Original Article

Diagnostic significance of colloid body deposition in direct immunofluorescence

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ABSTRACT

Background: Colloid bodies (CB) in direct immunofluorescence (DIF) studies are usually found in interface dermatitis. Furthermore, CB can be found in various skin diseases and even in normal skin. **Aim:** To evaluate the diagnostic value of CB deposits in DIF studies. **Methods:** From 1996-2007, data from 502 patients where DIF studies showed immunoreactants at CB were enrolled. The definite diagnoses of these patients were based on clinical, histopathological and immunofluorescent findings. The results of DIF studies were analyzed. **Results:** Immunoreactants at CB were detected in 44.4%, 43.8%, 4.2%, 3.8%, and 2.2% of interface dermatitis, vasculitis, autoimmune vesiculobullous disease, panniculitis, and scleroderma/morphea, respectively. The most common immunoreactant deposit of all diseases was Immunoglobulin M (IgM). Brighter intensity and higher quantity of CB was detected frequently in the group with interface dermatitis. **Conclusions:** Immunoreactant deposits at CB alone can be found in various diseases but a strong intensity and high quantity favor the diagnosis of interface dermatitis. CB plus dermoepidermal junction (DEJ) deposits are more common in interface dermatitis than any other disease. Between lichen planus (LP) and discoid lupus erythematosus (DLE), CB alone is more common in LP; whereas, CB plus DEJ and superficial blood vessel (SBV) is more common in DLE. The most common pattern in both diseases is CB plus DEJ. The quantity and intensity of CB in LP is higher than in DLE.

Key words: Colloid bodies, direct immunofluorescence, interface dermatitis

INTRODUCTION

Colloid bodies (CB) are eosinophilic hyaline ovoid bodies which are often found in the subepidermal papillary regions or sometimes in the epidermis. They are usually seen in lichen planus (LP) and lupus erythematosus (LE).[1] They can also be found in several dermatoses such as erythema multiforme (EM), bullous pemphigoid (BP) and diseases with suprabasal clefts.[2] Colloid bodies, also known as civatte bodies or cytoid bodies, are generally believed to be derived from two origins. The first type originates from apoptosis of keratinocytes causes by epithelium damage created by circulating disorders.[2] CB of this type are usually found locally both in the epidermis and papillary dermis. The other origin derives from the destruction of thickened basement membranes which are found only in the papillary dermis.[3]

Immunoglobulin (Ig) subclasses of CB: IgG, IgA, IgM, complement components (C3) and fibrinogen, can be demonstrated by direct immunofluorescence (DIF).[1] According to previous studies, IgM-CB is the most common immunoreactant deposit in LP,[4-7] BP,[1] and EM.[8] It is still unclear whether or not CB would provide any additional on diagnostic value for overlapping skin diseases. The aim of this descriptive study was to demonstrate a possible correlation between the Ig subclasses of CB and their diagnostic yield.

METHODS

Data were collected from patients who visited the Department of Dermatology, Siriraj Hospital, Mahidol University, Bangkok, Thailand from 1996-2007. Cutaneous biopsies in which DIF studies showed immunoreactants at CB were enrolled. The definite

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diagnoses of these patients were based on clinical, histopathological and immunofluorescent findings. DIF studies of skin lesions were performed according to the standard method described previously.[9] Briefly, skin biopsy specimens were embedded in Cryomatrix embedding medium (Shandon Lipshaw, Inc, Pittsburgh, PA, USA) and snap frozen at -70°c until sectioned. Frozen sections, 4-μm thick, were cut on a cryostat, air dried, washed twice with phosphate-buffered saline (PBS), pH 7.4, for 10 min, and overlain for 30 min with fluorescein isothiocyanate-conjugated rabbit antihuman IgG, IgA, IgM, C3 and fibrinogen (Dako patt., Copenhagen, Denmark). Thereafter, section slides were incubated in a humidified chamber at room temperature, washed twice with PBS for 10 min, and mounted with a medium before being viewed under a fluorescent microscope. DIF patterns were interpreted according to the standard criteria.[9] The number of CB were counted in a high-power field (HP) (×400) and recorded as a few (≤5/ HP), many (6-10/ HP) or numerous (≥11/ HP). The intensity was graded in three levels (1+, 2+, and 3+).

