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# Frosted branch angiitis with undiagnosed Hodgkin lymphoma

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PURPOSE. *To report the case of a patient with bilateral frosted branch angiitis and undiagnosed Hodgkin lymphoma.*
METHODS. *Review of clinical history, laboratory findings, histology of supraclavicular lymph node biopsy, and follow-up.*
RESULTS. *A 22-year-old man presented with a sudden, bilateral visual loss. Fundus examination and fluorescein angiography disclosed a bilateral frosted branch angiitis that was dramatically responsive to systemic corticosteroid therapy. Laboratory tests were unremarkable but radiologic studies showed extensive mediastinal and supraclavicular lymphadenopathy. A supraclavicular lymph node biopsy led to the diagnosis of nodular sclerosis Hodgkin lymphoma.*
CONCLUSIONS. *The occurrence of frosted branch angiitis in combination with classical Hodgkin lymphoma, although possibly coincidental, raises the possibility of a paraneoplastic syndrome. Thus, we suggest that, for patients with frosted branch angiitis, Hodgkin lymphoma should be considered in the diagnostic workup. (Eur J Ophthalmol 2009, 19: 310-3)*

KEY WORDS. *Frosted branch angiitis, Hodgkin lymphoma, Paraneoplastic syndrome, Retinal periphlebitis*

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## INTRODUCTION

Classical Hodgkin lymphoma is a malignant lymphoproliferation of B-cell origin characterized by progressive, painless adenopathy, and often accompanied by constitutional symptoms such as fever, night sweats, and weight loss. Intraocular manifestations are extremely uncommon in the early stages of the disorder and most often occur late in the course of the illness as chorioretinitis, vitritis, or anterior uveitis (1). We describe a patient with Hodgkin lymphoma, in whom the initial manifestation of the disease was bilateral frosted branch angiitis.

## Case report

A 22-year-old man presented to the Ophthalmology Service of the Centre Hospitalier Universitaire de Liège and reported a sudden, bilateral visual loss that had occurred 3 days previously. His previous medical history was insignificant.

On examination, visual acuity was 20/200 in both eyes, with no relative afferent pupillary defect and no anterior chamber inflammation. Intraocular pressure was normal. Fundus examination showed extensive white sheathing surrounding the retinal veins with optic disc edema in both eyes, and a few scattered retinal hemorrhages in the left eye (Fig. 1). Fluorescein angiography demonstrated extensive dye leakage and diffuse staining of the retinal veins and the optic disc in both eyes (Fig. 2). Laboratory evaluation including full blood count, erythrocyte sedimentation rate, and angiotensin converting enzyme was normal. Antinuclear and antineutrophil antibodies were negative. Serologic testing for cytomegalovirus, herpes simplex virus, Epstein-Barr virus, *Treponema pallidum, Borrelia burgdorferi,* and human immunodeficiency virus was negative. Serum testing for varicella zoster virus and

