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Review Article

Retinal Vasculitis

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Abstract:

Retinal vasculitis characterized by inflammation and necrosis of the vascular wall, which can be primary or secondary, may be limited to one organ or system or is polysystemic.

Retinal vasculitis can affect large vessels in giant cell arteritis and Takayasu disease, medium vessels in major visceral arteries (renal, coronary, hepatic, mesenteric) in polyarteritis nodosa, Kawasaki disease in children, isolated vasculitis, or ANCA-negative or ANCA-positive small vessels in Wegener's granulomatosis, Churg Strauss syndrome, microscopic polyangiitis. The major symptomatology in vasculitis is related to the vascular localization involved in the inflammatory process, the length of the disease and the evolution of the inflammation towards tissue necrosis. Management in vasculitis requires treatment with oral steroids, in moderate doses, for months or years, with gradual reduction of doses according to clinical evolution, methotrexate, cyclophosphamide, in refractory cortico-resistant cases, azathioprine, methotrexate, inflixumab in the presence of side effects of corticotherapy.

The initial treatment must be aggressive, in order to achieve clinical remission, if not properly treated, the disease can be fatal due to insufficiency of vital cardiac, renal, digestive organs.

Biological therapy in retinal vasculitis with Etanercept, Inflixumab, Adalimumab reduces inflammation and destructive vascular damage by blocking mediators and effectors of inflammation.

Keywords: retinal vasculitis; arteritoblaston, Wegener's granulomatosis; Takayasu disease; Kawasaki disease; Churg Strauss syndrome; corticotherapy; immunosuppressants

Introduction

• Vasculitis encompasses a heterogeneous group of diseases, characterized by inflammation and necrosis of the vascular wall, which can affect any blood vessel: artery, arteriole, vein, capillary venule

– inflammation of the vascular wall narrows the calibre and generates tissue necrosis

• Classification of vasculitis [1,2]

– vasculitis can be:

• primary (of unknown cause)

• secondary to drug treatment, a toxin, infection, immune or other disease

– vasculitis may be limited to one organ or system or may be multisystemic.

– vasculitis can be classified according to the size of the predominantly affected vessels [7].

Clinical Forms of Retinal Vasculitis:

- **Affecting large vessels - the aorta, its branches**
  - ***giant cell arteritis*** - GCA
  - ***Takayasu's disease*** - in people under 50 years old
- **Affecting the medium vessels - the main visceral arteries: renal, coronary, hepatic, mesenteric**
  - ***polyarteritis nodosa***
  - ***Kawasaki disease in children***
  - ***isolated vasculitis*** *limited* to a single organ or polyangiitis overlap syndromes.
- **Affecting small-calibre vessels (small arteries, precapillary arterioles, capillaries, venules, postcapillaries), with two clinical forms separated according to the presence of immune markers - ANCA - autoantibodies against the cytoplasm of neutrophils and monocytes** [3,4,5,6]:
  - ANCA – negative vasculitis
  - ANCA-positive vasculitis with three primary necrotizing vasculitis on a small vessel
  - ***Granulomatosis with polyangiitis – Wegener's granulomatosis - GPA***
    - necrotizing, granulomatous inflammation frequently located on the respiratory tract
    - frequent necrotizing glomerulonephritis
  - ***Eosinophilic granulomatosis with polyangiitis – Churg Strauss syndrome – EGPA***
  - ***Microscopic polyangiitis***
    - necrotizing vasculitis with/without minimal immune deposits, without granulomatous inflammation
    - necrotizing glomerulonephritis
    - pulmonary capillaropathy
    - There is a genetic predisposition in all these diseases.

The major symptomatology in vasculitis is related to the vascular localization involved in the inflammatory process, the age of the disease and the evolution of the inflammation towards tissue necrosis.

- Tissue biopsy can confirm the diagnosis, but must be limited because the vasculitis is segmental or focal.
- At retinal level - vasculitis affects retinal arterioles - arteritis, veins - phlebitis or both - periphlebitis [7,8,9].
- Clinical - the fundus examination reveals vascular blockages, hemorrhages

Management in vasculitis [4,10,11]

- Oral steroids – moderate doses – 200 mg/day orally, associated with H2 blocker – ranitidine (Zantac) 150 mg orally
- Topical steroids – prednisolone, acetate 1%
- Cycloplegic in the presence of anterior segment inflammation
- Injectable steroid under Tenon (triamcinolone 40 mg/ml)
- Cyclosporine 2–7 mg/kg/day or immunosuppressive agents in refractory forms.

