Clinical case

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MERSI

06/18/08

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

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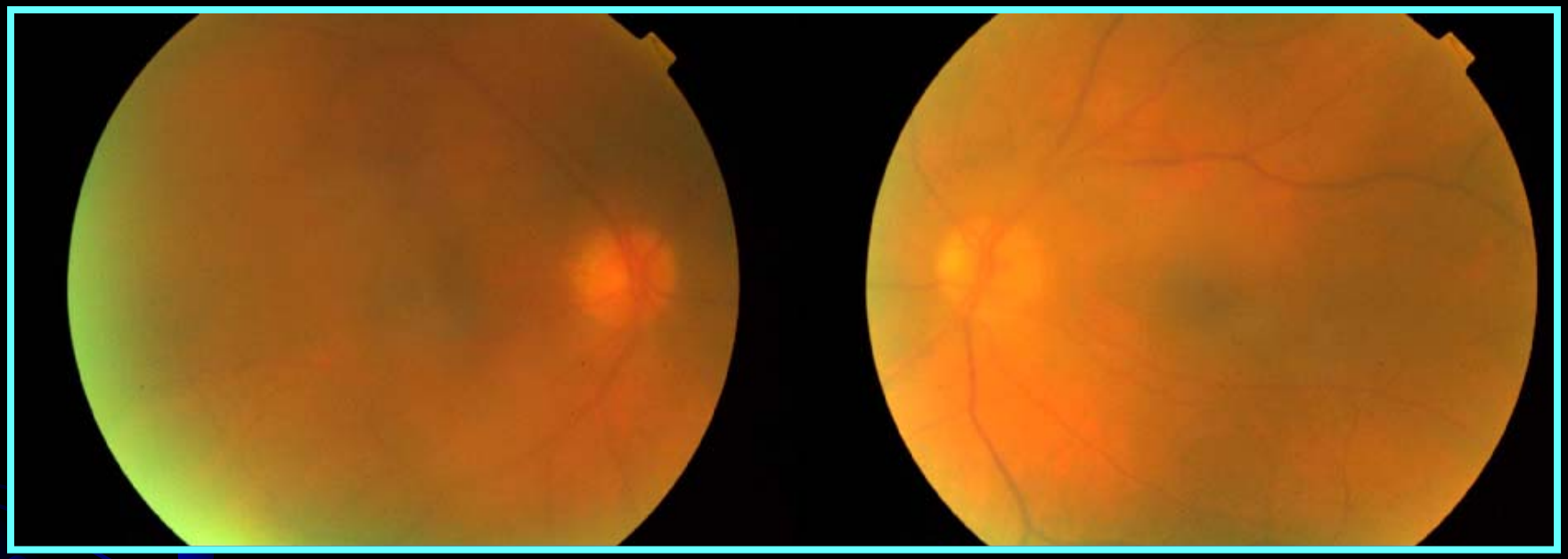
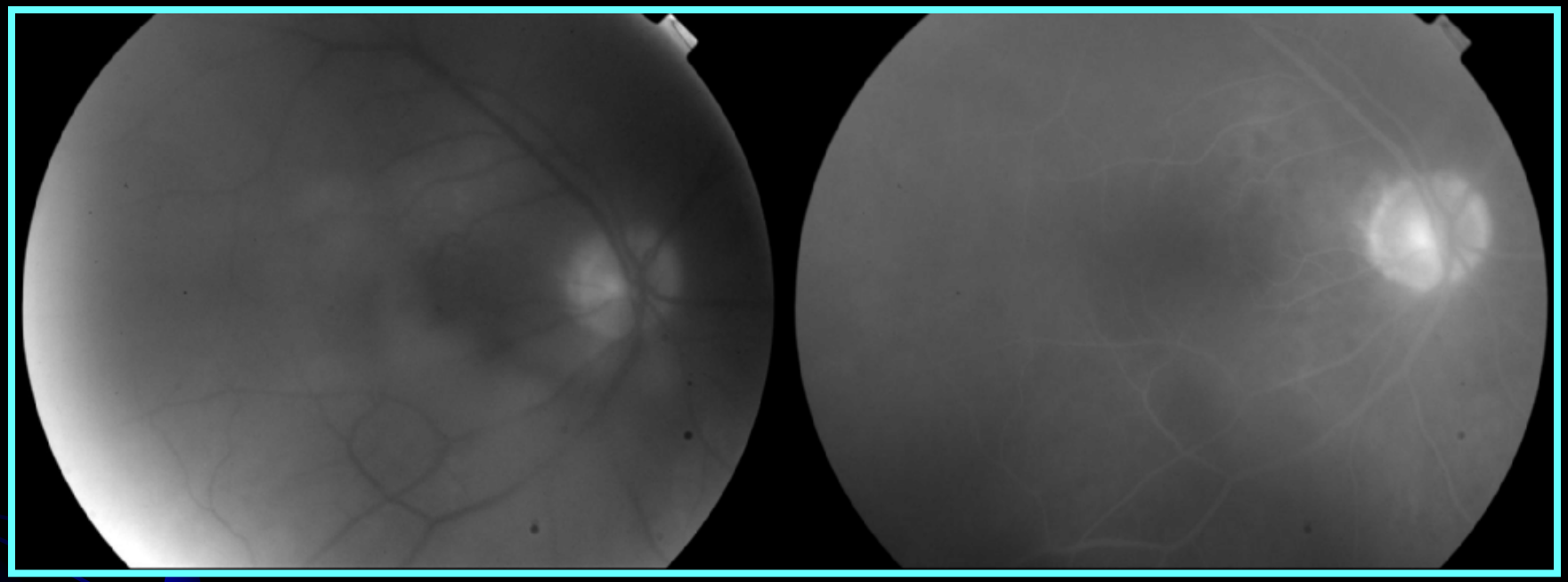
Eye fundus



