

# Intravascular Lymphoma and Thyroid Gland

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## ABSTRACT

*Intravascular lymphoma (IVL) is a rare disease characterized by the proliferation of neoplastic cells in the small blood vessels that frequently goes undiagnosed until the time of autopsy. The neoplastic cells are usually of B-cell origin. The clinical course was examined to determine factors that would facilitate antemortem diagnosis. IVL is observed with clinical, histopathological and immunohistochemical methods. This is a unique case because the thyroid gland is a rare place for IVL. Accent is given on immunohistochemical methods and tissue biopsy in the differential diagnosis of IVL when nervous system and thyroid gland dysfunction occur. This report indicates that micro-ecosystem of multinodular goitrous might influence the expression of chemokines and/or adhesion molecules on endothelial and lymphoma cells, leading to heavy infiltration of thyroid gland. Concurrently, that may guide the physician to tissue biopsy facilitating antemortem diagnosis and institution of appropriate therapy.*

**Key words:** *intravascular lymphoma, thyroid gland, tissue biopsy, immunohistochemical methods, chemokines*

## Introduction

Intravascular (angiotropic) lymphoma (IVL) is a rare variant of large cell lymphoma characterized by intravascular growth of neoplastic cells in the small blood vessels of the whole body (central nervous system and skin are usually involved) causing their blockade and possible symptoms. Malignant cells expressing B, T or rarely histiocyte differentiation. If the disease is detected and treated at an early stage, recovery can be achieved. In this case, we observed a 69-year old man with postmortem diagnosis of IVL, who presented with neurological symptoms (spastic paraparesis) but pathological findings at autopsy, revealed co-existing of multinodular goiter and heavy infiltration of thyroid gland with lymphoma cells. The simultaneous occurrence of multinodular goitrous enlargement and excessive neoplastic growth in the small blood vessels of thyroid gland is unusual, possibly related phenomena, and to the best of our knowledge this has not been previously reported.

A 69-year old, previously well, white man, presented with spastic paraparesis of few days duration. There was no history of significant weight loss, febrility or other

symptoms. General physical examination revealed no lymphadenopathy, splenomegaly, hepatomegaly or other abnormality. Laboratory studies showed normal erythrocyte sedimentation, blood cell counts, including the differential of white cells. Blood chemistry, including serum alkaline phosphatase and lactate dehydrogenase levels (except increased serum glucose level), were within normal limits. Chest radiography showed increased interstitial markings in the both lung fields. Ultrasound sonography showed no evidence of tumour or other significant abnormalities in the abdominal cavity. Urological examination was within normal limits.

Thoracholumbal and lumbosacral plain radiographs demonstrated a serious spondylosis and spondyloarthrotic degeneration. The myelography, computed tomography (CT) and nuclear magnetic resonance (NMR) scans did not reveal any significant information. The thyroid gland enlargement was not recognized premortem, so the measurement of serum thyroid stimulating hormone (TSH), thyrotropin releasing hormone (TRH), triiodothyronine (T3) and thyroxine (T4) was not performed but according

to the medical documentation, there was no clinical manifestations of hyper or hypothyroidism. During 24 days of hospital treatment patient was constantly febrile or subfebrile and finally he died as a result of heart failure.

### Pathological Findings

Postmortem examination found multinodular goitrous enlargement of thyroid gland involving both lobes equally. On cut section there was an overall heterogeneous multinodularity. The majority of nodules were poorly circumscribed and some of them accumulated scarring and condensation of the thyroid stroma. Histologically, we found typical features islands of colloid-filled hyperplastic follicles which varied in size. Focal hemorrhages, hemosiderin depositions and random irregular scarring were also found. Also, widespread to thyroid gland small blood vessels were filled with large polymorphic lymphoid cells with appearance of centroblasts or immunoblasts (Figure 1a) which showed B cell marker cluster of differentiation 20 (CD 20) immunoreactivity confirmed B cell origin of neoplastic cells (Figure 1b). T cell, histiocyte and epithelial markers were negative. Most vessels showed no thrombosis. The infiltrations of lymphoma cells were found in almost all others typically involved organs (lung, liver, kidney) with no lymph nodes, spleen, bone marrow or brain infiltrations. Also, an autopsy revealed chronic ischemic heart disease with global heart failure, which was the cause of death.