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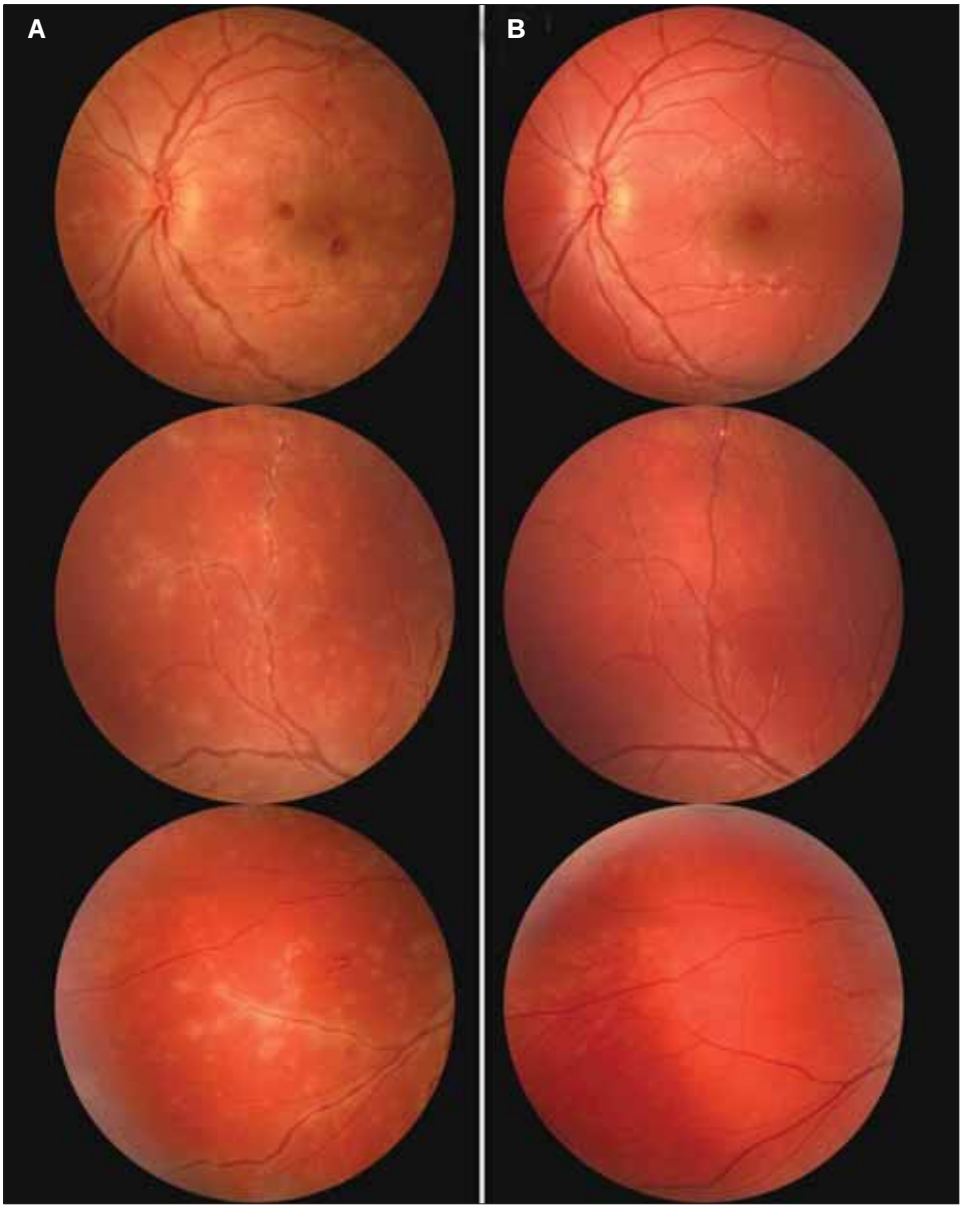


**Fig. 1 - (A)** *Fundus examination at the time of initial manifestation showed bilateral disc edema, bilateral congestion of retinal veins, bilateral perivascular sheathing of midperiphery retinal veins, and scattered small retinal hemorrhages in the left eye.* **(B)** *Two months later, after corticotherapy and initiation of chemotherapy, fundus findings were dramatically improved.*

adenovirus was positive for immunoglobulin G but immunoglobulin M was undetectable. Chest radiograph and brain magnetic resonance imaging (MRI) were normal. Cerebrospinal fluid study was unremarkable.

The diagnosis of acute idiopathic frosted branch angiitis was made and therapy was initiated with intravenous methylprednisolone, 1 g/day for 3 days, followed by oral methylprednisolone, 1 mg/kg/day for 11 days. The clinical response was rapid and after 10 days, visual acuity was 20/32 in the right eye and 20/25 in the left eye. The systemic corticosteroid treatment was tapered and discontinued after 4 weeks. Visual acuity recovered to 20/20 in both eyes by day 24.