Our study was approved by the Siriraj Institutional Review Board, Mahidol University.

Statistical analysis

Comparisons between subgroups of patients according to factors of prognostic value were performed using Chi-square test or Fisher exact test for categorical variables.

RESULTS

Five hundred and two patients (375 females and 127 males), age 6-87 years, were included in this study. The final diagnoses were classified into five groups including interface dermatitis, vasculitis, autoimmune vesiculobullous diseases, panniculitis and scleroderma/morphea as shown in Table 1. Interface dermatitis comprises LE, LP, EM and dermatomyositis. In the LE group, the diagnoses included LE-specific skin lesions and LE-non-specific skin lesions.

Table 2 shows the distribution of immunoreactants in discoid lupus erythematosus (DLE), LP and EM. We included only DLE (61 cases), which is the prototype of interface dermatitis, to analyze the significance of CB in this group. The data of dermatomyositis were not used in the analysis because there were only two cases. CB deposit in addition to dermoepidermal junction (DEJ) deposit [Figure 1] was the most common pattern in DLE and LP; whereas, CB deposit alone was the most common form in EM. IgM was the most common class of Ig deposited at CB in DLE, LP and EM in all patterns. The brightest intensity of IgM was detected in 37.9% of LP, followed by 26.2% of DLE and 20% of EM. The highest quantity of CB was detected in LP, in all classes of Ig except C3 [Table 3].

Table 4 shows details of the immunoreactant deposit at the various locations in other groups. CB deposit alone

Table 1: The final diagnoses of enrolled cases (n = 502)

Diagnoses	Cases* / n@ (%)	Cases* / n# (%)
Interface dermatitis	223 / 502 (44.4)	223 / 516 (43.2)
Lupus erythematosus	128	128 / 314
Discoid lupus erythematosus (DLE)	61	61 / 150
Lichen planus (LP)	58	58 / 108
Erythema multiforme (EM)	35	35 / 74
Dermatomyositis	2	2 / 20
Vasculitis	220 / 502 (43.8)	220 / 620 (35.5)
Leukocytoclastic vasculitis	157	157 / 516
Henoch-SchÖnlein purpura	40	40 / 58
Periarteritis nodosa	23	23 / 46
Autoimmune vesiculobullous disease	21 / 502 (4.2)	21 / 238 (8.8)
Bullous pemphigoid	11	11 / 118
Pemphigus vulgaris	6	6 / 92
Pemphigus foliaceous	2	2 / 14
Linear IgA bullous dermatosis	1	1 / 10
Lichen planus pemphigoides	1	1 / 4
Panniculitis	19 / 502 (3.8)	19 / 164 (11.6)
Scleroderma / Morphea	11 / 502 (2.2)	11 / 22 (50)
Others	8 / 502 (1.6)	8 / 88 (9.1)
Eczema	6	6 / 40
Sweet's syndrome	1	1 / 26
Pigmented purpuric dermatosis	1	1 / 22

Cases*: Cases that direct immunofluorescence (DIF) studies showed positive immunoreactant at colloid bodies (CB), n@: Enrolled cases, n#: Total cases of DIF studies

Table 2: Distribution of immunoreactants in the interface dermatitis group

Location	Number (%)			
	DLE (n=61)	LP (n=58)	EM (n=35)	*P* value*
CB alone	3 (4.9)	17 (29.3)	17 (48.6)	< 0.05
CB+ DEJ	33 (54.1)	36 (62.1)	8 (22.9)	
CB + DEJ + SBV	25 (41.0)	5 (8.6)	8 (22.9)	
CB + SBV	0	0	2 (5.7)	

DEJ: Dermoepidermal junction, SBV: Superficial blood vessel, *Comparison of immunoreactant deposit patterns between DLE and LP only

Table 3: Quantity of CB in the interface dermatitis group

	Quantity	%		
		DLE	LP	EM
IgG	Few	14.8	15.5	14.3
	Many	0	3.5	2.9
	Numerous	0	0	0
IgA	Few	26.2	32.8	20
	Many	8.2	12.1	2.9
	Numerous	0	1.7	0
IgM	Few	54.1	44.8	54.3
	Many	21.3	31.0	14.3
	Numerous	6.6	17.2	2.9
C3	Few	27.9	46.6	28.6
	Many	1.6	10.3	20
	Numerous	1.6	1.7	5.7

