SCLERITIS: EVALUATION AND DIAGNOSIS

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THE EPISCLERA AND SCLERA

- Its structure is composed of collagen, elastin, proteoglycans, and glycoproteins.

- The sclera is a dense, poorly vascularized connective tissue

- It is embryologically derived from neural crest and mesoderm

EPISCLERITIS

- Definition: Inflammation of the connective tissue between the sclera and conjunctiva.

- Key features
  - Self-limited.
  - Less painful than scleritis.
  - Complain of discomfort or irritation rather than true pain
  - Blanches with topical neosynephrine.
  - Does not cause damage to the globe

EPISCLERITIS – ASSOCIATED CONDITIONS

- In two series of 94 and 85 patients with episcleritis, 68-73% were found to have no associated disease
  - 13-15% had a connective tissue or vasculitic disease
  - 7% had rosacea,
  - 1-7% had atopy
  - 1-6% had an associated infection
• Herpes zoster, herpes simplex, cat scratch disease, and Lyme disease).

• Location of involvement can help

8 EPISCLERITIS – TREATMENT
• Treatment is for cosmesis or alleviation of discomfort.

• Many treat with topical corticosteroids, as these were demonstrated to be superior in a randomized double-masked trial
  • However, may result in significant and worsened rebound inflammation when tapered.
  • Only drug proven in clinical trial
  • Low potency work well: Flurometholone, LOTEPREDNOL

9 EPISCLERITIS – TREATMENT
• Also responds well to topical nonsteroidal anti-inflammatories (NSAIDs)
• Systemic NSAIDs, namely naprosyn, may be used for the treatment of severe or recurrent episcleritis
• NOTE: Treatment of underlying blepharitis and rosacea is very important.
  • Most episcleritis is due to local factors
  • Warm compresses and rosacea therapy (if indicated) will limit topical steroid use to 1-2 times per month

10 SCLERITIS - ETIOLOGY
• Scleritis can be infectious or non-infectious
• Non-infectious scleritis is associated with different systemic diseases than is uveitis.
  • SO the evaluation and treatment is DIFFERENT
  • You can save your system a lot of money with a very
directed work-up.
• This is not what is found in most textbooks

12 SCLERITIS - EPIDEMIOLOGY
• Scleritis typically occurs in the sixth decade of life, but may occur in adolescents and the elderly
• Females are more commonly affected
• Bilateral inflammation occurs in nearly 40% of cases.
• Most scleral inflammation is noninfectious.
  • However, scleral infection by bacterial, protozoan or fungal organisms, such as Pseudomonas, Mycobacterium, Acanthamoeba or Aspergillus, may cause severe scleritis

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21 SCLERTIS - PRESENTATION
• The involved area is usually tender to palpation, although pain may occur in seemingly uninvolved areas.

• The pain typically is deep and boring in nature and often wakes the patient from sleep

• The involved area may appear violaceous, because the inflammation is in deeper tissues
SCLERTIS - PRESENTATION

- Scleritis may be unilateral, simultaneously bilateral, or alternate from eye to eye.
- The whole eye may be involved or inflammation may localize to one or more quadrants.
- Duration is variable and may last only a few months or persist for years.
  - THIS LAST PART IS IMPORTANT – MUST TAKE A GOOD HISTORY
  - Will help decide who needs long-term immunotherapy

SCLERTIS - PRESENTATION

- The involved area may appear violaceous, because the inflammation is in deeper tissues

SCLERTIS - EXAMINATION

- On slit-lamp examination, the overlying conjunctival vessels are usually found to be engorged and the episclera may also be edematous and inflamed.
- Secondary inflammation in the conjunctiva and episclera can make it difficult to appreciate underlying scleral inflammation.
  - Topical phenylephrine blanches the overlying conjunctiva and, to a much lesser extent, the episclera and may permit better delineation of the depth of inflammation.
  - The red-free (green) light on the slit lamp may also be used to determine the level of inflammation.

CLINICAL CLASSIFICATION

- Location: Anterior vs Posterior
- Anterior is further sub-classified
  - Diffuse
• Nodular
• Necrotizing
  • Necrotizing scleritis usually is extremely painful and presents with areas of avascularity in the sclera.
• Scleromalacia Perforans
  • Avascular areas may result in scleral thinning, which can progress to staphyloma formation

SCLEROMALACIA PERFORANS
• Scleromalacia perforans is a very rare type of painless necrotizing scleritis that typically occurs in women with a long-standing history of rheumatoid arthritis in its classically described cases
  • However, many specialists doubt its existence today

POSTERIOR SCLERITIS
• Refers to inflammation of the sclera behind the equator
  • Typically difficult to diagnose in the absence of anterior scleritis
  • Symptoms of posterior scleritis may include headache, pain, blurred vision, and photophobia, although the patient may have only vague complaints and be fairly asymptomatic, as well
  • This is why it is commonly missed
POSTERIOR SCLERITIS

- Some patients with posterior scleritis develop proptosis, shallowing of the anterior chamber, exudative retinal detachments, choroidal detachments, disc swelling, and chorioretinal changes
- Chorioretinal changes may consist of subretinal exudates and hemorrhages, as well as a stippled appearance to the retinal pigment epithelium in long-standing disease.