Clinico Therapeutic Aspects in Retinal Vasculitis:

Temporal Arteritis – Giant Cell Arteritis:

- It is the chronic inflammation of the large vessels – the carotid and its branches, a more common condition in women over 55 [12,13,14].
- Laboratory examination – shows signs of inflammation with
  - ESR, CRP – increased
- Clinically:
  - headache
  - vision impairment
  - pain when chewing
  - fever
  - weight loss
  - asthenia
  - temporal artery sensitive to palpation
  - ESR very high
  - positive diagnosis confirmed by temporal artery biopsy
    - At ocular level:
  - AAION – arteritic anterior ischemic optic neuropathy
  - Various visual disturbances
    - amaurosis fugax
    - diplopia
    - scotoma
    - ptosis
    - foggy vision
  - pain in the masseters (intermittent claudication), in the scalp.
  -

Treatment should be started as soon as temporal arteritis is suspected, and then the biopsy that confirms the diagnosis is done, so that the eye disease does not become bilateral [10,11,12,14].

- The basic medication is systemic corticosteroid treatment with prednisone 60 mg/day as a single dose for 2–3 weeks [10]
- if symptoms improve, cortisone is tapered according to individual response by 5–10 mg/day per week to 10–20 mg/day then by 1 mg/day per week
- if symptoms reoccur when prednisolone is tapered, dose should be increased
- many patients need low doses of cortisone – for years in the presence of adverse effects of corticotherapy, AZATIOPRINE and METOTREXATE, INFLIXIMAB are used

Takayasu Arteritis:

- Pulseless disease, aortic arch syndrome

Occlusive thrombo-aortopathy

It is a rare condition, an inflammatory disease affecting the aorta and its branches that occurs commonly in adolescents, young women 8/1 and Asians [8,15]

- **Clinical signs are related to vascular ischemia**
- At ocular level:

– scleritis
– amaurosis fugax
– ocular ischemia
– AION

Medical treatment requires:

- Corticosteroid therapy that can improve disease and reduce long-term vascular complications

– Treatment with prednisone 60 mg/day orally, for months or years, is gradually reduced according to the clinical evolution
– Methotrexate is used in refractory cases

- In corticosteroid-resistant cases – METHOTREXATE, CYCLOPHOSPHAMIDE, AZATIOPRINE

Polyarteritis Nodosa – Periartheritis-Pan:

- It is a systemic necrotizing vasculitis located in the medium and small arteries at the arterial bifurcations with secondary tissue ischemia [16,17]:
- Proliferation of the vascular intima occurs with thrombosis and occlusion that causes infarction
- The integuments, peripheral nerves, liver, heart and digestive tract are most frequently affected

– the pulmonary arteries are not affected
– the kidney can show ischemia with glomerular infarction
– massive infarcts (rarely) or areas of focal hepatic capsular vasculitis may occur in the liver

- Affection is more common in men
- Nonspecific signs and symptoms

– fever
– weight loss
– abdominal pain
– hypertension
– edema
– biopsy and arteriography are required for diagnosis

- At ocular level:

– keratoconjunctivitis sicca
– necrotizing sclero keratitis
– retinal vascular occlusions
– AION
– retinal vascular aneurysms (rare)
– damage to the superior oblique tendon

- Generally:

– heart damage: myocardial infarction, hypertension, pericarditis, angina
– kidneys: nephritic or nephrotic syndrome
– intestines: heart attack, abdominal pain
– peripheral neuropathy
– arthritis, myalgia
– CNS – headache 20%, convulsions 10%
– skin lesions: purpura, subcutaneous nodules

Initial treatment must be aggressive to achieve clinical remission, untreated acute or chronic disease is fatal through failure of vital cardiac, renal, digestive organs. [9,10,11]

– the treatment must be administered for a long time and the evolution of the disease can be complicated by the adverse effects of the drugs administered
– if the patient does not respond to corticosteroid treatment in an adequate dose of 60–80 mg/day prednisone for 3–4 weeks, start the immunosuppressive treatment with:

- CYCLOPHOSPHAMIDE – 2–3 mg/kg/day with dose adjusted to maintain peripheral blood WBC > 3000.
- AZATIOPRINE, METHOTREXATE

Kawasaki Disease:

It is an idiopathic vasculitis with predominantly mucocutaneous manifestations that affects children around 5 years of age in Japan [18]

– can be fatal 1–2%

- At ocular level:

– bilateral acute conjunctivitis (90%)
– superficial punctate keratitis
– medium anterior uveitis, nongranulomatous (80%)
– retinal periarteritis

- Systemically:

– fever for more than 5 days
– oral lesions – erythema, fissures, strawberry tongue
– skin rash
– cervical lymphadenopathy
– affecting the extremities: edema, erythema, desquamation
– associated with polyarteritis
– the temporal arteries may be affected

Complications – coronary arteritis 15%.

Induction treatment with high doses of IV immunoglobulins and aspirin can reduce coronary risk and death.

– In some cases (well chosen) methylprednisone can be effective in reducing fever.