Few: ≤ 5/ high-power field, Many: 6-10/ high-power field, Numerous: > 11/ high-power field

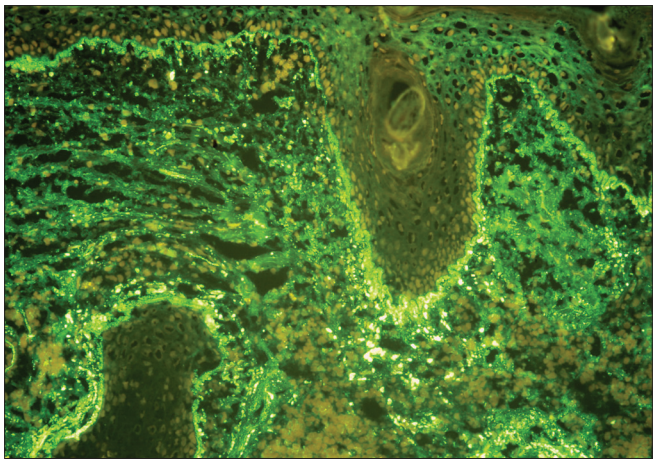

Figure 1: Photograph shows immunoreactant deposits at CB and DEJ (×400)

Table 4: Distribution of immunoreactants in the other groups

Location	Numbers (%)				
	Vasculitis (n=220)			Panniculitis (n=19)	Scleroderma / Morphea (n=11)
	LCV (n=157)	HSP (n=40)	PAN (n=23)		
CB alone	4 (2.5)	0	6 (26.1)	13 (68.4)	6 (54.5)
CB + DEJ	1 (0.6)	0	1 (4.3)	5 (26.3)	3 (27.3)
CB + DEJ + BV	79 (50.3)	10 (25)	11 (26.1)		
CB + BV	73 (46.5)	30 (75)	5 (21.7)		

LCV: Leukocytoclastic vasculitis, HSP: Henoch-SchÖnlein purpura, PAN: Periarteritis nodosa, BV: Blood vessel

was found in panniculitis, scleroderma/morphea, periarteritis nodosa (PAN), and leukocytoclastic vasculitis (LCV) in 68.4%, 54.5%, 26.1%, 2.5% of cases, respectively; whereas, it was not detected in Henoch-SchÖnlein purpura (HSP. Immunoreactants at CB plus DEJ was more commonly found in interface dermatitis (77/154 = 50%) than vasculitis (2/220 = 0.9%), pannicultis (5/19 = 26.3%), or scleroderma/ morphea (3/11 = 27.3%) ($P < 0.05$).

The most common immunoreactant deposit at CB in all diseases was IgM.

The brightest intensity of IgM (3+) was found in 43/154 cases (27.9%), 10/220 cases (4.5%), and 1/21 cases (4.8%), of interface dermatitis, vasculitis and autoimmune vesiculobullous disease, respectively. Moreover, there was no intensity grading of 3+ in panniculitis and scleroderma/morphea. Regarding the quantity of CB, the interface dermatitis group had the highest amount when compared to other groups (vasculitis, autoimmune vesiculobullous diseases, panniculitis and scleroderma/morphea) (data not shown in the Table).

DISCUSSION

Our study demonstrated immunoreactant deposit at CB in a wide variety of diseases, which is in agreement with previous studies.[1,2,5-7,10,11] Previous studies proposed that CB was usually detected in interface dermatitis and might increase the index of suspicion for LE and LP.[7] Interestingly, our study showed that CB was commonly detected in interface dermatitis and vasculitis. However, the intensity and the number of CB in interface dermatitis were higher than those of vasculitis.

In LE and LP, which sometimes are an overlapping syndrome and difficult to differentiate, DIF can be used as an additional diagnostic clue. In our study, CB alone was more common in LP than DLE [Table 2]. More numerous CB were detected in LP than DLE, which supports the claim that CB in LP have

a tendency to cluster in groups of 10 or more in the papillary dermis.[4,7,12] A brighter intensity of IgM was also noted.