BUT MOST CASES WILL PRESENT...

- Without the most typical signs
- B-scan will show mild thickening
- Must take a good history
- And in young patients under 40 years of age have a high suspicion for an Inflammatory Bowel Disease etiology

SUBTLE THICKENING: DO NOT USE 2.0MM RULE

SUBTLE DISEASE CAN HAVE COMPLICATIONS

STRUCTURAL COMPLICATIONS

- Ocular complications were encountered in nearly 50% of cases in one study,
  - anterior uveitis (26%),
  - decreased vision (16%)
  - peripheral keratitis (13%),
  - ocular hypertension/Glaucoma (14%)

- Decreased vision is most-associated with necrotizing and posterior scleritis
STRUCTURAL COMPLICATIONS

- A number of mechanisms may result in elevation of intraocular pressure (IOP).
  - Inflammatory cells may block scleral emissary vessels, which results in elevated episcleral venous pressure and hence elevated IOP.
  - Ciliary body effusion may cause angle closure as the lens–iris diaphragm rotates anteriorly.
  - Accompanying uveitis may be responsible for glaucoma if the trabecular meshwork is clogged with inflammatory cells and debris.
  - Corticosteroid use may also result in secondary elevation of IOP.

SCLEROKERATITIS

- Scleritis adjacent to the cornea may be associated with a focal or diffuse keratitis.
  - Focal keratitis may manifest as a ring infiltrate at the limbus, without the peripheral clear zone that is seen with staphylococcal marginal infiltrates.
  - Sclerokeratitis also may present with crystalline deposits that have the appearance of spun sugar or cotton candy in the deep cornea.
    - This variant is known as sclerosing keratitis.

SCLEROKERATITIS

- Worse ocular and systemic prognosis
  - Review of 47 patients revealed that 81% lost vision, 57% had necrotizing disease, 62% had uveitis, 62% had impending corneal perforation, and 67% had systemic disease association.
    - This was especially true in the peripheral ulcerative keratitis group.
      - Of the 24 patients, 10 had RA, 7 had GPA, 2 had relapsing
polychondritis, and 1 had polyarteritis nodosum

**DIAGNOSING SCLERITIS**

- The diagnosis of anterior scleritis is clinically based.
- It is important to examine the patient with the room lights on. The lid should be lifted and the eyes examined from a distance, as scleritis may be missed if the patient is examined only at the slit lamp in a dark room.

**SCLERITIS GRADING**

**DIAGNOSING POSTERIOR SCLERITIS**

- B-scan ultrasonography is the most helpful in the diagnosis of posterior scleritis.
  - The T-sign, representing fluid in Tenon's capsule, is highly characteristic
  - Thickening of the posterior sclera can usually be demonstrated
  - **REMEMBER: THE 2.0MM RULE IS NOT A STRICT RULE**
- Fluorescein angiography may be helpful, as it may demonstrate characteristic subretinal leakage spots that coalesce as the study progresses.
  - Only Vogt-Koyanagi-Harada syndrome has a similar picture on angiography

**DIAGNOSING POSTERIOR SCLERITIS - IMAGING**

- Computed tomography (CT) scan of the orbits with contrast material may show the so-called ring sign of enhancement of the sclera, suggestive of posterior scleritis.
- Magnetic resonance imaging (MRI) has not proved to be any more useful than CT scans and may even be less helpful than CT, although it avoids the radiation

**DISEASE ASSOCIATIONS**
• Underlying systemic disease is present in approximately 35-50% of patients with scleritis.
• Rheumatoid arthritis is the most frequently associated condition and scleritis may be the first manifestation, preceding joint disease
• Other common connective tissue diseases that can present with scleritis include GPA (Wegener’s granulomatosis), polyarteritis nodosa, systemic lupus erythematosus, and relapsing polychondritis (Fig. 4-11-13).
• Psoriatic arthritis and ankylosing spondylitis are usually associated with acute iritis, and are less commonly associated with scleritis, though it can occur

50  DISEASE ASSOCIATIONS
• Inflammatory bowel disease, especially Crohn’s disease, is associated with scleritis.
  • Scleritis has been observed in 18% with inflammatory bowel disease and may correspond to GI disease activity, as does accompanying large joint peripheral arthritis.

