

Clear Cell Papulosis of the Skin

Dr. W. K. Fung

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and both axillae (Figure 1). No lesion was found along the milk lines. The number of skin lesions was about 70. There was no other associated skin lesion such as café-au-lait spot.

CASE SUMMARY

History

A 1-year-old boy who was born in Hong Kong presented with multiple asymptomatic white macules over the lower abdomen and suprapubic area at the age of 5-months-old. Later, the lesions also appeared over both axillae. However, each individual lesion remained static in size. His past health was unremarkable. He had two elder sisters. Both his sisters and the parents were unaffected.

Physical examination

Multiple, small, hypopigmented macules or barely palpable papules, varying from 2 to 5mm in diameter were found over the lower abdomen, suprapubic area

Differential diagnosis

The differential diagnoses included post-inflammatory hypopigmentation, plane warts, hypomelanotic tinea versicolor, chickenpox scars, idiopathic guttate hypomelanosis, anetoderma, papular elastorrhesis and clear cell papulosis of the skin.

Skin biopsy

Skin biopsy showed focal papillomatosis and acanthosis of the epidermis. Isolated larger clear cells with hyperchromatic nuclei and abundant pale cytoplasm were found in the basal layer of the epidermis (Figure 2). The cells stained positive for CEA (Figure 3) but negative for S100. The dermis was unremarkable. The diagnosis was compatible with clear cell papulosis of the skin.



Figure 1: Multiple small white macules were found over the abdomen

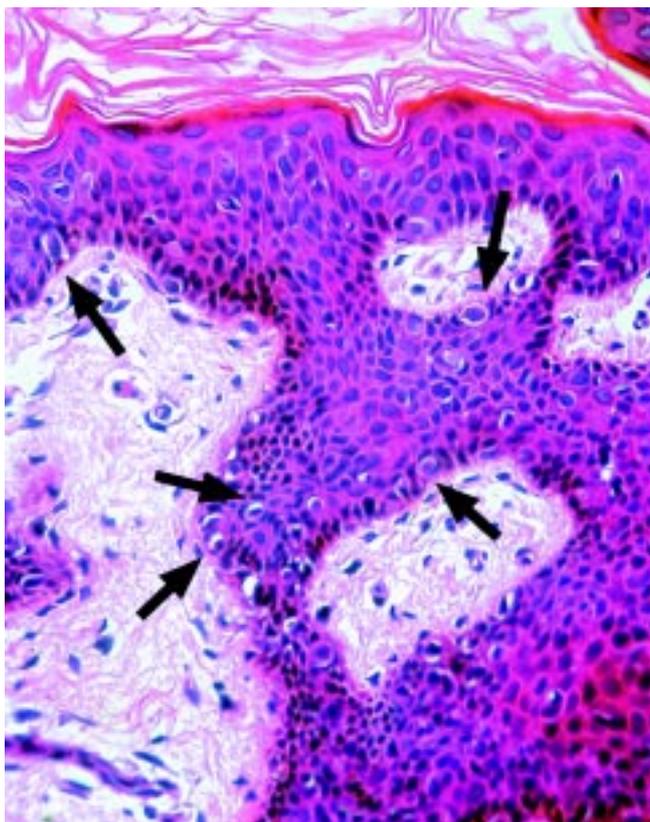


Figure 2: High power photomicrograph (400x) showing isolated large clear cells with hyperchromatic nuclei and abundant pale cytoplasm (arrows). (By courtesy of Dr. W. Y. Lam, SYPPI; and Dr. K. C. Lee, Department of Pathology, PMH)

Management

The skin lesions gradually increased in number from about 20 over the suprapubic area to about 70 scattering over both axillae over the 6 months' period after the onset. Since then, the number and the morphology of lesions remained static. In view of the benign nature of clear cell papulosis of the skin, no medication was prescribed and the parents were reassured.

REVIEW ON CLEAR CELL PAPULOSIS OF THE SKIN

Clear cell papulosis of the skin is a new entity first described by Kuo et al in 1987.¹ A total of 11 patients (10 Taiwanese, 1 Korean), all from Asia, have been reported ever since.¹⁻⁵ A summary of the clinical features of the 12 patients (11 reported patients and our patient)

