Présentation clinique rare d'une vascularite à ANCA

GEAI 14/12/20

CHU Angers

Histoire du cas

Mme B. 80 ans

Episodes récents de saignements de nez

Surdité bilatérale

Cs ophtalmo en avril 2020 pour baisse acuité visuelle œil gauche

rapidement progressive depuis 10j + épisclérite bilatérale (ttt collyre anti-histaminique)

Tableau de sclérite antérieure sectorielle bilatérale + NORB gauche sans signe de sclérite postérieure. Pas d'uvéite associée.

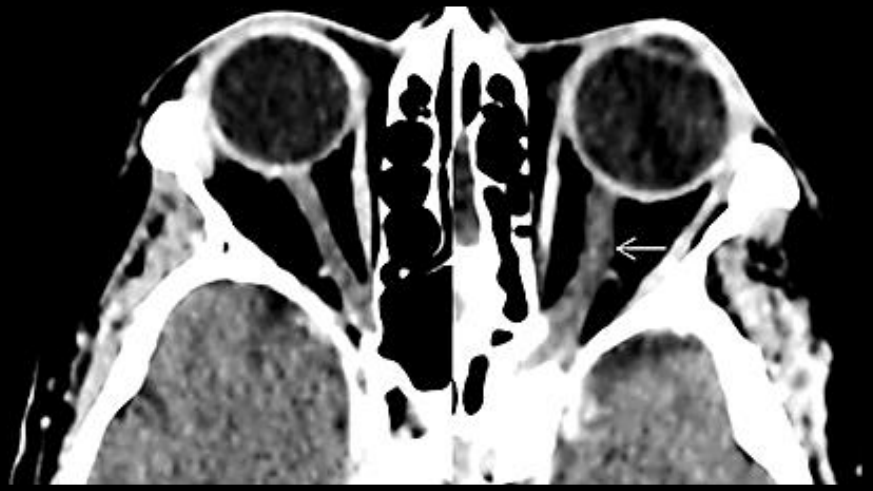
Bilan bio

CRP 30 mg/L (VN <5 mg/L) VS 67 mm (VN <30 mm)

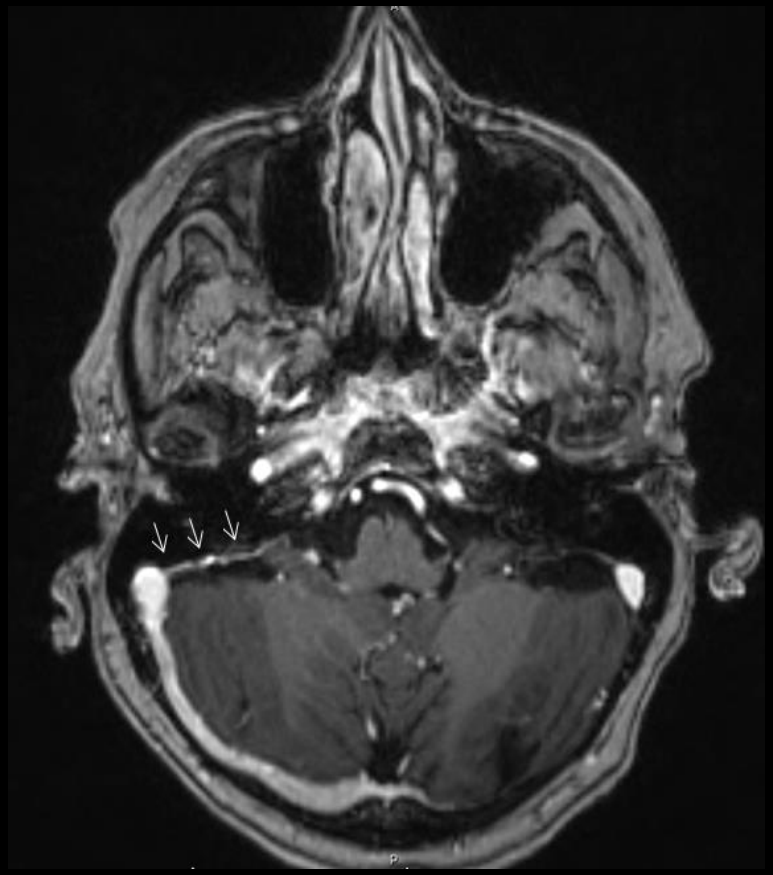
EPPS : Hypergammaglobulinémie polyclonale modérée (16,3 g/L VN 8-13,5)

