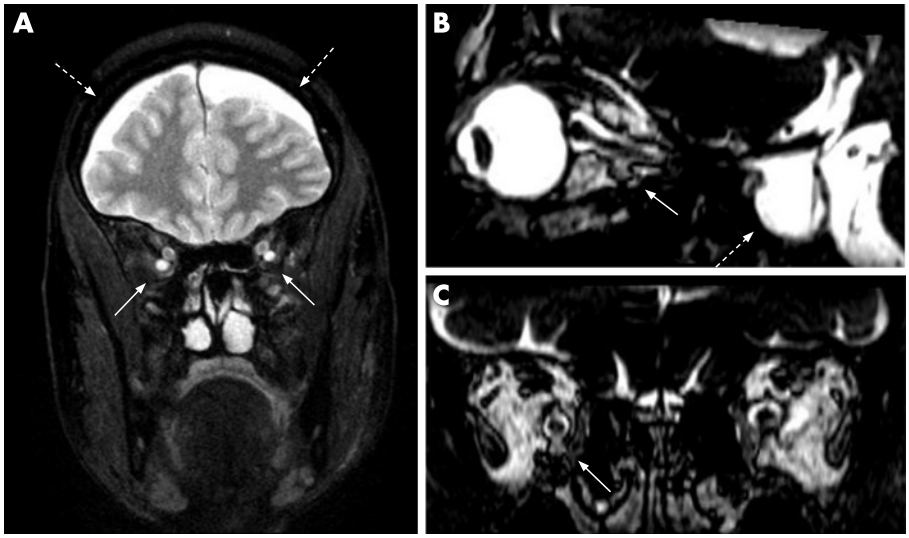

Figure 1 Magnetic resonance images showing aneurysm-like ectasias (solid arrows) of the optic nerve sheaths, subdural haematomas (dotted arrows in (A)), and empty sella (dotted arrow in (B)). (A) T2 weighted image with fat suppression. (B) (C) Multiplanar reconstruction of a three dimensional T2 weighted sequence in sagittal (B) and coronal projection (C).

only accidently detected. Alternatively, one may hypothesise that a focal weakness in the optic nerve meninges may have been induced by some indirect trauma to the orbit. The increased pressure within the optic nerve sheath may then have contributed to the formation of the optic nerve sheath aneurysm.

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Unilateral diffuse uveal melanocytic proliferation (DUMP)

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare paraneoplastic syndrome first described by Machemer 40 years ago in a patient with pancreatic carcinoma.[1] Gass and associates later expanded the syndrome to include round red patches in the fundus, multifocal areas of retinal pigment epithelial (RPE) atrophy, rapidly progressive cataracts, retinal detachments, and choroidal thickening.[2] There have been 34 reported cases since Machemer first described it, and all have had bilateral involvement.[3–8] After searching databases such as MEDLINE (1947 to the present), Exerpta Medica/EMBASE (1947 to the present), and Ophthalmic Literature (1947 to 1988) using the key words BDUMP, melanocytic proliferation, paraneoplastic, and uvea, we report the first case—to the best of our knowledge—of unilateral diffuse uveal melanocytic proliferation (DUMP) found in a patient with metastatic lung cancer.

Case report

A 55 year old woman with a two year history of metastatic small cell lung carcinoma undergoing chemotherapy was referred for a decrease in vision and anterior displacement of the temporal iris. Visual acuity was 20/20 in the right eye and 20/40 in the left. Examination revealed anterior bowing of her left iris, a nuclear cataract, and multiple grey oval patches separated by a reticular pattern of yellow-orange pigmentation in her left fundus (fig 1). Nummular areas of RPE atrophy with pinpoint staining were revealed by fluorescein angiography, along with shallow neurosensory detachments overlying an attenuated RPE by optical coherence tomography/scanning laser ophthalmoscope (OCT/SLO) examination (fig 1). In addition, 20 MHz B-scan ultrasound showed diffuse unilateral choroidal thickening. High frequency (35 MHz) B-scan ultrasound revealed an anterior uveal metastasis causing narrowing of the angle, and a small overlying exudative retinal detachment in her left eye (fig 2). These findings were secondary to both anterior uveal small cell lung cancer and ipsilateral unilateral DUMP. Her right eye was normal. The patient returned at a 4 month follow up and did not have DUMP in the fellow eye.

