COMPARISON OF TWO DIAGNOSTIC CRITERIA SCHEMES FOR MULTICENTRIC CASTLEMAN'S DISEASE IN 72 CASES

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BACKGROUND

Two clinical schemes have been proposed that define an acute episode of HIV-associated multicentric Castleman's disease (MCD).
The French ANRS (Agence Nationale de Recherche sur le SIDA) CastlemanB trial group definition requires: raised serum C-reactive protein (CRP) (in the absence of any other cause), pyrexia, and at least 3 of 12 clinical features (J Clin Oncol. 2007;25:3350-6). The National Cancer Institute scheme requires: raised serum CRP, at least one clinical symptom and one laboratory abnormality probably or definitely attributed to MCD (Curr Opin Oncol. 2012;24: 495-505). Of note the serum CRP cut-off was higher in the French than in the US scheme. Neither system has been validated on an indipendent data series.

METHODS

We applied the two diagnostic schemes to our cohort of 72 patients treated for MCD. All patients had histologically confirmed MCD with IgM lambda restricted plasmablasts with positive immunostaining for KSHV.

Population features:	
Total number of patients diagnosed with MCD	72
Mean age at MCDdx	42ys
Sex: M/F (%)	88/12
Median CD4 count/mm3 at dx	237 (range: 37-1400)
Patients (%)on HAART at dx	44%
Patients with undetectable HIV RNA	52%
Median duration of symptoms before dx (months)	3 (range: 0.5-48)

ANRS criteria: what`s an attack of MCD?

1. **Fever**

2. At least 3 of the following :
1. Lymphadenopathy
2. Splenomegaly
3. Oedema
4. Pleural effusion
5. Ascites
6. Cough
7. Nasal obstruction
8. Xerostomia
9. Rash
10. Central neurologic symptoms
11. Jaundice
12. Autoimmune haemolytic anaemia

3. Serum C-reactive protein level >20 mg/L

(in the absence of any other cause)

NCI criteria: what`s an attack of MCD?

At least one clinical symptom:
1. Fatigue (CTCAE> Grade 1)
2. Fever, night sweats
3. Weight loss
4. Respiratory symptoms
5. Gastrointestinal symptoms
6. Neurologic symptoms
7. Oedema or effusion
8. Xerostomia
9. Rash (including KS)

At least one laboratory abnormality probably or definitely attributed to MCD:
1. Anaemia (Hb< 12 g/dL)
2. Thrombocytopenia (<100 x 10^9/L)
3. Hypoalbuminaemia (<35 g/L)

3. Serum C-reactive protein level >3 mg/L

RESULTS AND CONCLUSIONS

Frequency of ANRS criteria in 72 MCD ptatients at diagnosis.		Frequency of NCI criteria in 72 MCD patients at diagnosis	
Serum PCR> 20 mg/L	**92 %**	**Serum PCR> 3 mg/L**	**100%**
Fever	**99%**	**One clinical finding**	**99%**
>2 of 12 criteria met	**92%**	Fatigue (CTCAE>Grade1)	56%
Lymphadenopathy	100%	Fever, night sweats	97%
Enlarged Spleen	90%	Weight loss	*
Oedema	21%	Respiratory symptoms	63%
Pleural effusion	18%		
Ascites	8%	Gastrointestinal symptoms	8%
Cough	63%	Neurologic symptoms	7%
Nasal obstruction	30%	Oedema or effusions	32%
Xerostomia	37%	Rash (including KS)	65%
Rash (including KS)	65%		
Central neurologic symptoms	7%	**One laboratory finding**	**97%**
Jaundice	16%		
Autoimmune haemolitic anaemia	43 %	Anaemia	88%
		Thrombocytopenia	32%
		Hypoalbuminaemia	89%
ALL FINDINGS MET	**92%**	**ALL FINDINGS MET**	**96%**

*But nasal obstruction and xerostomia only prospectively collected on 30 patients

*Weight loss data not available

The sensitivity of these schemes were 92% for the ANRS criteria and 96% for the NCI criteria. The difference between the two schemes relates to the higher cut-off used for serum CRP in the French scheme and the requirement for at least 3 specified clinical abnormalities.

- ANRS: fewer than 3 criteria met 8%
- NCI: raised CRP with one clinical and one laboratory abnormality NON met 4%

CONCLUSIONS

Although both schemes categorize the majority of our patients as having active MCD, the looser criteria in the NCI scheme identifies more of our cohort as having active MCD (false negative rates 8% ANRS and4% NCI).
The study has not attempted to establish the capacity of either scheme to correctly exclude patients without MCD and so the specificity and power of the two schemes cannot be established.