Immuno AAN négatifs

- Imagerie en urgence (TDM) : Discrète asymétrie des nerfs optiques + discret réhaussement périphérique au niveau du canal optique d'étiologie indéterminée en TDM
- Intérêt d'un avis spécialisé + IRM pour meilleure caractérisation
- **IRM : épaississement pachyméningé supra et infratentoriel droit pouvant s'intégrer dans le cadre d'une granulomatose (notamment sarcoïdose et GPA)**



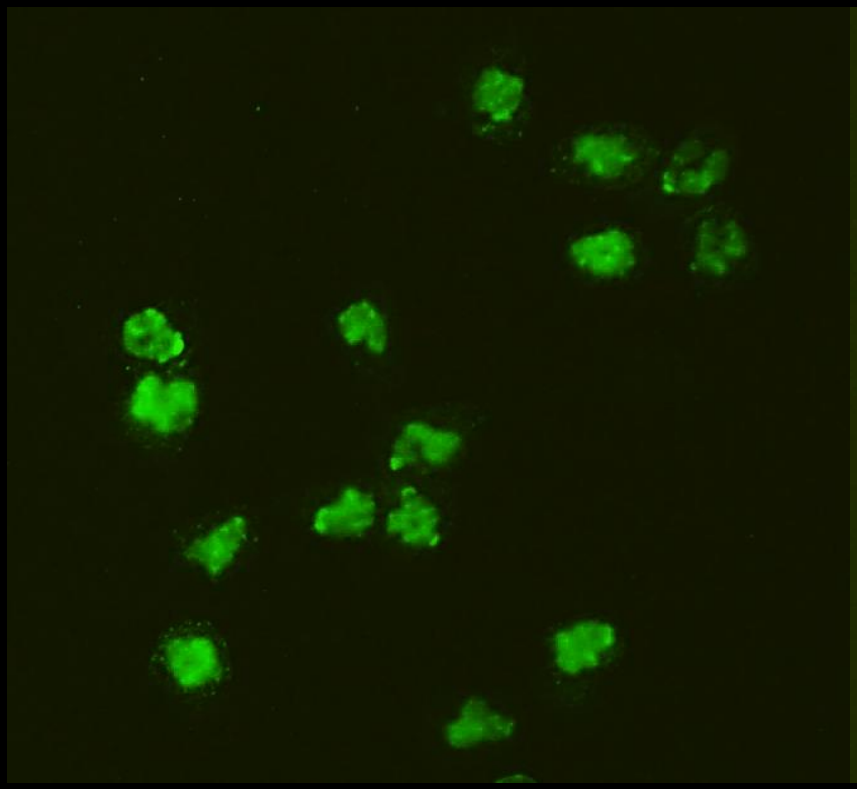
1. Sanner
Contrast-enhanced CT reconstruction showing left optic nerve thickening and slight peripheral contrast uptake (white arrow)



