The eye in lung disease

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This article reviews disorders in which both pulmonary and ocular disease can occur. These may occur at the same time or the disease process can start in one and involve the other later. Different treatments may be needed as the severity of lung and eye involvement may vary. The lung may be affected by treatment for an unrelated eye problem and treatment for lung disease may affect the eye.

SARCOIDOSIS

Between 20 and 30% of patients with systemic sarcoidosis develop ocular involvement at some stage (Jabs and Johns, 1986), although more have undetected asymptomatic ocular disease (O'Connor, 1983). The peak incidences for ocular sarcoidosis are between the ages of 20–30 years and 50–60 years (Karma et al, 1988). Sarcoidosis in childhood is rare. Older children tend to have a higher frequency of blindness and significant multisystem involvement (Hoover et al, 1986).

The nature of the disease varies, not just in presentation and progression but also in the degree of ocular and systemic involvement, aggression and prognosis. In older patients, the disease tends to be more insidious with granulomatous uveitis often involving the posterior segment of the eye. Resolution is less likely with significant visual morbidity (Jabs and Johns, 1986).

The most common ocular manifestation of sarcoidosis is uveitis (60%) (Jabs and Johns, 1986). It is an early feature – over 80% present before or within 1 year of systemic disease (Jabs and Johns, 1986). The frequency of sarcoidosis was 5% in uveitis patients from Western Europe and the USA (Rothova et al, 1992). The majority (75%) have anterior uveitis, a common feature in young black patients. Up to 10% of sarcoid uveitis patients develop significant visual loss in at least one eye, with cystoid macular oedema being the main cause of visual loss (Rothova, 2000). The eyelid, lacrimal gland and conjunctiva can be involved but granulomas leading to diplopia, severe keratoconjunctivitis sicca and orbital symptoms are very rare. Corneal involvement by granulomas is rare while band keratopathy may develop from longstanding chronic anterior uveitis.

Although sarcoid uveitis is typically described as granulomatous, the acute anterior uveitis in young patients tends to be non-granulomatous, presenting with anterior chamber cellular activity and non-confluent keratic precipitates (KP) which respond rapidly to topical steroids. Uveitis is usually bilateral and symmetrical and may only last for a few weeks with excellent prognosis.

Chronic granulomatous anterior uveitis tends to affect older patients, often with coexisting significant pulmonary involvement. 'Mutton-fat' KPs are impressive, often with marked posterior synechiae (*Figure 1*). Peripheral anterior synechiae may also form and this form of uveitis is more often accompanied by glaucoma. The uveitis may be asymmetrical. Nodules, considered typical of granulomatous uveitis, may form on the iris and the anterior chamber angle. More aggressive treatment tends to be needed with many eventually requiring further intervention for complications related to the uveitis (cataract, glaucoma and cystoid macular oedema).

Involvement of the posterior segment of the eye is less common (25%). The spectrum may range from intermediate uveitis (inflammation centred around the pars plana) with vitritis, subtle peripheral vasculitis only obvious on fluorescein angiography and snowball infiltrates to significant vasculitis with extensive sheathing (*Figure 2*) and perivascular exudates (commonly taught as 'candle-wax drippings' – a misinterpretation of the the original 'taches de bougie' description by Franceschetti and Babel, 1949). Complications of periphlebitis are retinal vein occlusion, neovascularization and haemorrhage.

Choroidal sarcoid lesions may also be seen. They are typically multifocal, round punched-out lesions (often in various stages of evolution) in the peripheral retina and represent the original taches de bougies (*Figure 3*). Large or solitary choroidal granulomas are rare as is optic nerve involvement. One or both optic nerves may be involved either by papilitis or infiltration by granuloma and CNS involvement may cause papilloedema.

Figure 1. Mutton-fat keratic precipitates and posterior synechiae.

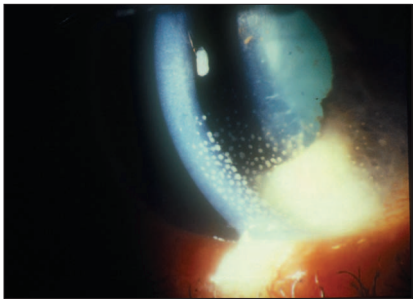


Figure 2. Vascular sheathing – arrow.

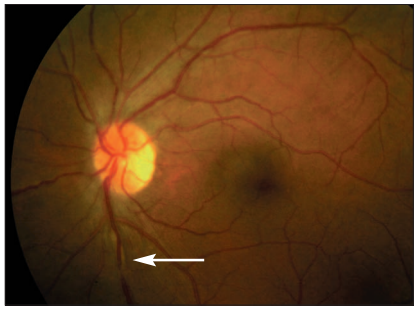
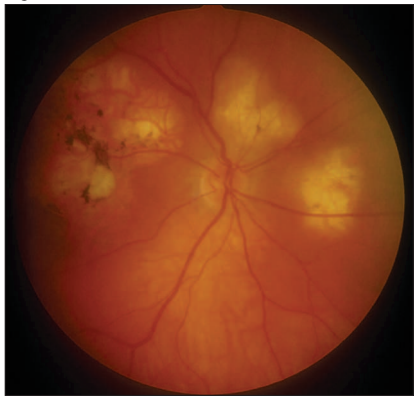


Figure 3. Multifocal choroidal lesions.