In cases that CB deposits were detected in combination with deposition at the other sites, the combination of CB with DEJ was the most common pattern in patients with LE and LP. Previous studies reported that fibrinogen was the most common immunoreactant deposit at DEJ in LP at a high percentage (91-100%).[5,6,13,14] Igs (IgG, IgA, IgM and C3) deposited at DEJ ranged from 16-47%.[5] Kulthanan *et al*. reported that IgG was the most common immunoreactant at DEJ in DLE.[11] The second most common deposit at the DEJ was IgM, which tended to exhibit a strong intensity in association with LE.[15-17] Considering all the results, we suggest that any immunoreactant deposit at CB plus fibrinogen deposition, whether alone or combined with other immunoreactants at DEJ, favors LP. Meanwhile, the deposition of any immunoreactant at CB plus IgG or intense IgM at DEJ, favors LE. Among cicatricial alopecia caused by LP, LE, lichen planopilaris (LPP) and Pseudopelade of Brocq (PB), DIF findings in LP consisted of IgM deposit at CB and fibrinogen deposit at the DEJ; whereas, Ig deposit at the DEJ in a granular pattern was commonly found in LE.[18] Merheregan *et al*. reported that the DIF studies in LPP, follicular lichen planus of the scalp, and LP were similar.[19] With regard to PB, DIF often showed negative results or occasionally demonstrated IgM at the DEJ. Thus, CB plus different immunoreactants' deposit at the DEJ is helpful in the diagnosis of LP, LE and cicatricial alopecia caused by LE, LPP and PB.

Finan *et al*. showed that the combination of CB plus DEJ was the most common DIF pattern in EM.[8] They correlated the findings of DIF and histopathologic findings. In the epidermal pattern, CB was present in all specimens, whereas in mixed patterns, approximately equal fluorescence of CB and DEJ were indicated. The EM in our study was of epidermal pattern in 91.4% (32/35). Thus, the most common pattern of our study was CB alone, which differs from the previous study by Finan *et al*.[8]

The quantity and intensity of CB in interface dermatitis was higher than in other groups. Surprisingly, immunoreactants' deposit at CB alone was detected in more than 50% of panniculitis and scleroderma/morphea. CB plus DEJ was detected most commonly in the interface dermatitis group. Basically, the diagnoses of some diseases of the autoimmune vesiculobullous group require immunoreactants at DEJ. Therefore, we did not compare this pattern with autoimmune vesiculobullous diseases.

The most common immunoreactant deposit at CB was IgM, in our study. These findings were consistent with those reported by other investigators.[20] Thus, we concluded that the most common immunoreactant of CB might be IgM in all diseases.

Other diseases in our study which revealed CB deposits were eczema, Sweet's syndrome, and pigmented purpuric dermatosis. Within our review, additional diseases reported by other studies to have CB deposits included lichen planopilaris,[19] desquamative gingivitis,[21] ashy dermatosis,[22] necrolytic migratory erythema,[23] elastosis perforans serpiginosa,[24] rheumatoid arthritis,[25] cutaneous amyloidosis,[26] pityriasis lichenoides et varioliformis acuta,[2,7] pernio,[7] ulcer,[7] actinic cheilitis,[7] acute generalized exanthematous pustulosis,[7] drug reaction with eosinophilia and systemic symptoms,[7] granulomatous rosacea,[7] lichen striatus,[7] prurigo pigmentosa,[7] pyoderma gangrenosum,[7] toxic epidermal necrolysis,[2,7] herpes zoster,[7] herpes simplex,[7] varicella,[7] dermatitis herpetiformis,[2] porphyria cutanea tarda,[2] sarcoidosis,[2] subcorneal pustular dermatosis,[2] keratosis follicularis Darier,[2] familial benign chronic pemphigus,[2] transient acantholytic dermatosis Grover,[2] epidermolytic hyperkeratosis,[2] polymorphic actinic eruption,[2] and even normal skin.[27]

In conclusion, we propose the diagnostic value of CB in DIF study as follows: (1) Immunoreactant deposits at CB alone can be found in various diseases but a strong intensity and high quantity favor interface dermatitis. (2) CB plus DEJ is more common in interface dermatitis than any other disease (not including autoimmune vesiculobullous disease). (3) Between LP and DLE, CB alone is more common in LP; whereas CB plus DEJ and superficial blood vessel (SBV) is more common in DLE. The most common pattern in both diseases is CB plus DEJ. The quantity and intensity of CB in LP is higher than in DLE.

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