mucous membranes, and swollen parotid glands for at least two years before SS was firmly diagnosed. She developed enlarged lymph nodes which histologically showed findings first of pseudolymphoma and later of a malignant lymphoma. Lymphograms



Fig. 2a: Case 2. Slightly enlarged lymph nodes with non-specific structure alterations.



Fig. 2b: Diminution of the lymph nodes after 4 months' cytostatic treatment.



Fig. 2c: Re-enlargement of the nodes especially in the lumbar region. The contrast medium is observed as transverse strands and in the preserved marginal sinuses.

confirmed these various phases, and successful chemotherapy was accompanied by a demonstrable diminution of the nodes.

**Case 3.** A 61 year old man had had cervical lymph node enlargement for 10 years. Several nodes were biopsied, and they all revealed atypical adenitis or hyperplasia. When dryness of the mouth and eyes developed two years later, a biopsy of the parotid gland confirmed the diagnosis of SS, although he never had joint pain. The next year, the groin lymph nodes became enlarged and again showed atypical hyperplasia on biopsy. Blood tests, liver and spleen were within normal limits. Lymphography revealed enlarged nodes in the parailiac and paraaortic regions. One year later his general condition deteriorated with weight

loss. The lymph nodes became further enlarged, the largest to the size of a pear. The PHA stimulation test was positive. A roentgenogram of the chest revealed large hilar nodes and a repeat lymphography showed large lymph nodes. Histological examination of an axillary node revealed destruction of the architecture including the capsule, and many reticulum cells and mitotic figures. Despite different drug combinations (cyclophosphamide-vincristine-prednisone and nitrogen mustard-vincristine-procarbazine-prednisone) his general condition deteriorated, hepatomegaly and oedema of the legs developed, and he died 6 months after starting the cytostatic treatment. At autopsy, malignant reticulum cells were found in the parotid glands, lymph nodes and liver; the final histological diagnosis was reticulum cell sarcoma.

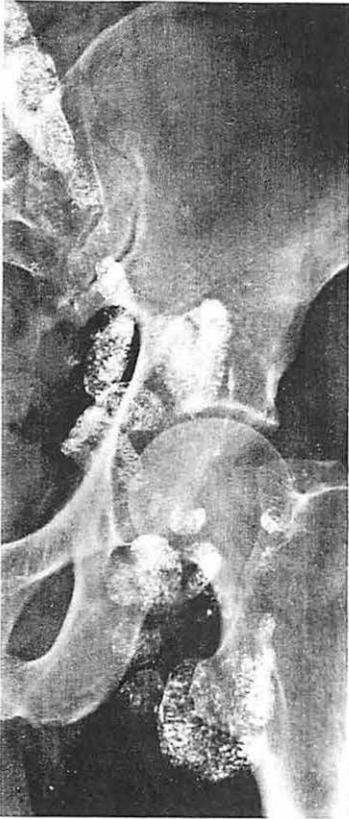


Fig. 3a: Case 3. The lymph nodes are enlarged and show a loosened structure corresponding to a non-specific node reaction or an early lymphoma.

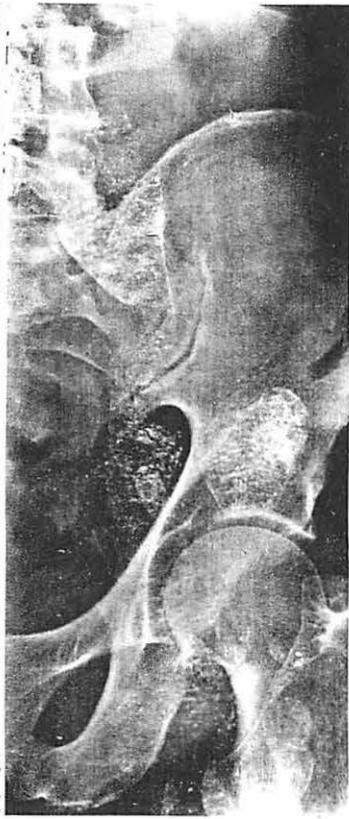


Fig. 3b: Considerable further enlargement of the nodes. The pattern is partially transverse linear and reticular. The marginal sinuses are mostly preserved.