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Posterior segment involvement has a significant association with CNS disease (Gould and Kaufmann, 1961) and sarcoid can mimic CNS and ocular features of multiple sclerosis. The differential diagnosis is wide and sarcoidosis should be considered in all forms of intraocular inflammation.

TUBERCULOSIS

Ocular tuberculosis may occur in the fit person with no systemic disease, in the presence of active primary disease or as a component of miliary dissemination.

Although it is an uncommon cause of uveitis, diagnosis of tuberculosis is crucial because prompt treatment may have implications both for sight and associated systemic disease. Asymptomatic choroidal involvement (*Figure 4*) is the most common form of intraocular inflammation. Anterior uveitis is classically granulomatous (mutton-fat KPs with iris nodules) and choroidal lesions are typically cream coloured and may be multiple; associated haemorrhage, exudation or panuveitis are rare (Helm and Holland, 1993). Classically, conjunctival phylectenules were described to be associated with tuberculosis.

The association between ischaemic retinal periphlebitis (*Figure 5*) and tuberculosis is accepted but the precise relationship between the two remains unclear. In this manifestation, the infection remains unproven and while periphlebitis with uveitis is well described in individuals with proven pulmonary tuberculosis, some individuals with periphlebitis and uveitis have no manifestations of systemic disease but exhibit a vigorous positive Mantoux test (Rosen et al, 1994) – known as tuberculin hypersensitive uveitis.

VASCULITIDES

Wegener's granulomatosis

Wegener's granulomatosis is a necrotizing granulomatous vasculitis of smaller vessels. Ophthalmic involvement is common. Orbital inflammation is often seen, including necrotizing sclerokeratitis and optic nerve disease (Power et al, 1994). Intraocular inflammation tends to be secondary to scleritis; retinitis with retinal vein occlusion, haemorrhage and oedema may occur but is rare. Ocular involvement usually follows systemic diagnosis although the presenting disease may be orbital inflammation or necrotizing sclerokeratitis (*Figure 6*). Careful history taking and vasculitis antibody screening are needed.

Churg–Strauss syndrome

This is a systemic vasculitis involving two or more extrapulmonary organs associated with a peak eosinophilia of 1.5×10^9/litre or more and asthma. The typical presentation is a young adult developing allergic rhinitis and polyps followed by vasculitis affecting the lung (nodular infiltration, haemoptysis and respiratory failure), heart, kidneys or CNS. Ocular involvement usually consists of neuro-ophthalmic complications of the cranial nerves or ischaemic optic neuropathy (Waldock et al, 2000).

Systemic lupus erythematosus

This is a multi-organ autoimmune vasculitis in which antinuclear antibodies occur. Pulmonary involvement is common and often serious (pleurisy or pleural effusion, pneumonia, fibrosing alveolitis, obliterative bronchiolitis, pulmonary oedema), although death is usually from involvement of other organs. Ocular involvement is rare; anterior uveitis, retinal and choroidal vasculitis with obliteration, ischaemia, oedema/serous exudation, cotton wool spots (*Figure 7*), ischaemic optic neuropathy and optic neuritis have all been reported. Posterior ocular segment involvement usually co-exists with severe renal or cerebral disease and indicates a poor prognosis (Stafford-Brady et al, 1988).

MALIGNANCY

It is unclear how often primary pulmonary malignancy co-exists with an ocular metastatic lesion. Ocular inflammatory manifestations may occur but seeding to the uvea is more common (De Potter, 1998). Malignant uveal seeding is typically non-pigmented, solitary or multiple and may be associated with exudative retinal detachment. Bilateral involvement has been reported and the optic nerve may also be involved. Choroidal melanoma (the most common intraocular malignancy in adulthood) usually metastasizes to the liver (93%) and the lung (24%) (Collaborative Ocular Melanoma Study, 1998).

RESPIRATORY FUNCTION AND ANTIGLAUCOMA MEDICATIONS

Glaucoma with significant visual field loss and optic nerve damage primarily affects the elderly, many of whom have

Figure 4. Tuberculous choroidal granulomata.

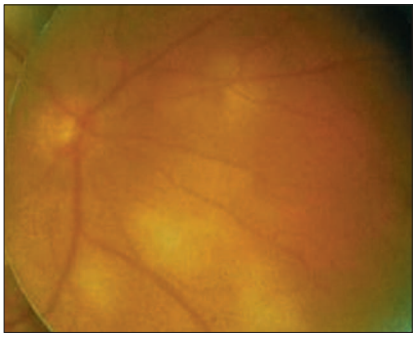


Figure 5. Tuberculous hypersensitivity uveitis.