Meanwhile, a computed tomographic scan of the chest was performed as the patient complained of exertional dyspnea and revealed diffuse mediastinal and supraclavicular lymphadenopathy. Excisional biopsy of two enlarged supraclavicular lymph nodes (2 and 3 cm) was performed. On microscopic examination, both lymph nodes were characterized by a fibrosing process consisting of broad collagenous bands surrounding cellular nodules (Fig. 3A). The latter were

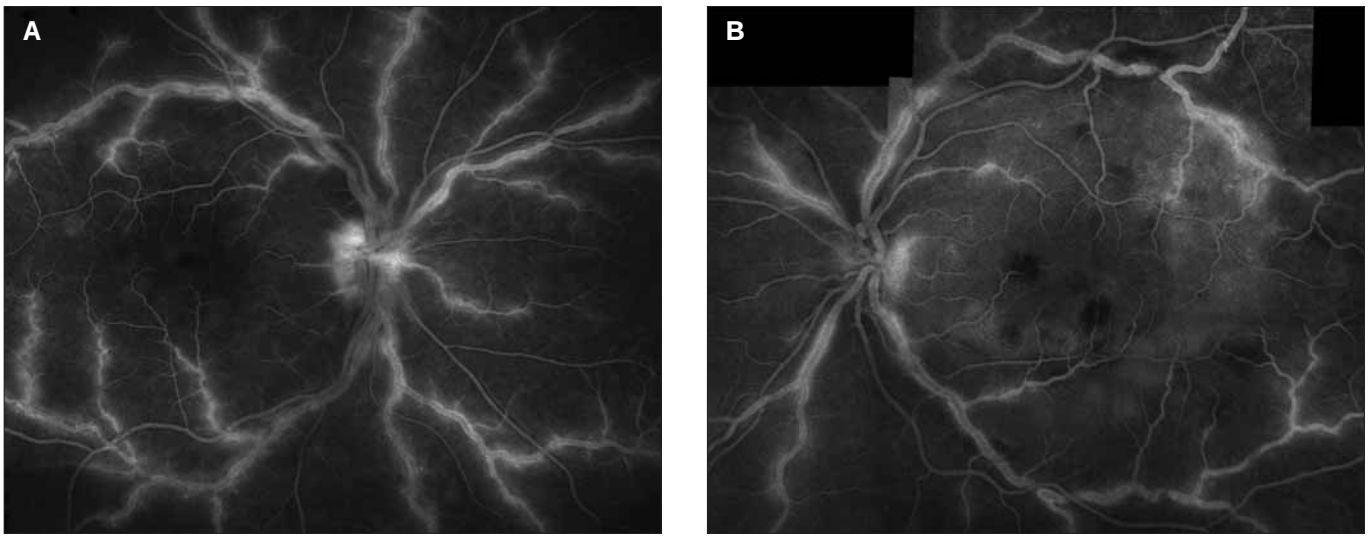


**Fig. 2 - (A)** *Fluorescein angiography at initial visit showed perivenous staining and* **(B)** *extensive dye leakage from retinal veins and optic discs.*