• Cogan’s syndrome can be associated with scleritis, as can sarcoidosis, although these are less commonly encountered

51  DISEASE ASSOCIATIONS
• Infectious conditions such as tuberculosis and syphilis are uncommon, but not rare
  • Must be on your differential

• Herpes zoster and herpes simplex may also cause scleritis
  • When herpes viruses cause scleritis, it is usually in the late recovery phase of the disease rather than during the acute infection.

• Necrotizing scleritis can be triggered by ocular surgery and
Scleritis: January 21, 2017

Scleritis is an inflammatory condition of the sclera, the white portion of the eye. It can be infectious or non-infectious, and its cause is often unknown. It is more common in women than in men and most often affects people ages 40 to 60 years.

There is no data for the use of cyclosporine in severe diseases. There is some evidence to suggest that some patients with severe scleritis may benefit from cyclosporine.

Oral NSAIDs should be considered the first line of treatment. However, at these doses it may be impossible to demonstrate characteristic inflammation.

Lyme disease. Would be beneficial as these patients may benefit from treatment of severe or recurrent episcleritis.

A chest x-ray, complete blood count and urinalysis may be considered to look for evidence of tuberculosis, sarcoid, and GPA (Wegener’s)

Diagnostic work-up

- The work-up of a patient with scleritis includes an evaluation for systemic vasculitis, connective tissue disease, and infection.
- Appropriate initial laboratory testing includes:
  - ESR - erythrocyte sedimentation rate,
  - RF - rheumatoid factor
  - Anti-CCP - Anti-citrullinated protein antibody,
  - ANCA - anti-neutrophil cytoplasmic antibody
  - ANA - ntinuclear antibody

- Additional testing will be directed by the clinical history and review of systems.

  - Review of systems and a relevant family history may prompt the clinician to order HLA-B27 or test for inflammatory bowel serology.
    - Those with family history of IBD has elevated serologies and markers of disease without overt GI disease
      - Likely on spectrum of disease
      - May have a genetic predisposition to inflammation

- A fluorescent treponemal antibody absorption (FTA-ABS) test, microhemagglutination test for Treponema pallidum (MHA-TP), or other specific serological test for syphilis should be obtained on all patients to rule out syphilis.

- A chest x-ray, complete blood count and urinalysis may be considered to look for evidence of tuberculosis, sarcoid, and GPA (Wegener’s)
55  **PATHOLOGY/HISTOLOGY**

- Histopathologic examination may reveal one of four patterns:
  - Diffuse, non-necrotizing disease – mixed inflammatory infiltrate with plasma cells and lymphocytic predominance – low disease association
  - Zonal, necrotizing granulomatous inflammation – mediated by Antigen–antibody complexes, and is most often associated with systemic disease such as RA and GPA.
  - Necrotizing inflammation with micro-abscesses is observed in infectious scleritis.
  - Granulomatous disease – rare form associated with sarcoidosis

56  **SCLERAL BIOPSY**

- Scleral biopsy should be done only in exceptional circumstances. The surgeon should be prepared to either place a scleral reinforcement graft or use some other tissue, such as periosteum, to replace the sclera that is biopsied.

57  **OCT IMAGING STUDY**

58  **STUDY BACKGROUND**

- Watson and Heyreh described clinical subtypes of anterior scleritis
  - Diffuse, nodular, necrotizing, and scleromalacia perforans
- Rao N, et al. revisited the topic and has two series describing histologic patterns and systemic disease association
  - Zonal, necrotizing granulomatous; diffuse, non-necrotizing; necrotizing with micro-abscesses; and non-zonal, non-diffuse granulomatous
STUDY BACKGROUND

• Diagnosis and treatment issues in scleritis
• Importance of diagnosing systemic disease as it can be life-threatening
• No test for early necrosis
  • Would be beneficial as these patients may benefit from early systemic steroids and IMT

PURPOSE

• Can anterior optical coherence imaging distinguish different scleritis subtypes
  • Zonal granulomatous vs diffuse, non-necrotizing?
  • Early detection of scleral necrosis?
  • Infectious vs non-infectious

CONTROL IMAGES

RHEUMATOID ARTHRITIS SCLERITIS

RHEUMATOID ARTHRITIS SCLERITIS

TUBERCULOUS SCLERITIS

HISTOLOGIC COMPARISON

IDIOPATHIC SCLERITIS OD

GPA (WEGENERS) SCLERITIS

ANTERIOR SEGMENT OCT IN SCLERITIS

• Clearly delineates location of active inflammation
• Findings correspond to pathology seen on histologic comparison
• Able to typically image disruption of deep sclera and contour of inner scleral wall in severe and necrotizing cases
• May identify those in whom extensive work-up should be pursued
• May identify patients with early requirement for systemic IMT

70 TREATMENT
• All patients who have active scleritis require therapy.

• Some physicians recommend that treatment be continued until all redness is gone from the eye. However, if there is no pain and no evidence of any damage to the eye, the side effects of the therapy may outweigh the benefits.