- *Vitritis more important on the right eye*
- *No lesions on the retina*
- *No vasculitis*
- *No hemorrhage*

FA Right eye



- *Vitritis 3+*
- *No vasculitis*
- *No subretinal infiltrates …*

- ***Diagnosis of Intermidiate uveitis :***

work up :

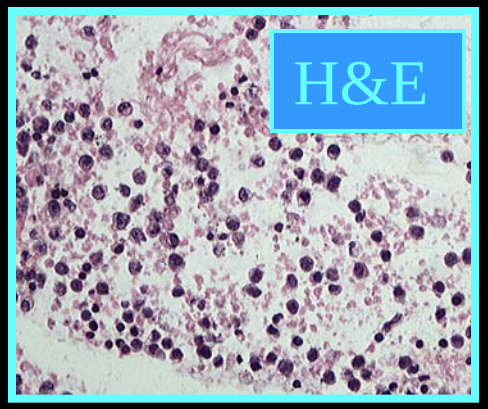
- ***Complete blod cells count : Normal***
- ***Antinuclear antibodies : Normal***
- ***Rhumatoid factor : Normal***
- ***Normal chest X ray***
- ***ACE: Normal***
- ***PPD: Negatif***
- ***Serological tests***

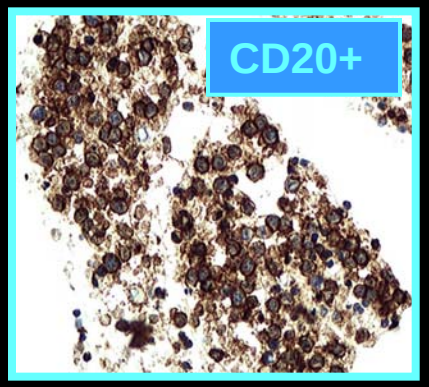
Syphillis (VDRL) negatif
HIV: negatif
Toxoplasmose; negatif

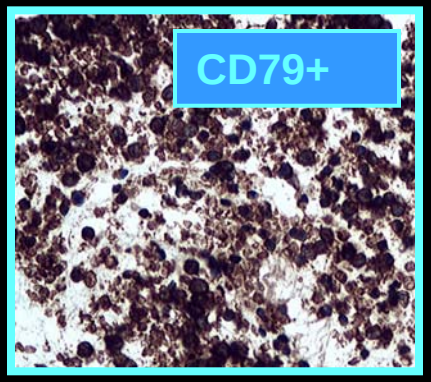
- *The patient underwent local and systemic steroids : PredForte one drop/hour*

