Abstract N°: 286

Multiparameter analysis of panniculitis reveals three clusters of patients

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Introduction & Objectives:

Panniculitis are characterized by a triple heterogeneity in (1) clinical presentation with multiple clinical forms,

2. histopathology as lesions may show primarily lobular or septal inflammation with or without vascular involvement and in (3) etiologies including autoimmune, metabolic, infectious, vascular, paraneoplastic and often idiopathic panniculitis. Publications are scarce on this subject with mostly case studies. Therefore, a better classification remains necessary to improve clinical management. The aim of this study is to use a specific epidemiological method, namely that of clusters, in order to characterize a large series of individuals with panniculitis and to describe homogeneous groups of patients.

Materials & Methods:

Patients were selected from the pathological registries and main or secondary diagnoses coded during clinical outpatient visit or hospital stay in three university hospital centers for a period of five years between January 2018-2023.

Results:

299 patients were included. Patients' sociodemographics and past medical history are cited in table 1. Most common clinical presentation was subcutaneous nodules (87.3%) located mainly on lower limbs (67.6%). Histologically, the majority of patients had mixed panniculitis (53.8%) and 51.2% of subjects had a polymorphic infiltrate in the deep dermis and hypodermis. No cause was found in 32.8% of patients considered as idiopathic panniculitis. 17.7% of patients had erythema nodosum, with no cause identified in more than half of the cases. An autoimmune disease was found in 14.2% and an infectious cause in 9% of patients. 72.2% of patients received multiple treatments for anti-inflammatory, anti-infectious or immunomodulatory purposes. We completed this study with a clusterization method using clinical, pathological, biological and imaging parameters and we found that the population could be divided into 3 clusters (tables 2, 3 and 4). The first cluster included half of the patients in this cohort and was characterized by multiple episodes of bilateral

nodular lesions with systemic signs, in young patients (< 50 y.o) without a history of cardiovascular diseases, without vascular involvement on histology, and treated with colchicine and hydroxychloroquine. The other half were distributed between 2 clusters. Cluster 2 patients had unilateral infiltrated erythematous plaques (87%) without systemic signs (97%). Histologically, they had mixed panniculitis (75%) and an inflammatory infiltrate in the hypodermis in almost all cases and vascular involvement in 40% of cases. They were treated with antiinfective treatments (39%) and topical steroids (21%). On the contrary, cluster 3 included elderly patients (65%), with a history of cardiovascular diseases who presented non-painful lesions (39%) limited to the lower limbs (43%) without edema (91%), without systemic signs (90%) and without inflammatory infiltrate in the hypodermis (55%).

Conclusion:

This large series highlights the clinical and histological heterogeneity of panniculitis with approximately 33% of idiopathic cases for which a consensual attitude is lacking. Using clustering analysis, we were able to describe three homogeneous groups of patients based on sociodemographic status, clinical findings, histological features and treatment modalities. This could help building foundations to future prospective studies and therefore a better management of this poorly understood entity.

Patients' characteristics	Total (n=299)
Age, y [median]	51.0 [38.0-62.0]
Female sex	233 (77.9%)
History of cardiovascular diseases	91 (30.4%)
Diabetes	41 (13.7%)
Hypertension	73 (24.4%)
Dyslipidemia	33 (11.0%)
Tobacco	40 (13.4%)
Alcohol consumption	16 (5.4%)
Substance use	8 (2.7%)
Medical or surgical history	
Chronic venous insufficiency	32 (10.7%)
Hematological malignancies	26 (8.7%)
Other dermatological diseases	21 (7.0%)
Solid tumors	14 (4.7%)
Infectious diseases	11 (3.7%)
Autoimmune diseases	11 (3.7%)
Rheumatological diseases	10 (3.3%)
Lupus	10 (3.3%)
Inflammatory bowel diseases	9 (3.0%)
Vascular thrombosis	9 (3.0%)
Renal diseases	8 (2.7%)
Respiratory diseases	8 (2.7%)
Psychiatric diseases	7 (2.3%)
Vasculitis	6 (2.0%)
Pancreatitis	5 (1.7%)
Sarcoidosis	4 (1.3%)
Others	30 (10.03%)
Recent Drug exposure (3 months)	16 (5.4%)
Recent vaccination (3months)	0(0%)