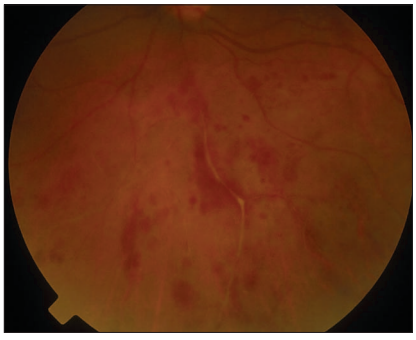


Figure 6. Necrotizing scleritis.

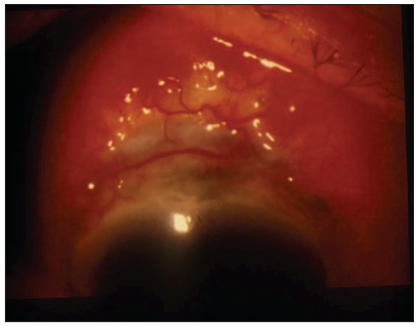
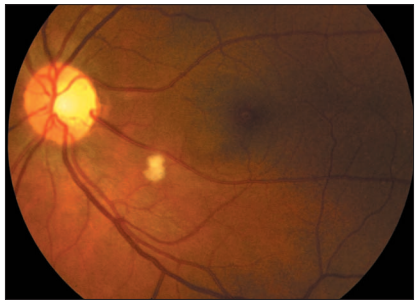


Figure 7. Cotton wool spot.



airway disease. Non-selective topical beta-antagonists are effective in reducing intraocular pressure (IOP) but can severely affect respiratory function. Their use should be avoided in those with compromised respiratory function and careful respiratory monitoring is needed in all others.

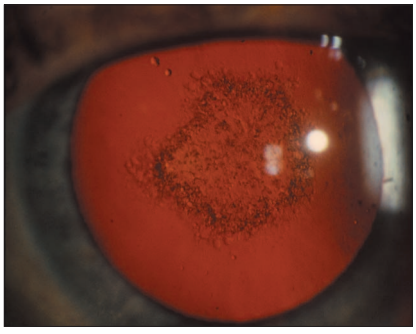
Cardioselective topical beta-antagonists, while having less of an effect on lowering IOP, appear to have a less negative effect on pulmonary function but may cause breathlessness (Weinstein et al, 1983). Prolonged lid punctal occlusion after application of non-selective topical beta-antagonist reduces the amount of medication reaching the systemic circulation by 67% (Zimmerman et al, 1984) but is difficult for the elderly to perform and does not seem to influence the negative effect on respiratory function (Diggory et al, 1995).

A significant number of people using topical alpha-agonist antiglaucoma medications also complain of shortness of breath (Weinstein et al, 1983). Topical carbonic anhydrase inhibitor and prostaglandin can be safely used in patients with compromised respiratory function.

SYSTEMIC AND INHALED CORTICOSTEROIDS

Ocular complication of corticosteroids are well documented. Cataract risk, typically posterior subcapsular cataract (*Figure 8*), increases with dosage and duration of treatment. The usual time to onset is at least 1 year with oral prednisolone 10 mg/day (Urban and Cotlier, 1986). There is a significant association between inhaled corticosteroids and the development of posterior subcapsular cataract, and a clear dose–response relation with an increased incidence with increased lifetime doses (Cumming et al, 1997). This risk appears to be more significant the older the patient. Children rarely develop steroid-related cataracts unless large and prolonged systemic doses are used. A study of asthmatic children using inhaled corticosteroids for 3 years or more found no increase incidence of cataract formation (Agertoff et al, 1998).

Figure 8. Posterior subcapsular cataract.



Raised IOP with and without visual field loss and optic disc damage can occur with corticosteroid administration (Carnahan and Goldstein, 2000). While the risk is highest with local ocular administration, it can also occur with systemic and inhaled corticosteroids (Garbe et al, 1997). The risk is low but significant and appears to be related to duration and use of higher dosage. Certain groups appear to be more at risk of steroid-induced raised IOP and include those with open angle glaucoma, diabetes mellitus, high myopia, connective tissue disease (especially rheumatoid arthritis) and first degree relatives with primary open angle glaucoma (Mitchell et al, 1999). Raised IOP may only occur after a significant period of steroid use but appears to regress once treatment is stopped (Tripathi et al, 1999).

CYSTIC FIBROSIS

Patients with cystic fibrosis-related diabetes mellitus (CFRD) have an increased morbidity and mortality. These patients have insulin deficiency and appear to have poorer pulmonary function compared to non-diabetic cystic fibrosis patients. Retinopathy, nephropathy and neuropathy tend to be only seen in these CFRD patients (Rosenecker et al, 2001). It was thought that CF patients developed background retinopathy only but proliferative retinopathy can occur and require treatment. Therefore CFRD patients require careful and regular eye examinations (Yung et al, 1998). HM

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