



# ANCA associated HIV infection in Senegal: a serological trap

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## Background

- Wegener's disease is a necrotising granulomatous vasculitis involving respiratory tract or kidneys for which cytoplasmic antineutrophilic cytoplasmic antibody (c-ANCA) is generally considered as a highly significant serological marker.
- However, not every ANCA-positive patient with renal symptomatology is suffering from Wegener's disease.
- Here we reported a patient with vasculitis-like syndrome including a positive ANCA fluorescence test who was found to be human immunodeficiency virus (HIV) seropositive.
- The potential serological pitfall of the supposedly specific c-ANCA in HIV infected is discussed.

## Case history

- We report a 55 years Senegalese man patient with diabetic proliferative retinopathy, neovascular glaucoma, who was suspected of having Wegener's disease because of lack of kidney function, and high serum levels proteinase 3 ANCA.
- He was admitted to the internal medicine department of Aristide le DANTEC hospital in January 2015 for fever and diabetic coma. He did mention having perturbation of the kidney functions, which were detected three months ago at nephrologist consultation.
- Physical examination revealed a feverish man with urinary infection. *Salmonella* spp was detected. Auscultation wasn't detected lung pathology.
- A significant hyper-gammaglobulinemia was observed and later on during of the disease, diagnosis of HIV-1 with low CD-4 cells count was made before he died at the beginning of antiretroviral treatment.

## Methods

- ANCA screening was done by the standard immunofluorescence test (IFT) according to the first international workshop on ANCA using INOVA reagents. Two types of ANCA staining reaction patterns can be identified: cytoplasmic (c-ANCA) and perinuclear (p-ANCA).
- When ANCA are positive, specific MPO (Myeloperoxidase) and PR3 (Proteinase-3) antibodies are measured using flow cytometry (Bio-plea 2200 Biorad).
- Serum autoantibodies directed to nuclear antigens (ANA) were determined by the standard immunofluorescence test on HEp-2 cells using ImmunoConcept, Eurobio reagents.
- HIV screening test was done by ELFA-Vidas (Biomérieux) method, which combines two-enzyme immunoassay with a final fluorescent measurement (HIV-1 and HIV-2) and simultaneous detection of p24 antigenemia. Confirmation was done by western blot using New LAV BLOT II Biorad reagents.

## Discussion

- c-ANCA were first described in patients with arthralgias and polyarteritis-nodosa-like diseases with glomerulonephritis, following infection with arbovirus [Davies and all, 1989]
- Subsequently, c- ANCA positivity was notified in patients suffering from Wegener's granulomatosis [Van der woude and all, 1989].
- Some cases of ANCA positivity has been associated with medication: hydralazine, minocycline and propylthiouracil, Cocaine abuse has sporadically been associated with ANCA [Short and all, 1995]
- c-ANCA without the central accentuation that is specific for WG, also occur in individuals infected with HIV [Klaassen and all, 1992].
- HIV infection may evoke ANCA in 20 to 83% of cases, probably due to polyclonal activation of B cells, but not associated with hypergammaglobulinaemia [Kopelman and all, 1988; Koderich and all, 1990].
- On 105 HIV-infected patients, Savage and all, found 44 patients (42%) with ANCA test positivity including 26 with MPO specificity
- On 29 HIV-infected patients, Koderich and all found a faint of c-ANCA positivity in 24 patients (83%), who had homogeneous cytoplasmic ANCA due to non specific Fc-receptor bonding of immunoglobulin G, since this staining pattern was found in 15 hypergammaglobulinaemic patients in this group.

## Results

- Laboratory investigations objective Kidney failure (Creatinine 60mg/l and Urea 1,73), Anaemia (Haemoglobin 8,5g /dl, leucocytes 3,83 and platelets (105G/L).
- Myelogram showed a less rich marrow associated dimorphic plasmocytes (14%) that make clinical jumping to Multiple Myeloma diagnosis. Electrophoresis followed by IFI reveals oligoclonal hyperpammaglobulinemia (38.8g/l) without any monoclonal immunoglobulin.
- In order to rule out the possibility of autoimmune disease, blood was drawn for ANA and ANCA. ANA were negative while ANCA were positive. To determine the specificity of the antibody, the flow cytometry confirmed a protease 3 (PR-3)-positive c-ANCA pattern at a rate of 2,1.
- A urinary tract infection due to *Salmonella* spp made the HIV screening test need, which was positive and HIV-1 was confirmed by western blot.
- Lymphocytes CD4 positive count confirmed that immunosuppression: CD-4 positive lymphocytes (151x10<sup>6</sup>/l) CD-8 positive lymphocytes (1205x10<sup>6</sup>/l) the CD4/CD8 ratio was 0,12 (normal > 1.0).
- The anaemia and urinary tract infection gradually resolved by blood transfusions and antibiotics treatment but the kidney function was still deficient despite more haemodialysis sittings.
- Others investigations (pulmonary radiography) were started but patient was died. The kidney biopsy was not to be realised because of severe and persistent thrombopenia

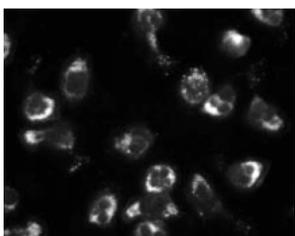


Figure: Cytoplasmic ANCA by the standard immunofluorescence test using INOVA reagents.

## Conclusions

- A positive ANCA serology should look for risk factors for HIV infection.
- In view of the increasing screening basis of ANCA, one should be aware of false-positive ANCA, that make jumping to Wegener's disease diagnosis.
- A careful work-up is needed, in whom Wegener's granulomatosis is suspected, even when c-ANCA positive.
- Lack of renal biopsy, not done due to severe thrombopenia is the limitation of this report
- This report serves again as a warning for the trap of positive ANCA in HIV-infected patients.