• Topical nonsteroidal agents may be of some benefit in patients who have mild episcleritis, but they are of NO benefit in true scleritis.
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71 TREATMENT - NSAIDS
• Oral NSAIDs should be considered the first line of treatment in patients with mild and moderate scleritis.
• They have been reported to be effective in diffuse scleritis and mild nodular scleritis
• Indomethacin 50 mg three times a day or, in the sustained-release form, 75 mg twice a day can be very effective.
• Naprosyn 500mg twice daily can be useful
• Another nonsteroidal agent that appears to work well is piroxicam 20 mg daily.

72 TREATMENT - CORTICOSTEROIDS
• Systemic corticosteroids are usually required for patients with moderate to severe scleritis.
• The usual starting dose is 1 mg/kg/day of prednisone but, in severe cases, doses up to 1.5 mg/kg/day may be required.
• Occasionally, patients who take their full dose of oral
prednisone in the morning experience pain at night. If the dose is divided and taken twice a day, this night pain may be relieved without increasing the total dose.

- Many patients require therapy for 6 months to a year or longer.
  - Patients who require more than 3 months of treatment or 5 mg of chronic daily prednisone should be considered for steroid-sparing agents.

### TREATMENT - CORTICOSTEROIDS

- Pulse intravenous methylprednisolone may be required in some patients with severe scleritis.
  - This high dose may be used once a day for 3 days or once every other day for 3 doses and then reduced to once a week. Oral prednisone is often required to supplement the pulses.
  - Subconjunctival injection of triamcinolone has been proposed as a method of corticosteroid delivery in cases of non-necrotizing anterior scleritis.
  - Its use, as the study authors suggest, should probably be limited to adjunctive therapy in select cases of non-necrotizing localized disease, cognizant of the at least theoretical risk of scleral thinning and perforation.

### TREATMENT - IMT

- Immunosuppressive or immunomodulatory therapy may be required in patients with scleritis who are unresponsive to or intolerant of prednisone, or who require long-term therapy.
  - Many patients with necrotizing scleritis require immunosuppressive therapy to preserve vision.
  - Oral or subcutaneous methotrexate (7.5–25 mg weekly) has been reported to be of benefit in reducing or eliminating the need for systemic corticosteroid therapy.
  - Azathioprine at a dose of 1.5–2 mg/kg/day also may reduce or eliminate the need for corticosteroids.
TREATMENT - IMT

- Mycophenolate mofetil, another anti-metabolite drug, may have lower toxicity and higher efficacy
  - Tend to favor in vasculitic diseases
- Cyclosporine has been used with some success in the treatment of scleritis, but is more for adjunctive therapy
  - It’s effective at high doses (mg/kg/day), but usually becomes nephrotoxic or is intolerable
  - As such, it is almost always used at lower doses (5 mg/kg/day)
    - However, at these doses it may be impossible to discontinue the use of corticosteroids.
- There is no data for Tacrolimus (FK-506) in scleritis

TREATMENT - IMT

- Tumor necrosis factor inhibitors (TNF-I) are very effective
  - These medications typically act rapidly in controlling inflammation.
  - The majority of data in uveitis and scleritis are for infliximab and adalimumab.
  - Sen et al. in a pilot study showed nealy all patients had a complete response by 14 weeks
- Rituximab, anti-CD 20 drugs targeting B-cells, also very effective
  - Cao et al. recently showed success in treating 14 out of 15 patients with an activity score of zero by 6 months

TREATMENT - IMT

- Alkylation agents, such as chlor-ambucil and cyclophosphamide, may be of benefit and usually enable oral prednisone to be tapered or discontinued.
  - In some cases, a 3–6-month course of chlorambucil, with reduction of the white blood cell count to <2500, results in prolonged remission
• Cyclophosphamide works more rapidly (frequently within a few days to a week) than does chlorambucil.
• Pulse intravenous cyclophosphamide also has been used in severe disease.

OUTCOMES
• Most patients with mild or moderate scleritis maintain excellent vision.
• In a minority of patients, the disease is active for months and then goes into long-term remission.
• In many patients, the disease course is persistent and relapsing.
• In other patients, the disease is active for several years.
• Necrotizing scleritis portends a worse prognosis than does non-necrotizing disease.
• Patients with necrotizing scleritis have a high incidence of visual loss and a 21% 8-year mortality.
  • Immunosuppressive therapy appears to lessen this risks.

ONE LAST CASE

LIFT THE LIDS

ONLY ADDITIONAL INFORMATION

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