Comment

There has been some controversy regarding the aetiology of RPE loss as specific antibodies—of the sort classically associated with autoimmune retinopathies such as cancer associated retinopathy (CAR) and melanoma associated retinopathy (MAR)—have not been discovered in BDUMP. Some speculate that the increased metabolic demand of hyperproliferating melanocytes leads to retinal hypoxia and the progression of cataract with RPE dysfunction.[9] Others have suggested that the RPE loss is a result of a distinct paraneoplastic process independent of what leads to melanocytic proliferation.[4] Histopathological specimens of BDUMP have shown benign proliferation of melanocytes within the choroid with widespread dysfunction and necrosis of the overlying RPE (even in areas with minimal melanocytic proliferation).[2 10] Gass theorised that toxic or immunological factors liberated by the interaction of a systemic carcinoma with normal melanocytes of the uveal tract are responsible for this extensive degeneration.[2]

The uveal metastasis in our patient was in close proximity to the melanocytes of the ipsilateral affected RPE and can explain the local production of factors previously described by Gass. Clinically, one sees islands of atrophic RPE lying in a sea of ''orange-pigment'' lipofuscin laden retina (fig 1). The complete absence of any signs of diffuse uveal melanocytic proliferation in the right eye suggests that systemic factors were not responsible in our case. Though the aetiology of the RPE toxicity remains unclear, this case shows that BDUMP does not have to be bilateral. Therefore, it should be called diffuse uveal melanocytic proliferation (DUMP).

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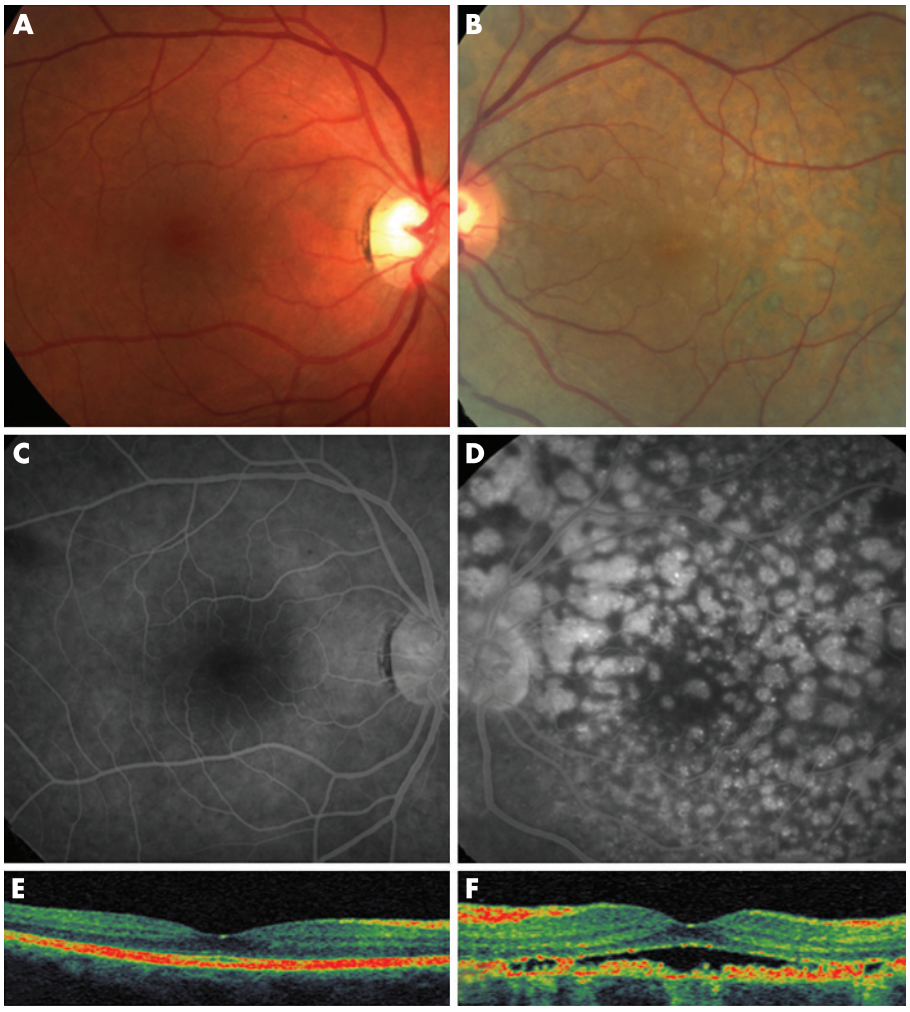

