Clinical case

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Clinical case

- Woman 57 years old came to CHU St Pierre in Brussels
- Complained of blurred vision
- Medical history: unremarkable
- Best corrected visual acuity: 20/20 both eyes
- Intraocular pressure: normal
Slit lamp exam

- Anterior chamber and vitreous:
  - 2+ cells in both eyes
- No retrokeratic precipitates
- No iridocorneal synechies
- No iris atrophy

Intermediate Uveitis
Eye fundus

- Vitritis more important on the right eye
- No lesions on the retina
- No vasculitis
- No hemorrhage
• Vitritis 3+
• No vasculitis
• No subretinal infiltrates ...
Diagnosis of Intermediate uveitis:

- **work up**
  - Complete blood cells count: Normal
  - Antinuclear antibodies: Normal
  - Rheumatoid factor: Normal
  - Normal chest X-ray
  - ACE: Normal
  - PPD: Negatif
  - Serological tests
    - Syphilis (VDRL) negatif
    - HIV: negatif
    - Toxoplasmosis: negatif
The patient underwent local and systemic steroids: PredForte one drop/hour, Solumedrol 1mg/kg/j.

The VA worsened.

The reaction in AC and Vitreous subsided.

Diagnostic vitrectomy was performed.
Cytological + Immunohistochemical staining of the vitreous

- Large B cell Lymphoma of the vitreous

- CD20+, CD79a+, BCL2+, CD3-, CD10-, BCL6-
Primary Intraocular lymphoma (PIOL)

- Subset of a primary central nervous system lymphoma (PCNSL)
- Non-Hodgkin’s, large B-cell lymphoma
- 1% of all the Non-Hodgkin’s lymphoma
- Ocular involvement occurs in 25% in PCNSL
- Initially affected by PIOL: 56% to 85% PCNSL
- The past two decades: Incidence PIOL tripled in the USA
Clinical suspicion of PIOL

- The knowledge > women after the age of 60
- Chronic *posterior* bilateral uveitis is unresponsive to corticosteroids
- The association that exist between PIOL and cellular vitritis, subretinal and retinal infiltrates and RPE
- Typical angiographic findings
Work-up: Complementary exams

Eye Fundus

- Large yellow retinal and subretinal infiltrates
- Necrotizing granulomatous retinal vasculitis
- Retinal pigmentary degeneration
- Haemorrhagic retinal necrosis
- Retinal periphlebitis
- Perivascular exudates

Primary intraocular lymphoma mimicking multifocal choroiditis and panuveitis
D J Browning and C M Fraser
Granularity on FA

Most common and characteristic finding in IOL

Indicated diffuse sub RPE infiltration of lymphoma cells. presenting as punctate hypofluorescence and hyperfluorescence lesions in the early phase of fluorescein angiography (FA)
Focal retinal vasculitis and necrosis are less common finding and indicate the secondary involvement or the retina and which are correlated with angiographic perivascular leakage.
Diagnostic vitrectomy: Vitreous biopsy

- **Undiluted vitreous for cytological staining**

Typical lymphoma cells:

- Large pleomorphic cells with scanty basophilic cytoplasm
- Hypersegmented nuclei with finger like projections
- Prominent nucleoli
- Multiple mitoses

Molecular Analysis of Primary Central Nervous System and Primary Intraocular Lymphomas
N. Tuillon* and C.C. Chan
Malignant B cells are usually monoclonal:

Demonstration of monoclonality is important in distinguishing low grade lymphoma from reactive lymphoid lesions.

Standard range of immunostains:
CD3, CD20, CD19, CD79a, CD68...

(a) Numerous large atypical lymphoid cells. Giemsa stain 400. (b) Predominance of large CD20-positive B cells. CD20 immunostaining 400.

Cytopathological analysis of vitreous in intraocular lymphoma.
● Cytokine measurements in the vitreous

- B cells malignancies can secrete high levels of IL-10 (immunosuppressive cytokine)

- While inflammatory conditions are associated with high levels of IL-6 (pro-inflammatory cytokine)

- High of IL-10 levels > 400 pg/ml with IL-10:IL-6 ratios > 1.0

  Suggestive of PIOL
IL-10 measurement in aqueous humor for screening patients with suspicion of primary intraocular lymphoma.

Cassoux N, Giron A, Bodaghi B, Tran TH, Baudet S, Davy F, Chan CC, Lehoang P, Merle-Béral H.

IL-10 > 50 pg/ml: Sensitivity 89 %, Specificity 93 %

Undiluted ocular fluids

Figure 1: IL-10 level in the vitreous by diagnostic group

Figure 2: IL-10 level in the AH by diagnostic group.
Molecular Analysis

- **PCR used to detect monoclonality of Immunoglobine heavy chain gene (IgH)**

- **Sensitivity >> Cytology**

- **Maintaining the same specificity (99%)**

- The polyclonal inflammatory cells **overshadowing** the monoclonality of the PIOL cells.

- **PIOL has unique molecular patterns of bcl-2, bcl-6, and bcl-10**
Treatment

- **Local Radiotherapy : ORT >50 Gy**

  - *In the litterature:* Bilateral ORT controled PIOL in most patients (Margolis et al, 1980), but CSN relapse occurred in 100 % of the patients within 11-84 months (Pterson and al,1993)

  - *Side effects:* Optic neuropathy
    - Retinopathy > 35 Gy
    - Cataract
    - Glaucoma
    - Permanent visual loss

**Systemic Chemotherapy**

- The efficacy depend on IO penetration through the blood retinal barrier
- **Recent American study**:
  - Blood brain barrier crossing medication chemotherapy = MTX (methotrexate) Ara C (Cytosine arabinoside)
  - Micromolar concentration of MTX present in OU (vitreous and HA) 4h > IV high dose (Smet and al, 1996; Henson and al, 1999; Bachelor and al, 2003)

- **Intravenous MTX** - first line agent: 8 mg/m
  HD-MTX prolongs median survival from 18 to 30-60 months over WBRT alone (Deangelis et al, 1992; Batchelor and al, 2000)
- **Intravenous Ara C** - alone or in combination

Ocular presentation of primary central nervous system lymphoma: diagnosis and treatment Adri´lia Hormigo, 1 Lauren Abrey, 1 Murk-Hein Heinemann 2, and Lisa M. DeAngelis
Local Chemotherapy

Intravitreal MTX

- Directly elevates the [ ] to effective level avoiding systemic complications
- Well tolerated by IO tissue: No retinal toxicity
- Adverse reactions: - corneal epitheliopathy
  - Cataract
  - Sterile endophtalmitis
  - Intravitreal HH …
**Largest scale study**
- 16 IC patients IOL+PCSNL treated IVI MTX +Systemic therapy +/- WBRT
- Dose of 400 micrograms in 0.1 ml

- **Induction phase**: twice weekly - one month
- **Consolidation phase**: Once weekly - one month
- **Maintenance**: Monthly - one year

- Cleared clinically of malignant cells after 8.5 injections

Role of IV MTX in the Management of PCNSL with Ocular Involvement
Justine R. Smith, MBBS, PhD, James T. Rosenbaum, MD, David J. Wilson, MD, Doolittle, PhD, Tali Siegal, MD, Edward A. Neuweit, MD, Jacob Pe'er, MD
**Other treatment**

- **Intravitreal Rituximab**
- **Ct+ Rt** with combined **PCNSL+ PIOL**
- **Alkylant agent as Trofosamide**

  Possible adjuvant to high dose of MTX.....
What about our patient?!!

- She disappeared for two months after the diagnosis

**IRM**: Normal

**LP**: No malignant cells

No visual complaints ....
Thank you for your attention...