Maintenance treatment is not necessary, knowing that the disease is self-limiting:

– possible coronary abnormalities can be treated with aspirin (low doses 80–120 mg/day), anticoagulants, beta-blockers.

The recommendations of the European League against Rheumatism for the treatment of ANCA vasculitis [19]

Vasculitis	Induction treatment	Remission maintenance treatment
localized	methotrexate + STEROIDS	STEROIDS (low dose) + – AZOTHIOPRINE – LEFLUNOMIDE – METHOTREXATE
Initial systemic		
Widespread	CYCLOPHOSPHAMIDE (oral/iv) + STEROIDS	
Severe	ADDITIONAL – PLASMAPHERESIS	
Resistant cases	– IMMUNOGLOBULIN iv – MOFETIL MYCOPHENOLATE RITUXIMAB PLASMAPHERESIS	

Granulomatosis With Polyangeitis – Gpa: [15,16]
Wegener's granulomatosis [20,21,22]

Rare condition with onset of granulomatous inflammation of the mucosa of the upper and lower respiratory tract, progressing to generalized necrotizing granulomatous vasculitis and glomerulonephritis [21]

Granulomatous inflammation affects the respiratory system, sinuses, kidney, orbit

- Clinical diagnosis for GPA – two of the following:

oral, nasal inflammation with painful ulcers/or not, purulent or bloody rhinorrhea
pulmonary – nodules, paremchymatous infiltrates, cavities
microhematuria (>5 red blood cells per field in sediment, cylinders, red blood cells)
biopsy – granulomatous inflammation of the arterial wall, perivascular, extravascular

- At ocular level:

painful proptosis
painful ophthalmoplegia
chemosis
conjunctivitis
necrotizing scleritis, episcleritis
keratitis
Fundus
cotton wool spots
thin arteries
tortuous veins
ON edema
thickened choroid
CME
CRAO
lacrimal-nasal duct obstruction

- Generally:

hemoptysis
renal insufficiency
cerebral vasculitis
weight loss
peripheral neuropathies
fever
arthralgia
saddle nose by destroying the nasal vessels

- ANCA (+) 6–7%

If the diagnosis is posed early, the current treatment allows the remission of the disease and the reduction of renal complications.

Cyclophosphamide 2mg/kg/day is the drug of choice

Cyclophosphamide is administered one year after achieving clinical remission;
The daily dose is reduced by 25 mg every 2–3 months

Eosinophilic Granulomatosis with Polyangiitis – Churg Strauss Syndrome – Egpa:

It is a systemic necrotizing vasculitis with granulomatous eosinophilic inflammation which frequently affects the airways and small and medium-sized vessels, associated with bronchial asthma, possible glomerular renal damage [2,7]
Systemically:
bronchial asthma
eosinophilia >10%
mono or polyneuropathy
migratory pulmonary infiltrates
abnormalities of the paranasal sinuses
biopsy – extravascular eosinophilic accumulation

- At ocular level:

conjunctival granulomas
scleritis
orbital inflammation
retinal periarteritis
Treatment of ANCA positive small vessel vasculitis (Wegener, Churg-Strauss)
induction treatment is done with CYCLOPHOSPHAMIDE iv in a high dose or orally in a lower dose associated with the administration of CORTICOIDS [10,15,16]
maintenance treatment after achieving remission is continued for 24 months with prednisolone 10 mg/day, and discontinuation after

6–18 months to 2 years depending on therapeutic response

combination of prednisolone with azathioprine can reduce morbidity in vasculitis

they have also been used in the treatment of vasculitis [9]
TNFα inhibitors in acute disease
INFLIXIMAB
RITUXIMAB (IgG monoclonal antibody) with B-cell destruction induces disease remission
IMATINIB – inhibits T cells and proliferation

Biological therapy in vasculitis

In vasculitis, inflammation occurs with destructive organ damage through the interaction of ANCA with neutrophils and endothelium [5,14].
Biological agents can be used to block mediators and effectors of inflammation
Fighting inflammation by inhibiting it by binding to TNFα
ETANERCEPT – ENBREL
INFLIXIMAB – REMICAD
ADALIMUMAB – HUMIRA
The final effect in reducing the migration and activation of neutrophils
Anti-ANCA therapy, which interferes with ANCA binding to epitopes
HUMAN IMMUNOGLOBULINS prevent ANCA-mediated activation of neutrophils
Treatment against B cells
RITUXIMAB – MABTHERA achieves depletion of B lymphocytes
BELIMUMAB – inhibits the maturation of B cells
Treatment against T cells
ABATACEPT - ORENCIA - inhibits the activation of T lymphocytes
ALEMTUZUMAB – CAMPATH – destroy T cells

Conclusions:

