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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Multicentric Hyaline-Vascular Castleman Disease: The Missing Link?

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Introduction: Castleman disease (CD) is a rare lymphoproliferative disorder that encompasses distinct clinicopathological entities. Unicentric form of the disease (UCD) usually involves a single lymph node station, exhibits hyaline vascular (HV) pathological changes with follicular dendritic cell expansion, and may associate with specific and life-threatening complications including paraneoplastic pemphigus (PNP) and follicular dendritic cell sarcoma (FDCS). Plasma cell interfollicular infiltration is absent in the HV subtype as opposed to the Plasma-Cell (PC) or Mixed subtypes. PC subtype has been associated with inflammatory symptoms thought to be secondary to plasma cell infiltration and represents the majority of HHV8-negative "idiopathic" multicentric forms of the disease. Interestingly, patients with PC-UCD behave as PC-MCD, suggesting a stronger role of histology rather than Unicentric vs Multicentric phenotype in disease expression. We here studied the phenotype of HV-MCD, a rare subtype of CD characterized by hyaline-vascular pathological changes involving 2 or more lymph node stations.
Methods: Patients were screened through the French national reference center for CD between January 1994 and June 2023. Cases were followed from first symptoms to last follow-up visit. Comparators consisted of patients with HV-UCD and patients with PC/Mixed iMCD (P/M-iMCD). All cases and biopsies were reviewed by three expert clinicians and one expert pathologist.
Results: Sixteen patients with a diagnosis of HHV8-negative HV-MCD were identified. All patients had supra- and infradiaphragmatic involvement. Four were excluded because of a subsequent diagnosis of POEMS, systemic lupus erythematosus, tuberculosis, or inborn error of immunity. The 12 remaining patients were considered as having HV-iMCD and compared to 101 patients with P/M-iMCD and 139 patients with HV-UCD. Characteristics and comparison between the 3 groups are depicted in **Table 1**.
When compared to HV-UCD, HV-iMCD displayed frequent systemic involvement with significantly higher ECOG, higher frequency of fever and splenomegaly, and higher levels of C-reactive protein, gammaglobulins, leukocytes and ferritinemia (**Figure 1**). Age at diagnosis was not different between HV-UCD and HV-iMCD. No cases of TAFRO syndrome were observed in HV-UCD whereas 4 cases were observed in HV-iMCD. All cases of PNP (n=12) and FDCS (n=3) were observed in the HV-UCD group.

We observed a younger age at diagnosis in HV-iMCD compared to P/M-iMCD (median 24 [range 13-70] vs median 50 [range 11-88] years respectively, p = 0.01). We also noted a trend towards lower levels of C reactive protein and gammaglobulins as well a higher albumin level in HV-iMCD vs P/M-iMCD but these differences were not significant (**Figure 1 and Table 1**).
Treatments were similar between HV-iMCD and P/M-iMCD with prescription of steroids or anti-IL6R as first line therapy in 8/12 (67%) and 61/101 (60%) respectively. As expected, surgery was the first line therapy in 98/139 (72%) of HV-UCD patients. One patient with HV-iMCD and two with HV-UCD died (logrank p = 0.10), whereas 13 died in the P/M-iMCD group (logrank p = 0.8).

Conclusions: These data altogether indicate that HV-iMCD appears to be a distinct entity in CD landscape, sharing pathological aspects of HV-UCD and clinical/biological features of P/M iMCD. In line with this view, there seems to be no overlap between HV-UCD and HV-iMCD-related complications. The findings also suggest that nodal PC infiltration is not sufficient to explain the inflammatory pattern of iMCD.

Disclosures Meignin: *EUSAPHARMA:* Consultancy. **Terriou:** *Alexion:* Honoraria; *Sobi:* Honoraria; *Eusapharma:* Consultancy. **Viallard:** *EUSAPHARMA:* Consultancy. **Galicier:** *EUSAPHARMA:* Consultancy; *AMGEN:* Consultancy. **Oksenhendler:** *EusaPharma:* Consultancy; *CSL Behring:* Consultancy.

Table 1. Comparison of patients' clinical and biological characteristics according to histology and extension of CD