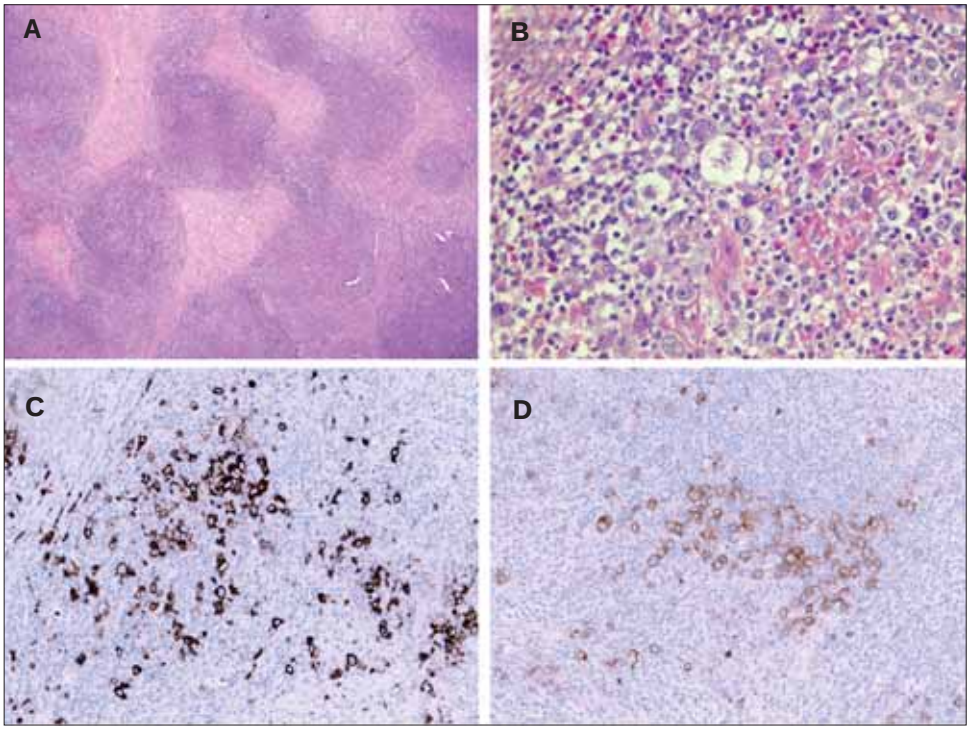


**Fig. 3 -** *Lymph node biopsy.* **(A)** *Low power view showing nodular sclerosis pattern (hematoxylin and eosin, x25).* **(B)** *High power view showing several Hodgkin and Reed-Sternberg (HRS) cells in an inflammatory background; note the presence of lacunar cells (hematoxylin and eosin, x400).* **(C)** *CD15 positivity of the HRS cells (immunoperoxidase, x200).* **(D)** *CD30 positivity of the HRS cells (immunoperoxidase, x200).*

composed of variable numbers of Hodgkin and Reed-Sternberg (HRS) cells, some with a lacunar appearance, admixed with a reactive background of small lymphocytes, plasma cells, histiocytes, and eosinophils (Fig. 3B). By immunohistochemistry, the HRS cells were negative for CD20 and CD5, and positive for both CD15 and CD30 (Fig. 3, C and D). In situ hybridization for Epstein-Barr virus encoded RNAs was negative. Altogether the pathologic findings were diagnostic for nodular sclerosis Hodgkin lymphoma.

## DISCUSSION

The term frosted branch angiitis was first used by Ito et al in 1976 to describe a 6-year-old Japanese boy who developed idiopathic bilateral retinal periphlebitis (2). The unusual thick sheathing surrounding all of the retinal veins suggested the appearance of frosted tree branches in winter. The phenomenon is rare with about 60 recorded in the world literature.

In 1983, Barr and Joondeph described bilateral retinal periphlebitis as the initial clinical findings in a patient with Hodgkin lymphoma (3). Bilateral optic disc swelling, periphlebitis, focal chorioretinitis, and vitritis were noted. Best-corrected visual acuity was 20/30 and 20/80. The ocular manifestations of the disease resolved in response to systemic radiation therapy. That report shares similarities with our patient and can probably be considered as a frosted branch angiitis.

Besides Hodgkin lymphoma, there are reports of frosted branch angiitis in association with primary central nervous system lymphoma and leukemia (4, 5). However, those cases seem to be due to infiltration with malignant cells rather than to a true angiitis. According to Kleiner in his editorial, these cases should be described as having a "frosted branch-like appearance," but they do not represent true frosted branch angiitis (6).

The frosted branch angiitis observed in this patient could have occurred from a variety of mechanisms. Antibodies to tumor antigens that cross-react with endothelial cells can cause this type of inflammation. Chemokines produced by malignant cells may activate suppressed clones of B and T cells, resulting in antibody production, or induce T-cell sensitization against endothelial cells producing this striking clinical picture. Also, immune-complex deposition induced by viruses or other infectious agents may also result in localized or systemic vasculitis in patients with Hodgkin lymphoma (7).

Frosted branch angiitis represents an additional entity in the spectrum of paraneoplastic inflammatory disease that may occur in the context of Hodgkin lymphoma. Thus, we suggest that for patients with frosted branch angiitis, Hodgkin lymphoma should be considered in the diagnostic workup.

*Proprietary interest: none.*

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