Retinal vasculitis encompasses a heterogeneous group of eye diseases, correlated with arterial, venous, capillary systemic vascular manifestations, intersecting large vessels (aorta and its branches), medium vessels (main visceral vessels - coronary, renal, hepatic, mesenteric) or ANCA negative or positive small vessels.
Horton temporal artery, giant cell artery affects the carotid and its branches causing arteritic anterior ischemic optic neuropathy with varied visual symptoms (amaurosis fugax), diplopia, intermittent claudication, blurred vision. The treatment must be started immediately (before the biopsy of the temporal artery), to limit the bilateralization of the disease with systemic corticosteroid therapy, prednisone 60 mg/day in a single dose prolonged according to evolution, azathioprine, methotrexate, infliximab if necessary. In Takayasu arteritis, symptoms related to secondary vascular ischemia are amaurosis fugax, arteritic anterior ischemic optic neuropathy (AAION). Corticotherapy can improve the disease and reduce complications, but in resistant cases methotrexate, cyclophosphamide, azathioprine are necessary.
Polyarteritis nodosa can be associated ocularly with retinal vasculitis, AAION, retinal aneurysms, and requires initially aggressive long-term treatment, to achieve clinical remission with corticotherapy, if necessary immunosuppressive treatment with cyclophosphamide, azathioprine, methotrexate. Wegener's granulomatosis develops at the level of the respiratory and renal mucosa with glomerulonephritis, producing ocular painful ophthalmic proptosis, necrotizing scleritis, papillary edema, cystoid macular edema, central retinal artery obstruction. It requires early treatment with cyclophosphamide (treatment of choice) administered one year after clinical remission.

Churg Strauss syndrome is associated ocularly with conjunctival granulomas, scleritis, orbital inflammation, retinal periarteritis. Treatment of ANCA-positive small-vessel vasculitis, Wegener's syndrome, Churg Strauss's syndrome requires single high-dose or low-dose cyclophosphamide combined with corticosteroids.

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References:

1. Peter Berlit – Diagnosis and treatment of cerebral vasculitis – pub. med. 2010.
2. Dumitrache M. – Sindroame și boli sistemice – Ed. Medicală 2014.
3. Lionakis et al – Classification of ANCA vasculitis - Arthritis Rheum – 2012, 64/10, 3452-62.
4. Sinclair D, Stevens J.H. – Role of ANCA and glomerular basement membrane antibodies in diagnosis and monitoring of systemic vasculitides – Ann. Curr. Biochem. – 2007, 44, 432-42.
5. Sinico RA, Sabadini E, Boeri R, Radice D – ANCA associated vasculitis – G. Ital Nefrol – 2002, 19/2, 125-36.
6. Schultz D.R., Diego J.M. – ANCA and systemic vasculitis – Semin Arthrites Rheum – 2000, 29/5, 267-85.
7. Friedman, Kaiser-Trateler – Review of ophtalmology – Elsevier Saunders – 2005.
8. Yokota H., Yamada K – Diagnosis imaging of CNS vasculitis – Brian Nerve 2015, 67/3, 248-60 – pub. med.
9. Jayme D. – The diagnosis of vasculitis – Rev. Clin. Rheumatol 2009, 23/3, 445-453.
10. Dumitrache M. – Tratament medical în bolile oculare – Ed. Medicală 2015.
11. Kennet C. Chern – Emergency Ophtalmology – McGraw Hill – 2002.
12. Dumitrache M. – Tratat de oftalmologie – Ed. Universitară „Carol Davila" 2012.
13. Khurana A.K. – Comprehensive ophtalmology – Anshan – 2008.
14. Mukhtvar C et al – EULAR recommandations for the management of large vessel vasculitis – Ann. Rheum. Dis. – 2009, 66/3, 316-23.
15. L. Gherasim, I.A. Oproiu – Actualități în Medicina Internă – Ed. Medicală 2015.

16. Karr as A, Gerard E, Levi C, Thervet E – Granulomatosis with polyangitis – (Presse Med. 2012, 4/10, 1014-23).
17. Kawakami I – New algoritm to diagnose primary cutaneos vasculitis – J. Dermatol 2010, 37/2, 113-24.
18. G. Mihăescu, Carmen Chifiriuc – Imunologie și imunopatologie – Ed. Medicală 2015.
19. Kim HW, Song YW – ANCA associated vasculitis – Clin. Exp. Nephrol – 2015, 17/5, 706-11.
20. Lamprecht P, Gross WL – Wegener granulomatosis – Herz 2004/29/1/47-56.
21. A.Miller et al – An approach to the diagnosis and management of systemic vasculitis – Clinical & experimental Imunology – 2010/160/2, 143-160.
22. Buraa Kubaisi, Khawla Abu Samra, S. Foster – Granulomatosis with polyangiitis – IRDR 2016, 5/2, 61-69.