### Discussion

Intravascular lymphoma (IVL), first reported by Pflieger and Tappeiner<sup>1</sup>, has many clinical manifestations (neurological, cutaneous, fever of unknown origin, etc). To our knowledge until now, only Shanks<sup>2</sup> described IVL with intense infiltration of thyroid gland. He showed the patient with pyrexia of unknown origin, hypothyroidism and thyroid nodule which was a cavernous hemangioma heavily colonized by lymphoma cells. Our case reported here, demonstrated simultaneous occurrence of pre-existing multinodular goitrous enlargement of thyroid gland and excessive infiltration of their small blood vessels by neoplastic cells for the first time. It is evident that phenomenology of IVL involves close interaction between neoplastic cells and vascular endothelium of involved organ. This interaction is performed by adhesion molecules, chemokines and other cytokines. Endothelial cells and/or adjacent tissue can produce specific chemokines which can play a key role in the process of lymphoma cells recruitment of the blood vessels. Normal leucocytes and endothelial cells make a close interaction with help of adhesion molecules called selectins. Binding, then, proceeds to another class of adhesion molecules—the integrines which are structurally designed for rapid conformational change that determine their affinity. These conformational changes lead to firm arrest of cells on the wall of the blood vessels and then transmural migration.

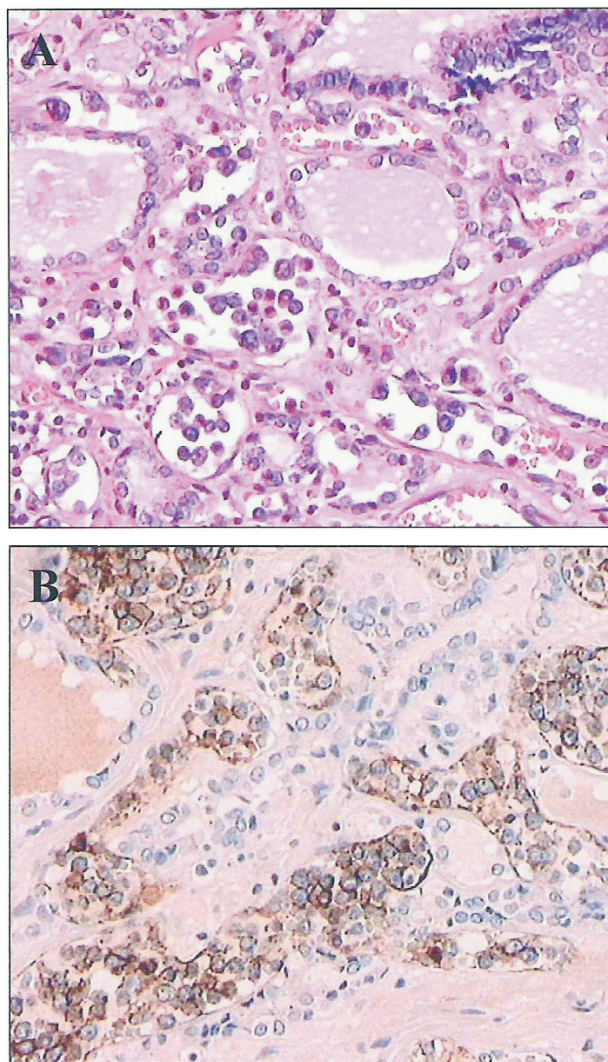


Fig. 1 a) Thyroid gland tissue with intravascular lymphoma. Multiple blood vessels are filled with tumor cells. b) Tumor cells are positive for B-cell antigen cluster of differentiation 20 (CD 20).

Chemokines are probably responsible for integrin's activation<sup>3</sup>. We believe that the same mechanisms are involved in the migration of lymphoma cells. But, in the case of IVL, the possible activation blockade (conformation change) of integrines, normally achieved by chemokines, lead to »prisoning» of lymphoma cells in the lumen of the small blood vessels. The measurement of these molecules produced by endothelial and lymphoma cells, but also by surrounding tissue, needs to be evaluated in the cases of IVL as prerequisite for therapeutic action. This case indicates that micro-ecosystem of multinodular goitrous, might influence the expression of chemokines and/or adhesion molecules on endothelial and lymphoma cells, leading to heavy infiltration of thyroid gland.

## REFERENCES

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## INTRAVASKULARNI LIMFOM I ŠTITNA ŽLIJEZDA

### SAŽETAK

Intravaskularni limfom (IVL), rijetka bolest obilježena proliferacijom malignih stanica unutar malih krvnih žila, često se ne dijagnosticira do trenutka obdukcije. Maligne stanice su obično B-limfocitnog reda. Cilj rada bio je utvrditi čimbenike koji bi ubrzali premortalnu dijagnozu. IVL je proučavan klinički, histopatološki i imunohistokemijski. Naglasak je dan na kliničke i imunohistokemijske metode te biopsiju tkiva u diferencijalnoj dijagnostici IVL-a. Ovo je jedinstven slučaj jer je štitnjača rijetko sijelo IVL-a. Rad pokazuje da mikro-ekosustav multinodozne strume možda može utjecati na ekspresiju kemokina i/ili adhezijskih molekula što bi dovelo do masivne infiltracije štitnjače neoplastičnim stanicama. Konačno, upućivanje liječnika na ideju pravovremene biopsije tkiva štitnjače ubrzalo bi premortalnu dijagnozu i pomoglo u liječenju.