Table 1- Patients' sociodemographic characteristics and past medical history

Variable	Cla/Mod (%)	Mod/Cla (%)	Global (%)	p-value	v.test
Absence of cardiovascular history	71,63	100,00	69,57	<0,001	12,66
Absence of hypertension	65,93	100,00	75,59	<0,001	10,90
Absence of erythematous infiltrated plaque	64,62	91,95	70,90	<0,001	8,24
Absence of diabetes	57,36	99,33	86,29	<0,001	7,10
Absence of dyslipidemia	56,02	100,00	88,96	<0,001	6,72
Age: 26-49 years	68,22	59,06	43,14	<0,001	5,55
Bilateral lesions	58,99	85,91	72,58	<0,001	5,19
More than 5 episodes	78,43	26,85	17,06	<0,001	4,54
Absence of edema	55,74	91,28	81,61	<0,001	4,34
Treatment with colchicine	75,51	24,83	16,39	<0,001	3,95
Absence of vascular involvement on histology	54,58	91,95	83,95	<0,001	3,77
Intact dermis on histology	56,46	79,19	69,90	<0,001	3,48
Skin erythema	55,66	82,55	73,91	<0,001	3,38
Negative deep tissue culture	51,76	98,66	94,98	<0,001	2,92
Absence of anti-infectious treatment	53,97	86,58	79,93	<0,001	2,85
Multiple nodules: > 10 nodules	57,75	55,03	47,49	0,01	2,59
Absence of chronic venous insufficiency	52,43	93,96	89,30	0,01	2,59
Absence of topical steroids treatment	52,24	93,96	89,63	0,02	2,43
Presence of associated systemic symptoms	69,70	15,44	11,04	0,02	2,40
Presence of digestive symptoms	73,91	11,41	7,69	0,02	2,38
Age: 18-25 years	75,00	10,07	6,69	0,02	2,30
Multiple nodules: 5-10 nodules	64,15	22,82	17,73	0,02	2,28
Presence of fever	63,64	23,49	18,39	0,02	2,25
Treatment with hydroxychloroquine	68,97	13,42	9,70	0,03	2,15
Presence of arthralgia	61,54	26,85	21,74	0,03	2,12

Table 2 – Cluster one: list of over-represented variables

Variable	Cla/Mod(%)	Mod/Cla(%)	Global(%)	p-value	v.test
Presence of erythematous infiltrated plaque	62,07	87,10	29,10	<0,001	10,92
Unilateral lesions	52,44	69,35	27,42	<0,001	7,86
Absence of nodules	73,68	45,16	12,71	<0,001	7,62
Presence of edema	61,82	54,84	18,39	<0,001	7,56
Absence of relapse	28,30	96,77	70,90	<0,001	5,64
Absence of cardiovascular history	27,88	93,55	69,57	<0,001	5,01
Presence of vascular involvement on histology	50,00	38,71	16,05	<0,001	4,98
Absence of hypertension	26,55	96,77	75,59	<0,001	4,88
Lesions exceeding lower limbs	26,73	87,10	67,56	<0,001	3,86
Ant infectious treatment	40,00	38,71	20,07	<0,001	3,85
Presence of dermis alteration on histology	34,44	50,00	30,10	<0,001	3,69
Absence of dyslipidemia	23,31	100,00	88,96	<0,001	3,63
Absence of colchicine treatment	24,00	96,77	83,61	<0,001	3,45
Presence of pathogen on deep culture	60,00	14,52	5,02	<0,001	3,34
Mixed panniculitis on histology	27,33	70,97	53,85	<0,001	3,05
Absence of diabetes	23,26	96,77	86,29	<0,001	2,92
Treatment with topical steroids	41,94	20,97	10,37	<0,001	2,82
Pain	24,77	85,48	71,57	<0,001	2,81
Absence of skin erythema	32,05	40,32	26,09	0,01	2,76
Treatment installed	24,54	85,48	72,24	0,01	2,69
Presence of triggering factor	36,59	24,19	13,71	0,01	2,52
Absence of associated systemic symptoms	22,56	96,77	88,96	0,02	2,33
Absence of digestive symptoms	22,10	98,39	92,31	0,03	2,14
Absence of general status alteration	23,28	87,10	77,59	0,04	2,06
Presence of inflammatory infiltrate in the deep dermis and hypodermis	22,02	98,39	92,64	0,04	2,05
Absence of hydroxychloroquine treatment	22,22	96,77	90,30	0,04	2,02

Table 3 – Cluster two: list of over-represented variables

Variable	Cla/Mod(%)	Mod/Cla(%)	Global(%)	p-value	v.test
Presence of cardiovascular history	95,60	98,86	30,43	<0,001	17,60
Presence of hypertension	97,26	80,68	24,41	<0,001	14,79
Presence of dyslipidemia	100,00	37,50	11,04	<0,001	9,27
Presence of diabetes	92,68	43,18	13,71	<0,001	9,20
Age: 50 – 75 years	44,19	64,77	43,14	<0,001	4,84
Age > 75 years	76,19	18,18	7,02	<0,001	4,52
Absence of edema	32,79	90,91	81,61	0,01	2,77
Absence of inflammatory infiltrate in the deep dermis and hypodermis	54,55	13,64	7,36	0,01	2,52
Lesions limited to lower limbs	39,18	43,18	32,44	0,01	2,51
Absence of pain	40,00	38,64	28,43	0,01	2,47
Absence of fever	32,38	89,77	81,61	0,02	2,41
Male sex	40,91	30,68	22,07	0,02	2,25
Absence of treatment installed	38,55	36,36	27,76	0,04	2,10

Table 4 – Cluster three: list of over-represented variables