Vasculitis / Polyarteritis nodosa (PAN)

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Case presentation:

87 yo, wf was referred in May 1998 with decreased VA OD and photophobia > one year duration. The patient had been on topical steroid for six months before referral but she got worse.

Family history: One brother had cancer and one sister had cancer breast.

Medical history: Mini-stroke and hypertension, chronic fatigue

Topical medication: PF bid OD for the last six months

Systemic medications: ASA 325 mg/day

Toprol XL 50mg/day

HCTZ 25mg/day

Docusate (laxative)

Examination:

VA: CF OD , 20/25 OS

slight ptosis OU

scleral thinning with engorged vessels superior and superior nasal OD

Pupils: sluggish OD Fixed OS (PS)

Fine Kps OD; AC: 2+ cells OD

PC IOL OU. IOL decentration and PCO OD

Vitreous: 3+ haze OD. Fundus OS: arterial narrowing and hard exudates (HTN retinopathy

Investigations:

Negative ANAs, ANCA, ACE, RF, C3, C4, CH50, C1q, Raji cell assay, ESR, CRP CBC, sIL-2 R, HLA-B 27, cat scratch Abs, Lyme Abs, FTA-abs, CXR, sinus films, liver function panel

Only p-ANCA +ve

FTA-abs weakly +ve (false +ve, MHA-TP -ve)

F/U: B scan and UBM « CB mass

Plan:

scleral biopsy, sector iridectomy, PPV and IOL explantation OD

- Scleral bx « obliterative vascuitis without eosinophilia confirmed by unequivocal deposition of immunoreactants in vessel wall (IF).

- Vitreous bx « -ve for malignancy

- Based on the above findings + no improvement OD on topical med « systemic prednisone and MTX with great improvement systemically (energy) and in her eyes

- Fundus OD: Ciliochoroidal detachment + extensive obliterated arterioles confirmed by FA

- 8 months later oral prednisone D/C and MTX reduced (7.5 « 5/w) « remarkable deterioration constitutionally.

Vasculitis Classification:

- Primary and secondary

- Secondary: infection, drugs, malignancy, connective tissue disease, cryoglobulin, organ-transplant, hypocomplement and pseudovasc (e.g., anticardiolipin)

- Primary: vessel size, examples

large size: GCA
medium: PAN
small: Schonlein-Henoch syndrome
miscellaneous: BehÔet

- Pathogenesis:

- specific mechanisms:

Immune comp « EC injury by comp or ADCC
Direct EC infection
Anti-EC abs
ANCA-&/or neutrophil-mediated EC dam
T cell & macrophage (HLA-depend) EC damage
unique properties of each vascular bed

- Common mechanisms:

inflammatory mediators and cytokines lead to
- Pro-coagulant activity of EC
- transmigration of cells and proteins
- immune and inflammatory response of EC (e.g., - expression of adhesion molecules, receptors and secretion of chemokines)

Confirmatory test: biopsy or angiogram

- ANCA is not a sensitive or a specific test in some cases

- c-ANCA binds PR3 (P 29= serine protease)

- p-ANCA binds MPO (PAN)

PAN

- affect any organ but the skin, joints, peripheral nerves, gut and kidney common

- progressive fulminant, or limited disease

- may be a complication of other diseases such as rheumatoid or hepatitis B or C

- Rare disease but - - in hepatitis endemic areas

- M:F 2:1. Age at diagnosis 40s to 60s

- Pathology: focal pan-mural necrotizing inflammation, predilection for bifurcation. Pleomorphic cells, neutrophil predominance, some lymphocytes and eosinophils

- Clinical features: limited or fulminant

- constitutional: fever, malaise, weight loss
- skin rash, peripheral neuropathy, asymmetric polyarthritis, kidney or gut.
- Limited: single organ usually skin or peripheral nerve
- Skin: pulpable purpura, ulceration, livedo reticularis, ischemia distal digits

"Livedo reticularis" "purpura with ischemic changes"

Artharalgia or arthritis 50%, asymmetric episodic non deforming large joints of LL

- peripheral neuropathy 50-70%, sensory followed by motor« mononeuritis multiplex « finally symmetric polyneuropathy (S&M)

Less common slow distal sensory neuropathy. Brachial plexopathy. CNS uncommon, with peripheral « seizure and hmgic stroke

- Renal 70%: proteinuria, RC casts, hypertension in 25%
- GIT: pain, site depends on organ; generalized pain &distention in mesenteric thrombosis/peritonitis
- silent myocardial infarction
- myalgia or intermittent claudication
- Eye: in 10-20% due to hypertension or local vasculitis
- ptosis, exophthalmos, EOM paresis, chemosis, corneal furrow degeneration, episcleritis, scleritis and PUK.

"Furrow degeneration"

- PUK 1st sign, destructive, progressive, ass with scleritis (DD Mooren).systemic steroid
- Choroidal and retinal vasculitis is the most common ocular manifestations«
- hemorrhage, cotton wool spots, edema, CRAO, op atrophy & amaurosis fugax (intermittent ischemia)
- orbital congestion, proptosis, A&PION, orbital apex syndrome

Retinal vasculitis in PAN, pt refused steroid treatment and condition progressed, vitritis is seen on the right side picture

Laboratory tests: non specific reflect systemic inflammation and - immune complex. HBsAg in 10-54%, HCV Ab in 5%. p-ANCA < 10%, c-ANCA rare

- Diagnosis: fever, chills, wt loss, fatigue and multisystem involvement. Angiography or biopsy (skin, sural n, muscle, kidney, temporal a, testicle)

Mesenteric angiography in PAN

Prognosis: depends on age (65) and visceral involvement, most deaths in 1st year

- untreated 5-year survival < 15%, 7-year survival on steroid 80%. Despite steroid relapse rate 40% in 33 months (median)

- Treatment: Steroid with or without cytotoxic drugs.
- Iv Ig esp in cases associated with Parvovirus
- IFN-alpha in cases ass with hepatitis B

Polyarteritis Nodosa Review Questions

David Chu, M.D.

1) Which of the following diseases is incorrectly matched with the size of vessels the vasculitis associated with the disease affects?

A. Giant cell arteritis Â large
B. Beh¨et¡s syndrome Â large
C. Henoch-Schonlein Â medium
D. Polyarteritis nodosa Â medium

2) What is the most common ocular manifestation of PAN?

A. Retinal vasculitis
B. Central retinal artery occlusion
C. Scleritis
D. Episcleritis

3) Which of the following is not associated with PAN?

A. Hepatitis B
B. Syphilis
C. Hepatitis C
D. Rheumatoid arthritis

4) Which of the following systems is least likely to be involved in PAN?

A. CNS

B. Kidney
C. Skin
D. Peripheral Nervous System

5) Which of the following is seen in PAN?

A. Ptosis
B. Strabismus
C. Exophthalmos
D. All of the above

6) When PAN is associated with parvovirus, which treatment modality is indicated?

A. Steroid
B. Steroid with cytotoxic agent
C. IVIg
D. INF alpha

7) Which statement concerning the prognosis of PAN is true?

A. Most deaths occur within 1 year
B. Untreated 5-year survival is 50%
C. Relapse, when PAN is treated with steroid, is rare
D. Ocular involvement indicates poor prognosis

8) Diagnostic biopsy can be performed in the following.

A. Temporal artery
B. Testes
C. Both
D. Neither

9) True or False

ANCA is not sensitive but specific for PAN.

10) True or False

Patients with PAN can present with silent myocardial infarction.

Answers 1-C, 2-A, 3-B, 4-A, 5-D, 6-C, 7-A, 8-C, 9-False, 10-True