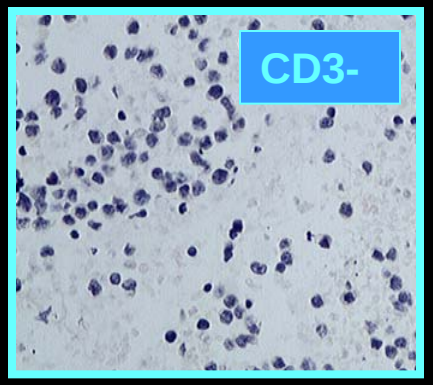
  Solumedrol 1mg /kg/j
- *The VA worsened*
- *The reaction in AC and Vitreous subsided*
- *Diagnostic vitrectomy was performed*

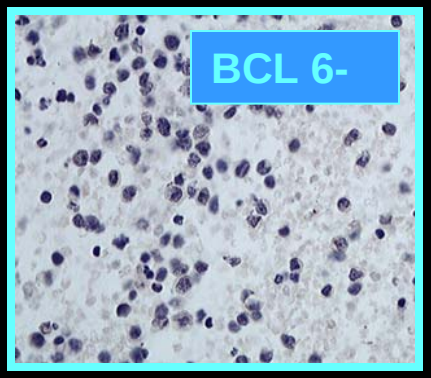
Cytological +Immunohistochemical staining of the vitreous

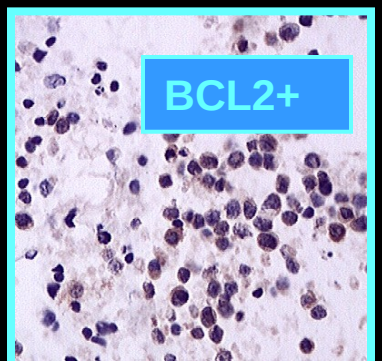












- Large B cell Lymphoma of the vitreous

- 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*

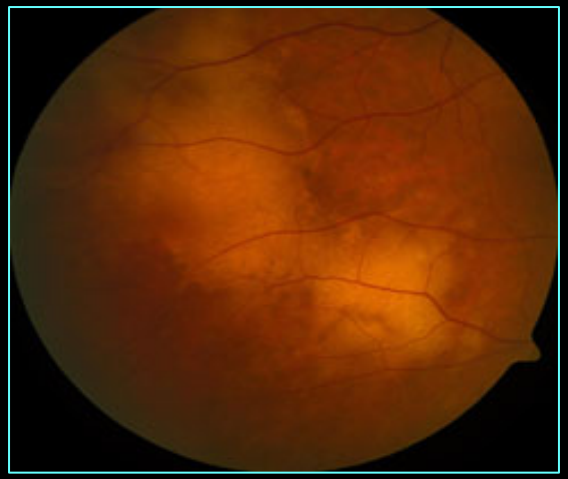
Clinical suspicion of PIOL

- *The knowledge > women after the age of 60*
- *Chronic posteriour bilatteral uveitis is unresponsive to corticosteroides*
- *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



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National Eye Institute
U.S. National Institutes of Health
Research Today...Vision Tomorrow