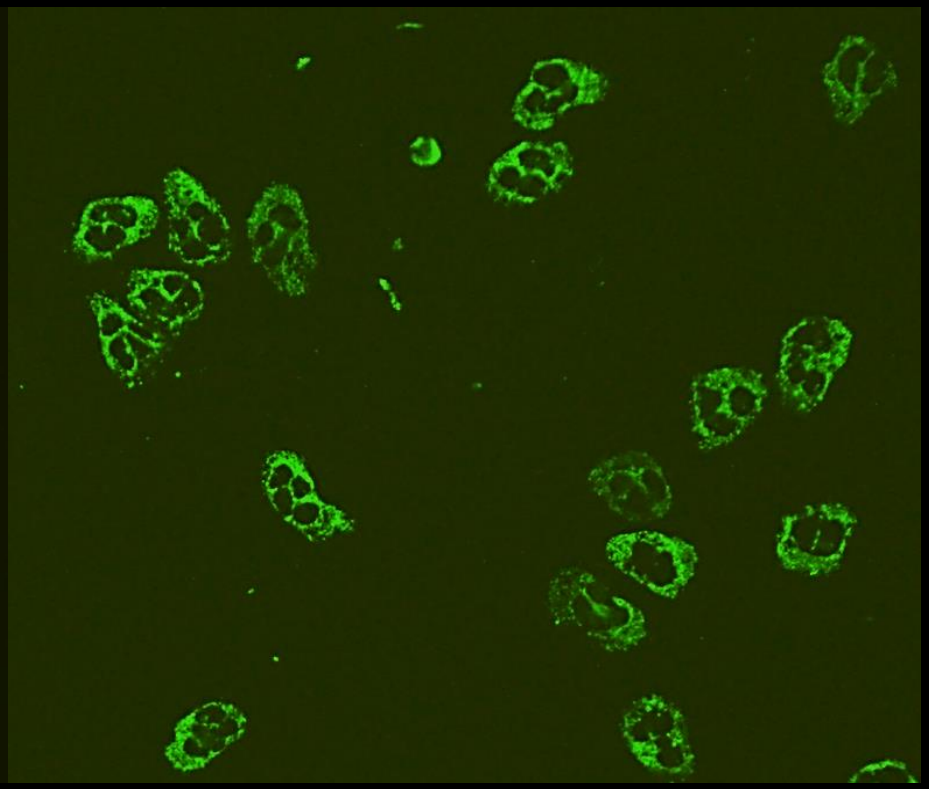
2. IRM
Contrast-enhanced T1-weighted MRI showing right granulomatous pachymeningeal thickening and intense contrast uptake (white arrows).

Dépistage d'ANCA par IFI

Lames Euroimmun (Granulocytes Mosaique 12)



PNN fixés éthanol



PNN fixés formol

☛ Dépistage positif de type P-ANCA

Histoire du cas

- Identification de la cible des ANCA

Anti-MPO positifs par

-multiplexage (Bioplex2200®) : >8 IA

-fluoroenzymologie (Phadia250) : >134 UI/mL

- Hospitalisation en médecine interne concluant à une probable vascularite à ANCA anti-MPO en faveur d'une granulomatose avec polyangéite dans un contexte de NORB, pachyméningite, sclérite, atteinte ORL et chondrite (apport décisif de l'IRM)

Prise en charge et évolution

- Ttt bolus corticoides 1g/j pdt 3j puis relai *per os*
- Vaccination PNEUMO23
- Rituximab 1ère cure 26/05

- 18/07 Cs pour dyspnée fébrile avec des images plutôt bilatérales interstitielles à la radiographie pulmonaire
- Interrogatoire : patiente n'ayant pas encore débuté l'antibioprophylaxie par BACTRIM

☛ Diag de pneumocystose

Revue de la littérature

- **Focus 1 : ANCA en dehors des vascularites**

[Consensus 2020 Moiseev, Autoimmun Rev. 2020] cf tableau dia suivante

- **Focus 2 : Atteinte ophtalmo dans les vascularites à ANCA**

- Hétérogénéité clinique
- Série 2016 GPA MPO+ et ANCA nég : sclérite et uvéite absentes du groupe MPO+GPA (n=33). A noter plus de femmes dans ce groupe versus GPA-PR3+. [Miloslavsky, *Arthritis Rheumatol*. 2016].
- Présence de P-ANCA rapportée comme significative dans les formes avec sclérite antérieure diffuse tandis que C-ANCA associés à un spectre de symptômes plus large [Hoang *Arch Ophthalmol*. 2008]
- Ocular surface manifestations and posterior segment manifestations were major eye presentations in patients with pANCA associated Vasculitis [Sorin Simion, Romanian Journal of Ophtalmolgy 2020**]**
- Epidemiology and management of interstitial lung disease in ANCA-associated vasculitis. [Sebastiani M, Manfredi A, Vacchi C, Cassone G, Faverio P, Cavazza A, Sverzellati N, Salvarani C, Luppi F. Clin Exp Rheumatol. 2020 **]**

Table 3
Overview of non-AAV diseases in which ANCA can be found.