Figure 1 DUMP. Top: High definition 11-megapixel colour photography of the right eye (A) is normal. However, the left macula (B) contains islands of atrophic retinal pigment epithelium (RPE) lying in a sea of sick orange pigment (lipofuscin) laden retina. Middle: High definition, 11-megapixel fluorescein angiography of the right eye (C) appears normal with no evidence of diffuse uveal melanocytic proliferation (DUMP). The left retina (D) contains diagnostic nummular areas of early hyperfluorescence suggesting RPE atrophy which contain pinpoint spots of late staining hyperfluorescence. Optical coherence tomography (OCT) of the right macula (E) is within normal limits. Optical coherence tomography of the left macula (F) reveals a neurosensory detachments as well as focal areas of RPE atrophy and hypertrophy.

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Possible association between scleritis and lymphoma

Scleritis and uveitis are ocular inflammatory diseases often presumed to be autoimmune and associated with underlying systemic disease.[1] Other autoimmune diseases have been shown to confer increased risk for malignancy, including lymphoma.[2–4] We present two patients diagnosed with scleritis and lymphoma and examine whether there is an association between ocular inflammatory disease and malignancy.

Case series

We reviewed the records of 133 scleritis patients presenting to our ocular inflammatory diseases clinic at Oregon Health & Science University (OHSU) between 1993 and 2006. Access to this database was reviewed and approved by the OHSU institutional review board. Two patients with a diagnosis of lymphoma were identified.

Patient A developed scleritis 13 years before being diagnosed with lymphoma at the age of 48. Hodgkin's lymphoma was found incidentally on a chest *x* ray during repeated work up for ocular disease. Patient B was diagnosed and treated for Hodgkin's lymphoma at the age of 24 without recurrence. She developed scleritis 10 years later (table 1).

The two patients were diagnosed with anterior scleritis (table 2) at the age of 32 and 33 years, respectively.

Patient A had anterior bilateral diffuse scleritis and patient B had unilateral nodular scleritis. At the time of scleritis diagnosis, neither clinical presentation was clinically consistent with ocular lymphoma. Scleritis resolved with chemotherapy specific for lymphoma in patient A.

We previously reported a patient with scleritis and Waldenstrom's macroglobulinaemia,[6] a haematological malignancy occasionally included in epidemiological studies on lymphoma. His malignancy was discovered in the course of evaluating the cause of a raised erythrocyte sedimentation rate which accompanied his relatively refractory scleritis.

Comment

The National Cancer Institute reported 511 872 lymphoma patients in the 2003 United States population of 290 796 025.[7 8] Assuming the same prevalence of lymphoma within our inflammatory eye diseases clinic from 1993 to 2006, we would have expected to see 0.234 lymphoma cases from among 133 scleritis patients during this period. Using Fisher's exact test, we found that the two cases of lymphoma are more than would be expected by chance alone ($p = 0.002$). This suggests that autoimmune scleritis may be associated with an increased risk of lymphoma. In comparison, we identified three uveitis patients with a prior or subsequent diagnosis of lymphoma from among 1459 uveitis patients seen in our clinic between 1993 and 2006. This frequency does not differ significantly from published population prevalence figures ($p = 0.530$).

Other autoimmune diseases have been shown to be associated with lymphoma. Wolfe *et al* reported that patients with rheumatoid arthritis were three times more likely to develop lymphoma than the general population.[9] Sjögren's syndrome is also associated with a clearly increased risk of lymphoma.[10] While scleritis is often associated with autoimmune diseases,

