MASQUERADE SYNDROMES

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DEFINITION
Masquerade syndromes comprise a group of disorders
- simulating a chronic idiopathic uveitis
- having an underlying primary cause that is not immune mediated and that is associated with an
  apparent clinical picture of intraocular inflammation
They are usually poorly, if not at all, responsive to corticosteroid treatment.
One must be suspicious when the apparent intraocular inflammation:
- is unilateral
- occurs either in very young children or in the elderly

DIFFERENTIAL DIAGNOSIS
Masquerade syndromes can simulate intraocular inflammation caused by:
- sarcoidosis
- tuberculosis
- syphilis
- toxoplasmosis
- toxocariasis
- ARN
- Whipple’s syndrome
- intermediate uveitis, pars planitis
- idiopathic vasculitis
- birdshot retinochoroidopathy
- idiopathic scleritis

CLASSIFICATIONS
The main disorders that can masquerade as an uveitis are intraocular tumors, postoperative infections or
degenerative conditions.
Several classifications can be suggested to facilitate the practical approach to the diagnosis of these
masquerade syndromes.

1/ Malignant and non-malignant disorders
2/ Diagnostic directions according to the patient’s age
Because of an important impact on the life-expectancy of the patients, we will focus on the malignant disorders that can masquerade as an uveitis and need to be early diagnosed for an early treatment.

MALIGNANT AND NON-MALIGNANT DISORDERS
This classification is the first to consider by the practitioner to avoid serious misdiagnosis and mismanagement of an apparent uveitis.

The family history, the past medical history, the ocular history, the review of systemic complaints, the general physical examination, the direct ocular examination, the clinical course and the response to treatment should always be considered to rule out not only infectious etiologies (that can respond to specific treatment) but also any malignant disorders that can cause an apparent intraocular inflammation.

Diagnostic tests may help to recognize the different masquerade syndromes; they are easy and logical to indicate when the cause of the pseudo-uveitis is called to mind.

1/ Malignant disorders

1-1/ Malignant disorders in adults
   1-1-1/ Intraocular lymphoma
      a) Primary ocular-CNS non Hodgkin’s lymphoma
         Large B cell lymphoma
         Increased incidence
         Elderly patients
         Bilateral most of the time
         Ocular involvement may precede detectable lesions in other parts of the CNS
         Blurred vision and floaters with non painful and white eyes
         Minimal or no anterior segment inflammation
         Sheets of vitreous cells, subretinal infiltrates, vasculitis
         Poorly responsive to corticosteroid treatment
         Diagnosis :
            fluorescein angiography (leopard appearance), MRI elevated IL-10 levels in aqueous humor, vitreous, CSF
cytologic examination of the AH, the vitreous and the CSF immunohistochemical staining for B and T cell markers and for kappa and lambda light chains
detection of immunoglobulin gene rearrangement and translocation (combination of microdissection and PCR techniques)
         Differential diagnosis : lymphoid hyperplasia of the uvea
         Atypical presentations : acute optic neuropathy in the absence of any infiltration of the posterior segment, mild auto-immune-like uveitis
and epilepsy, tuberculosis-like uveitis, acute retinal necrosis like presentation.

Treatment: systemic and intrathecal chemotherapy ± radiotherapy
intravitreal chemotherapy

b) Systemic non-Hodgkin’s lymphoma metastatic to the eye
infiltration of the choroid
hypopion or hyphema in an uninflamed eye

1-1-2/ Uveal malignant melanoma simulating scleritis, anterior uveitis or choroidal granuloma.
FA, ICG, ultrasonography, fine-needle aspiration

1-1-3/ Metastatic tumors
renal, lung and breast carcinomas
cutaneous malignant melanoma
leukemia
Waldenstrom’s disease

1-1-4/ Paraneoplastic syndromes (Cancer-associated retinopathy, Bilateral diffuse uveal melanocytic proliferation) ; bilateral most of the time serum anti-recoverin antibodies, diagnosis of the primary tumor

1-2/ Malignant disorders in childhood

1-2-1/ Retinoblastoma (usually before the age of 5 years)
inflammatory signs
pseudo-hypopion in very large retinoblastomas or in diffuse infiltrating retinoblastomas ; the later can occur after 5 years of age, as old as 12 years.
calcifications (ultrasonography, CT scan)
anterior chamber tap = dangerous (lactic deshydrogenase, enolase, rosette forming cells)
vitrectomy contraindicated
sometimes difficult to differentiate from ocular toxocariasis

1-2-2/ Leukemia
acute myelomonocytic leukemia
acute lymphocytic leukemia (possible intraocular recurrence)