- *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

Typical angiographic findings

- ***Granularity on FA***

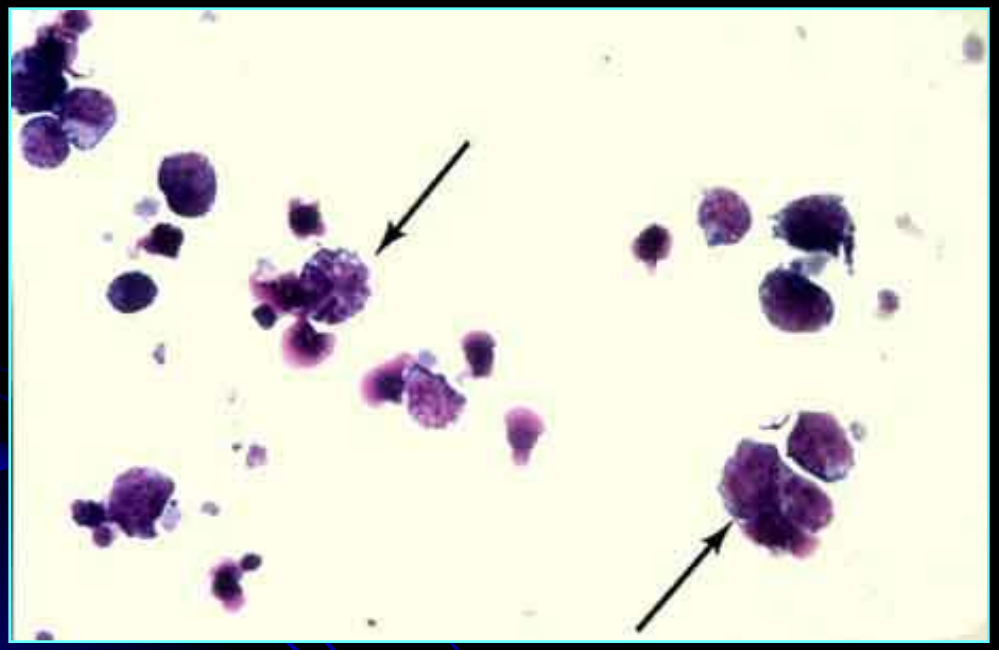
Most common and characteristic finding in IOL

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 corraleted with angiographic **perivascular leakage**.*

Diagnostic vitrectomy : Vitreous biopsy

- *Undiluted vitreous for **cytological** staining*



Molecular Analysis of Primary Central Nervous System and Primary Intraocular Lymphomas
N. Tuaillon and C.C. Chan*

Typical lymphoma cells

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

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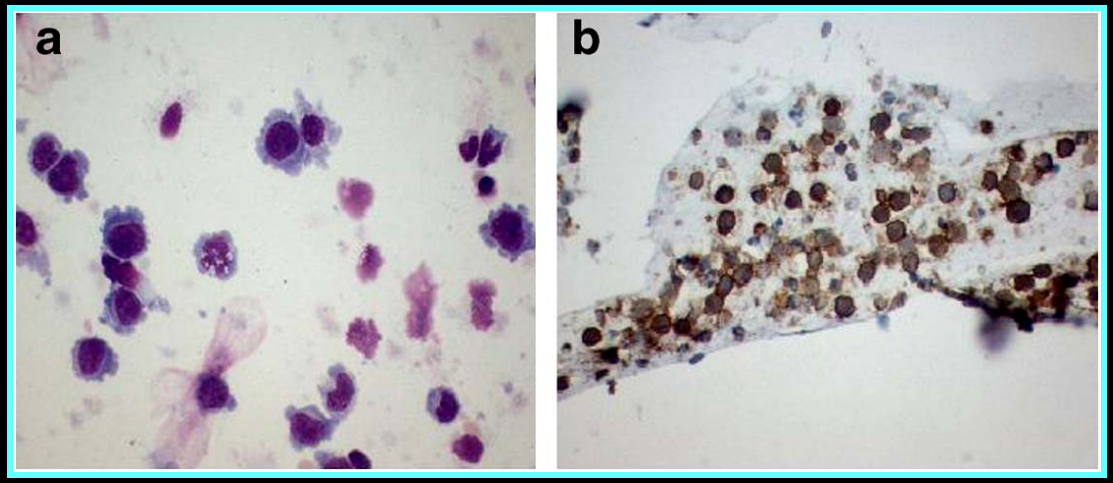
- ***Immunohistochemical staining***

Malignant B cells are usually monoclonal :

Demonstartion 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.

Eye. 2008 Feb;22(2):289-93. Epub 2007 Aug 31

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 inflammmatory 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.