Disease	ANCA-positivity (%)	AAV (%)	Comments
Rheumatoid arthritis	P-ANCA by IIF: 16–50% MPO-ANCA by ELISA: 0–4% (up to 18%)	Very rare	The clinical value of P-ANCA that can be detected by IIF in a significant proportion of RA patients is not definitely established. MPO-ANCA positivity was rarely found by antigen-specific immunoassay. Testing for MPO-ANCA may be justified in RA patients with a nephritic sediment.
Systemic lupus erythematosis	P-ANCA by IIF: 14–31.4% MPO-ANCA (ELISA): 0–23.8% PR3-ANCA (ELISA): 0–12.7%	Very rare	SLE can be associated with ANCA positivity in up to 15–20% of patients (particularly MPO-ANCA). One study suggested that the presence of ANCA may be associated with the severity of lupus nephritis and disease activity. However, the clinical implication of ANCA positivity in SLE is not clearly established.
Systemic sclerosis	0–9.1%	0.2–0.4%	MPO-ANCA predominated in all except one study. In one large study (n = 1303), ANCA were associated with a higher prevalence of ILD, PE, and death. Rapidly progressive glomerulonephritis in ANCA-positive patients with SSc should be differentiated from SRC.
Primary Sjögren's syndrome	P-ANCA by IIF 5.4–17.0% MPO-ANCA (ELISA) 2.0–6.7%	Very rare	The prevalence of MPO-ANCA in patients with primary Sjögren's syndrome was 3%. ANCA positivity was associated with a higher prevalence of extraglandular manifestations of Sjögren's syndrome. Testing for ANCA may be justified in the presence of renal disease or other features suggesting AAV.
Autoimmune liver diseases	Atypical P-ANCA (IIF): 65–81% in AIH type-1, 26–67% in PBC, 26–94% in PSC	Very rare	Atypical P-ANCA targeting nuclear antigens or neutrophil granule proteins are frequently found by IIF in patients with AILD and may assist diagnosis of AIH type-1 in the absence of conventional autoantibodies. Their clinical or prognostic value is not established. In one study, PR3-ANCA by CLIA was a specific biomarker for PSC though with a low sensitivity.
Inflammatory bowel diseases	Atypical P-ANCA (IIF): 41–73% in UC and 6–38% in CD PR3-ANCA (CLIA): 29.2–57.6% in UC 1.9–2.7% in CD MPO-ANCA (CLIA): 9.1–12.8 in UC 0–3.6% in CD	Very rare	Atypical P-ANCA and ASCA may aid in discriminating UC from CD in case of diagnostic uncertainty. PR3-ANCA, as detected by CLIA, may be a sensitive and specific biomarker for UC. Routine testing of the serological profile for diagnosis or for predicting the course or response to treatment cannot be recommended.
Anti-GBM disease	MPO-ANCA (more frequent) and PR3-ANCA: 13–47%	–	ANCA-positivity may identify patients who have better response to initial immunosuppressive therapy and a greater propensity to renal recovery, but can relapse during follow-up and require careful long-term monitoring.
Idiopathic interstitial pneumonia	MPO-ANCA 4–36%, PR3-ANCA 2–4%	–	Interstitial lung disease may precede diagnosis of AAV, e.g. MPA develops in up to 25% of MPO-ANCA positive patients initially diagnosed with IIP. ANCA-positivity in IIF cannot guide treatment decision
Infections	IIF: 18–24% ELISA: 8–14% (33% in one study)	–	In IE, ANCA-positivity may be linked with multiple valve involvement and more frequent renal impairment. However, the presence of ANCA seems more important in the context of differential diagnosis with AAV
Malignancy	–	Very rare	The evidence indicating a causal relationship between malignancy and AAV is inconclusive. However, it cannot be excluded in some patients.
Drugs	–	Rare	
Other diseases	–	–	Antigen-specific ANCA were reported in patients with midline destructive disease induced by cocaine inhalation, cholesterol emboli syndrome, cystic fibrosis, relapsing polychondritis, and IgG4-related disease. In patients with cystic fibrosis, BPI-ANCA may have prognostic significance.

Note: For each disease, the ANCA positivity rate is indicated as well as the occurrence of AAV.
RA – rheumatoid arthritis, SLE – systemic lupus erythematosus, AIH-1 – autoimmune hepatitis type 1, PBC – primary biliary cholangitis, PSC – primary sclerosing cholangitis, CD – Crohn's diseases, UC – ulcerative colitis, ASCA – anti-*Saccharomyces cerevisiae* antibodies, CLIA – chemiluminescent assay, IIF – indirect immunofluorescence, BPI – bactericidal/permeability-increasing protein.

[Consensus ANCA testing 2020 Moiseev, Autoimmun Rev. 2020]