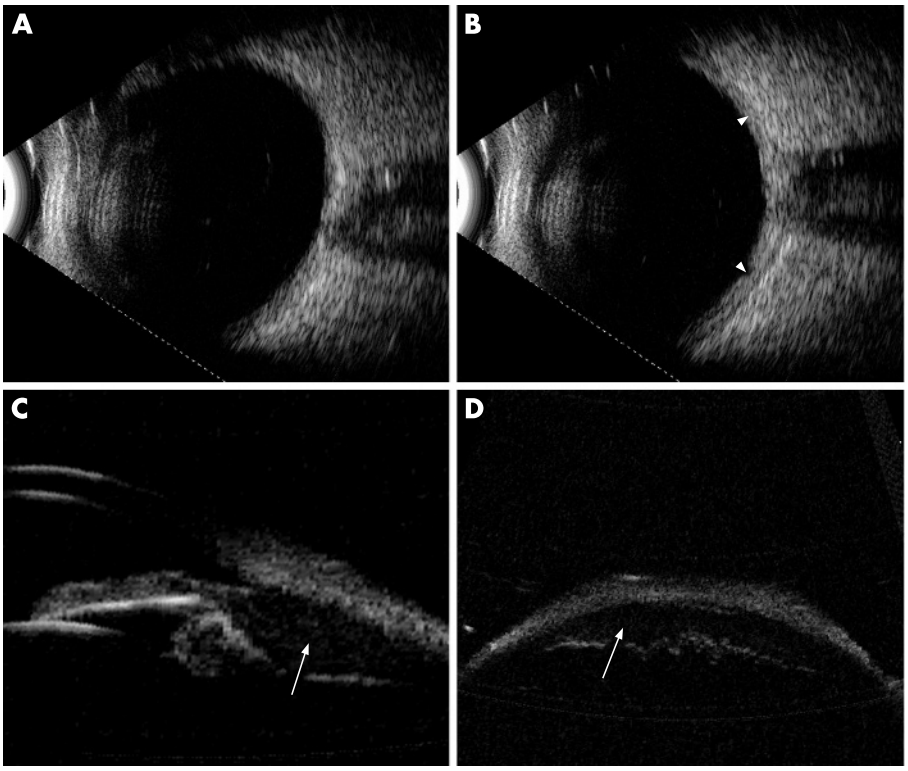

Figure 2 DUMP. Top: High resolution 20 MHz B-scan ultrasound reveals choroidal thickening (arrow heads) in the affected left eye. Bottom: High frequency 35 MHz B-scan ultrasound was carried out. Longitudinal section (C) reveals low reflective tumour in the ciliary body (arrow). Transverse section demonstrates the width of the anterior uveal metastasis (arrow) and displacement of the ciliary processes.

none was discovered in the work-up of our two patients with scleritis and lymphoma.

There are multiple hypotheses to explain why there could be a relation between autoimmunity and malignancy. Autoimmunity may either represent or lead to chronic B cell stimulation and proliferation.[4] A dysregulated immune system may be incapable of adequate surveillance to eliminate lymphoma.[3] Viruses that trigger autoimmune eye disease might also contribute to carcinogenesis.[2] It is possible that ocular inflammatory disease could herald the development of systemic illnesses or reflect changes in immune function. Though immunosuppressive drugs can also predispose to the development of malignancy, our Hodgkin's disease patients did not receive such treatment before developing their lymphomas.

Patients seen in our clinic often have more severe or treatment refractory disease, suggesting that there may be an ascertainment bias. Our data are also limited by the founder effect, considering the small sample size of our clinic compared with the general population at large. Conversely, we do not have complete follow up information on all our patients, which could lead to underascertainment of incident lymphoma in our referral population, causing an underestimation of the true rate of lymphoma occurring within our clinic.

The resolution of ocular inflammation with chemotherapy could suggest that autoimmune disease and haematological malignancy originate from a similar type of immune dysregulation. The larger than expected number of patients with both scleritis and lymphoma suggests that the concurrence of these two rare diseases may be more than coincidental. The possibility of an asymptomatic lymphoma should be considered during the systemic work-up of medically refractory anterior scleritis. The true relation between autoimmune ocular disease and malignancy would best be studied in a multicentre prospective cohort study, considering the rarity of these two diseases.

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Table 1 Lymphoma data and demographics

Patient	Sex	Ethnicity	Age at Dx (y)	Type	Location	Presentation	Previous eye symptoms	Treatment	Improved eye symptoms
A	F	White	48	NSHD	Mediastinum	Incidental	Yes	ABVD, local radiation	Yes
B	F	White	24	HD	Left cervical	Not concurrent	No	Local radiation	N/A

ABVD, doxorubicin, bleomycin, vinblastine, and dicarbazine; Dx, diagnosis; HD, Hodgkin's disease; N/A, not applicable; NSHD, nodular sclerosing Hodgkin's disease; y, years.

Table 2 Ocular diagnoses

Patient	Dx	Age at Dx (y)	Location	Type	Laterality	Onset	Duration	Course	Symptoms*	Complications
A	Scleritis	32	Anterior	Diffuse	Bilateral	Sudden	Persistent	Continuous	1, 2, 3	None
B	Scleritis	33	Anterior	Nodular	Unilateral	Sudden	Persistent	Recurrent	1, 2	None

Characteristics of inflammation are based on the SUN criteria.[5]
*Symptoms: 1, redness; 2, pain; 3, floaters.
Dx, diagnosis; y, years.