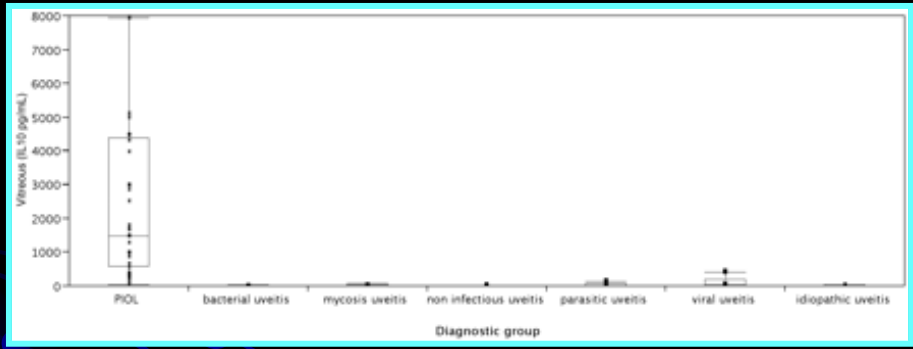


Figure 1: IL-10 level in the vitreous by diagnostic group

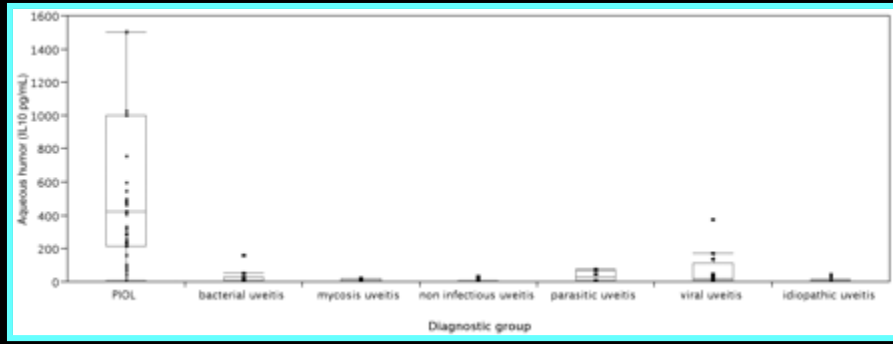


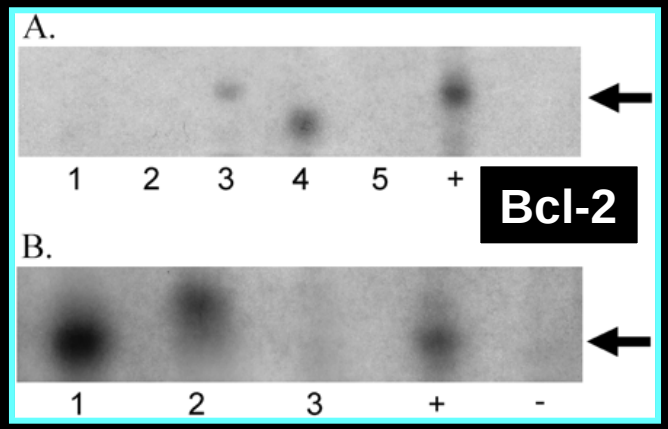
Figure 2 :IL-10 level in the AH by diagnostic group.

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

Undiluted ocular fluids

o *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***

Detection of the *bcl-2* t(14;18) Translocation and Proto-Oncogene Expression in PIOL
*Dana J. Wallace,*1 *DeFen Shen,*1 *George F. Reed,*2 *Masaru Miyanaga,*3 *Manabu Mochizuki,*3 *H. Nida Sen,*1 *Samuel S. Dahr,*1 *Ronald R. Buggage,*1 *Robert B. Nussenblatt,*1

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

Graefes Arch Clin Exp Ophthalmol. 2006 Jun;244(6):663-9. Epub 2005 Oct 16. Intraocular lymphoma 2000-2005: results of a retrospective multicentre trial.

- ***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 fron 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 Adı´lia Hormigo,1 Lauren Abrey, 1Murk-Hein K 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 …

Role of IV MTX in the Management of PCNSL with Ocular Involvement
Justine R. Smith, MBBS, PhD,1 James T. Rosenbaum, MD,1,2,3 David J. Wilson, MD,1
Nancy D. Doolittle, PhD,4 Tali Siegal, MD,5 Edward A. Neuwelt, MD,4 Jacob Pe'er, MD6

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- ***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

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- ***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…