Fig. 3c: Marked diminution of the nodes after cytostatic treatment. The nodal pattern remained unchanged.

*Lymphography:* On lymphography, at the time when the histologic picture of the nodes was that of an atypical adenitis or hyperplasia, enlarged nodes with coarse granulation were observed. These corresponded to a non-specific node reaction or an early lymphoma (Fig. 3a). A year later, at the time of the malignant histology, the nodes had enlarged (Fig. 3b). The rapid progression of the changes suggested a malignant disease, and the nodal architecture a malignant lymphoma. After 4 months of cytostatic treatment, the nodes became smaller, although the lymphomatous structure was retained (Fig. 3c). Soon afterwards the lymphographic finding was confirmed at autopsy.

*Comment:* In this patient, the lymphadenopathy preceded the dryness of the mouth and eyes, which led to the parotid gland biopsy and SS diagnosis. In the early stage of the disease lymph node biopsies revealed atypical adenitis or hyperplasia, but later when the clinical course turned malignant, the histology was that of reticulum cell sarcoma. Lymphographically the non-specific node pattern became suggestive for a malignant lymphoma. During the follow-up the clinical state, lymphographic appearances and histologic findings were compatible.

#### *Comment and Conclusion*

The three patients and their course of disease demonstrate the development of lymphomas

in association with primary SS. The diagnosis of SS was made on clinical, histological and radiological grounds. The persistent and recurrent lymphadenopathy, as well as the later neoplastic involvement of the lymphoid tissue, was assessed histologically. In all three cases the final diagnosis was reticulum cell sarcoma.

Our experience with lymphographic examination in the evaluation of SS, leads us to believe that the lymph node size and structural alterations closely follow the course of the disease. Not surprisingly, the lymphographic features are not pathognomonic, which also applies to many benign entities as well as to malignant diseases. However, lymphography may provide a hint of progression and malignant transformation. Additionally, lymphography is indicated when there is strong clinical suspicion of lymph node involvement, although no node enlargement can be detected by other means; further, lymphography may display which node is most likely to yield a successful

biopsy result. Lymphographic surveillance also permits objective assessment of the effectiveness of various chemotherapeutic regimes.

### References

- 1- *Graciansky de, P., S. Boule, I.P. Hardouin*: Syndrome de Gougerot-Sjögren d'étiologie complexe. Bull. Soc. Fran. Derm. Syph. 57 (1950) 292-294
- 2 *Kuffer, R., H. Szpirglas*: Syndrome de Gougerot-Sjögren et hémopathies lymphoïdes. Rev. Stomat. 73 (1972) 318-332
- 3 *Talal, N., J.J. Bunim*: The development of malignant lymphoma in the course of Sjögren's syndrome. Amer. J. Med. 36 (1964) 529-540
- 4 *Talal, N., L. Sokoloff, W.F. Barth*: Extrasalivary lymphoid abnormalities in Sjögren's syndrome (Reticulum cell sarcoma, "Pseudolymphoma", Macroglobulinemia). Amer. J. Med. 43 (1967) 50-65
- 5 *Teplick, J., M.E. Haskin*: Roentgenologic diagnosis. 2nd ed. Vol. 2. Saunders, Philadelphia 1971
- 6 *Silbiger, M.L., C.P. Peterson*: Sjögren's syndrome. Its roentgenographic features. Amer. J. Roentgenol. 100 (1967) 554-558
- 7 *Sodee, D.B., P.J. Early*: Technology and interpretation of nuclear medicine procedures. 2nd ed. Mosby, St. Louis, 1975

*K. Tallroth, M.D., Department of Radiology, Meilahti Hospital, Haartmaninkatu 4, 00290 Helsinki 29, Finland*