2/ Non-malignant disorders
Intraocular foreign body
Irido-corneo-endothelial syndrome (ICE)
Drug associated uveitis (rifabutin, cidofovir)
Pigment dispersion syndrome, pigmentary glaucoma (bilateral most of the time)
Heterochromic Fuch’s cyclitis
Anterior segment ischemia (carotid artery disease, irradiation, extraocular muscle disinsertion)
Amyloidosis (bilateral most of the time)
Peripheral retinal detachment (inflammatory reaction, tobacco dust)
Myelinated nerve fibers
Old vitreous haemorrhage
Retinal degeneration, retinitis pigmentosa (bilateral most of the time)
Best’s disease, fundus flavimaculatus (bilateral most of the time)
Central serous choroidopathy
Complications of severe systemic hypertension (choroidal ischemia)
Endogenous endophthalmitis
Myopic degeneration, paving stone degeneration
Coat’s disease

In childhood: Juvenile xanthogranuloma (skin or iris biopsy)
Persistent hyperplastic primary vitreous

In the elderly: Postoperative infections (cataract surgery): fungal, P. acnes, Staphylococcus epidermidis

**DIAGNOSTIC DIRECTIONS ACCORDING TO THE PATIENT’S AGE**
(The following classification is only indicative: there are exceptions to the rule).

1/ Under 15 years
Retinoblastoma
Acute leukemia
Medulloepithelioma
Juvenile xanthogranuloma (skin or iris biopsy)
Persistent hyperplastic primary vitreous

2/ Adult
20 + years
Drug associated uveitis (rifabutin, cidofovir)
Pigment dispersion syndrome, pigmentary glaucoma (bilateral most of the time)
Irido-corneo-endothelial syndrome (ICE)
Acute leukemia
Systemic lymphoma
Hodgkin’s lymphoma
Coat’s disease
Amyloidosis (bilateral most of the time)

50 + years
Chronic leukemia
Metastatic solid tumors
Uveal malignant melanoma
Paraneoplastic syndromes (Cancer-associated retinopathy, Bilateral diffuse uveal melanocytic proliferation) (bilateral most of the time)
serum anti-recoverin antibodies, diagnosis of the primary tumor
Waldenstrom’s disease

60 + years
Primary ocular-CNS non Hodgkin’s lymphoma (bilateral most of the time)

3/ Any age
Intraocular foreign body
Anterior segment ischemia (carotid artery disease, irradiation, extraocular muscle disinsertion)
Peripheral retinal detachment (inflammatory reaction, tobacco dust)
Retinal degeneration, retinitis pigmentosa (bilateral most of the time)
Old vitreous haemorrhage
Heterochromic Fuch’s cyclitis
Endogenous endophthalmitis

ANATOMICAL CLASSIFICATION

1/ Anterior pseudo-uveitis
- Retinoblastoma
- Metastatic tumors (carcinoma, systemic lymphoma, leukemia …)
- Iris melanoma
- Primary ocular-CNS non Hodgkin’s lymphoma (bilateral most of the time)

- Juvenile xanthogranuloma (skin or iris biopsy)
- acanthamoeba
- ICE
- Intraocular foreign body
- Amyloidosis (scalloped pupils) (bilateral most of the time)
- Pigment dispersion syndrome, pigmentary glaucoma (bilateral most of the time)
- Heterochromic Fuch’s cyclitis
- Anterior segment ischemia (carotid artery disease, irradiation, extraocular muscle disinsertion)
- Causes of pseudo-anterior uveitis with possible hypopion:
  Retinoblastoma
  Leukemia
  Primary ocular-CNS non Hodgkin’s lymphoma
  Systemic lymphoma
  Secondary infection to undiagnosed intraocular foreign body
  Postoperative infections: fungal, P. acnes
  Endogenous endophthalmitis
  Drug-induced uveitis

2/ Pseudo-vitritis
- Primary ocular-CNS non Hodgkin’s lymphoma (bilateral most of the time)
- Intravitreal metastasis (carcinoma, leukemia, Waldenstrom’s disease …)
- Retinoblastoma

- Postoperative infections: fungal, P. acnes
- Old vitreous haemorrhage
- Amyloidosis (bilateral most of the time)
- Heterochromic Fuch’s cyclitis
- Persistent hyperplastic primary vitreous
- Endogenous endophthalmitis

3/ Pseudo-posterior uveitis
- Retinoblastoma
- Metastatic tumors (carcinoma, systemic lymphoma, leukemia …)
- Uveal malignant melanoma
- Primary ocular-CNS non Hodgkin’s lymphoma (bilateral most of the time)
- Paraneoplastic syndromes (Cancer-associated retinopathy, Bilateral diffuse uveal melanocytic proliferation) (bilateral most of the time)
  serum anti-recoverin antibodies, diagnosis of the primary tumor

- Intraocular foreign body
- Peripheral retinal detachment
- Retinal degeneration, retinitis pigmentosa (bilateral most of the time)

Cross-checking these non-exhaustive lists according to the age of the patient, to the location and to the type of the apparent intraocular inflammation can help to draw up several hypotheses in the presence of an chronic uveitis unresponsive to conventional therapy. In fact, for every uveitis patient, this approach must be systematically used even before asking for laboratory tests and before giving any treatment. This is particularly true for unilateral uveitis or for uveitis occurring either in early childhood or in the elderly.
SELECTED READINGS