	HV-iMCD vs HV-UCD			HV-iMCD vs P/M-iMCD	
	HV-iMCD, N = 12	HV-UCD, N = 139	p-value	P/M-iMCD, N = 101	p-value
Age at diagnosis	23.5 (16.2, 46.5)	35.0 (22.5, 44.0)	0.4	50.0 (29.0, 64.0)	**0.011**
Sex (Female)	6 / 12 (50%)	83 / 139 (60%)	0.6	28 / 101 (28%)	0.2
ECOG status			**0.008**		>0.9
0-1	3 / 6 (50%)	82 / 87 (94%)		22 / 52 (42%)	
2-4	3 / 6 (50%)	5 / 87 (5.7%)		30 / 52 (58%)	
PET SUVmax	4.5 (4.1, 8.4)	4.4 (3.6, 5.5)	0.3	5.8 (4.7, 8.1)	0.6
Fever	7 / 12 (58%)	6 / 139 (4.3%)	**<0.001**	67 / 101 (66%)	0.7
Splenomegaly	6 / 12 (50%)	1 / 139 (0.7%)	**<0.001**	38 / 101 (38%)	0.5
Pemphigus	0 / 12 (0%)	12 / 139 (8.6%)	0.6	101 / 101 (100%)	
Sarcoma	0 / 12 (0%)	3 / 139 (2.1%)	>0.9	0 / 101 (0%)	>0.9
AIHA	0 / 12 (0%)	0 / 139 (0%)	>0.9	4 / 101 (4.0%)	>0.9
ITP	2 / 12 (17%)	2 / 139 (1.4%)	**0.032**	19 / 101 (19%)	>0.9
Edema	5 / 12 (42%)	4 / 139 (2.9%)	**<0.001**	39 / 101 (39%)	>0.9
Polyneuropathy	0 / 12 (0%)	2 / 139 (1.4%)	>0.9	7 / 101 (6.9%)	>0.9
Nephropathy	4 / 12 (33%)	1 / 139 (0.7%)	**<0.001**	36 / 101 (36%)	>0.9
TAFRO syndrome	4 / 12 (33%)	0 / 135 (0%)	**<0.001**	25 / 101 (25%)	>0.9
Leukocytes (/mm3)	8,800 (6,850, 10,800)	5,915 (4,915, 7,515)	**<0.001**	7,890 (5,723, 9,950)	0.2
Neutrophils (/mm3)	4,980 (4,523, 7,185)	3,800 (2,940, 4,960)	**0.001**	5,575 (3,813, 7,413)	0.5
Lymphocytes (/mm3)	1,680 (1,100, 1,810)	1,570 (990, 2,050)	0.7	1,370 (850, 1,850)	0.2
Hemoglobin (g/dL)	10.8 (8.6, 13.2)	13.5 (12.5, 14.7)	**0.002**	9.6 (8.2, 11.7)	0.4
Platelets (G/L)	199.5 (27.25, 341.5)	271 (230, 322)	0.061	194 (66.5, 361.5)	0.6
C reactive protein (mg/L)	62.(4.5, 105.8)	2.0 (1.0, 4.0)	**<0.001**	95 (42, 156)	0.092
Albumin (g/L)	40.0 (27.6, 42.2)	43.7 (40.5, 46.1)	**0.003**	29 (24, 34.3)	0.055
Gammaglobulins (g/L)	16.0 (11.8, 16.8)	11.1 (9.4, 13.1)	**0.009**	21 (13, 29)	0.13
IgG (g/L)	15.8 (13.1, 16.0)	10.5 (9.0, 12.4)	**0.001**	19.5 (12.5, 27.1)	0.2
IgA (g/L)	2.0 (1.1, 3.1)	1.8 (1.3, 2.6)	>0.9	3.6 (2.1, 5.3)	**0.030**
IgM (g/L)	0.8 (0.7, 1.9)	1.0 (0.8, 1.6)	0.6	0.9 (0.6, 1.6)	>0.9
Ferritin (ng/mL)	559 (522.0, 597.0)	80 (16.0, 156.0)	**<0.001**	468 (196, 1,047)	0.6

Continuous variables are shown as Median (Interquartile range) and discrete variables as n/N (%)
HV-iMCD: hyaline-vascular idiopathic multicentric Castleman disease, P/M-iMCD: plasmacytic/mixed idiopathic multicentric Castleman disease, HV-UCD: hyaline-vascular unicentric Castleman disease, ECOG : Eastern Cooperative Oncology Group, PET-FDG: Positive EmissionTomography, SUVmax: maximum Standardized Uptake Value, AIHA: auto-immune hemolytic anemia, ITP: immune thrombocytopenic purpura, TAFRO: Thrombopenia, Anasarca, Fever, Reticulin fibrosis, Organomegaly

Figure 1. Age, hemoglobin, platelets and C-reactive protein levels at diagnosis according to CD subtype.

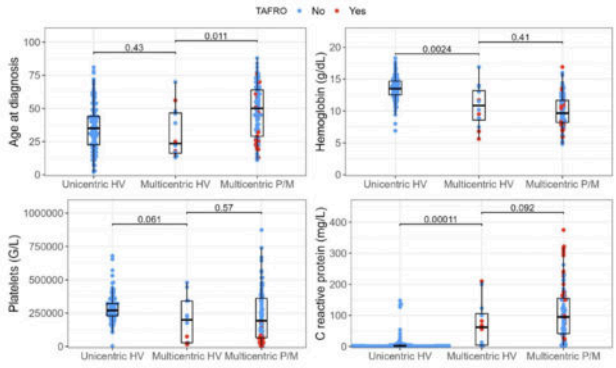

Figure 1

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