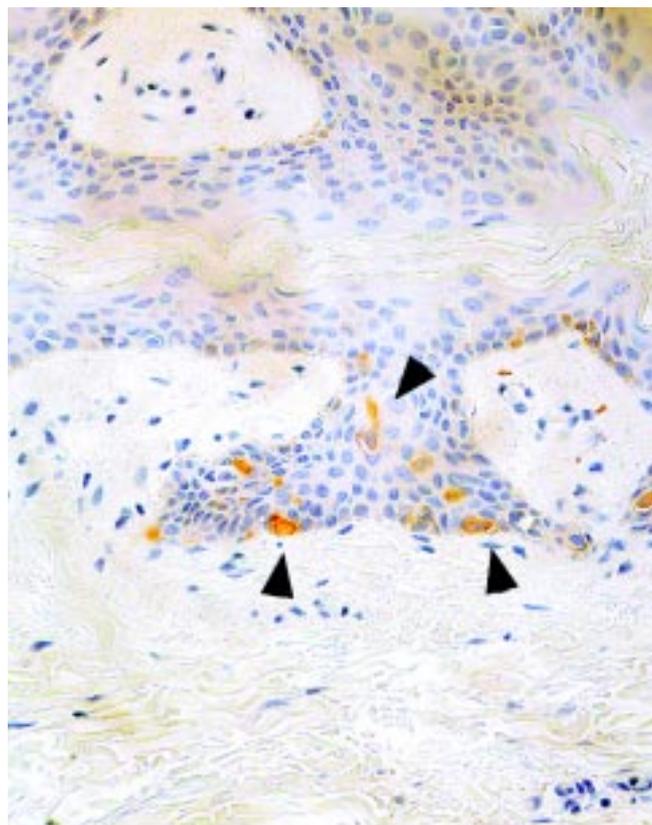


Figure 3: The cells are immunoreactive for carcinoembryonic antigen (CEA) (arrow heads). (By courtesy of Dr. W. Y. Lam, SYPPI; and Dr. K. C. Lee, Department of Pathology, PMH)

is shown in table 1. It occurs in early childhood (9 months to 5 years) and is characterized clinically by multiple small, whitish or hypopigmented macules or papules first noted on the lower abdomen. It may be found symmetrically along the milk lines. The number of skin lesions ranges from 5 to more than 100. The occurrence of this condition in two siblings in the earlier report of Kuo et al suggested that the condition could be hereditary.¹ However, no additional evidence for this is obtained in our patient.

Histopathological findings

The main findings on the H&E sections are slight acanthosis and the presence of solitary, benign-appearing clear cells in the hypopigmented epidermis. The cells are slightly larger than the adjacent keratinocytes and have abundant clear cytoplasm and round or oval, pale nuclei (pagetoid). These cells are mostly located in the basal layers of the epidermis. There

Table 1. Clinical features of the 12 patients with clear cell papulosis of the skin

Authors	Patients / Race	Age of onset / sex	Number / size	Location	Associated condition
Kuo et al 1987 ¹	Patient 1 Taiwanese	9 mths / M	5 / 3-6 mm	Chest, lower abdomen	Café-au-lait spots on lower abdomen
	Patient 2 Taiwanese	3 yrs / M	15/4 - 10 mm	Lower abdomen, chest and shoulder	Café-au-lait spots on lower abdomen
Kuo et al 1995 ²	Patient 3 Taiwanese	2 yrs / M	5/2 - 5 mm	Lower abdomen	_____
	Patient 4 Taiwanese	3 yrs / F	20/2-3 mm	Lower abdomen, lateral anterior aspect of chest	_____
	Patient 5 Taiwanese	26 mths / M	> 100/2-3 mm	Lower abdomen, inguinal area	_____
Huang et al 1997 ³	Patient 6 Taiwanese	ND	ND	ND	ND
Kim et al 1997 ⁴	Patient 7 Korean	8 mths / F	Numerous / 2-3 mm	Lumbar area, buttock	_____
Lee et al 1998 ⁵	Patient 8 Taiwanese	2 yrs / F	100 / 1-6 mm	Axillae, chest, abdomen, inner upper thighs, pubis	Growth and mental retardation, café-au-lait spot, thinning of scalp hair
	Patient 9 Taiwanese	20 mths / F	A few / 1-2 mm	Pubis	_____
	Patient 10 Taiwanese	2 years / M	A few / 1-4 mm	Lower abdomen, pubis	_____
	Patient 11 Taiwanese	21 mths / F	Many / 1-3 mm	Axillae, chest, abdomen, pubis	_____
Present case	Patient 12 HK Chinese	5 mths / M	70 / 2-5 mm	Lower abdomen, pubis, axillae	_____

N. B. Patient 1 and patient 2 were brothers
 Patient 8 and patient 9 were sisters and they had an unaffected elder brother
 ND: not described

is no obvious nest or glandular formation and no mitotic figure is observed.

Histochemical and immunohistochemical findings

All clear cells are stained by the low-molecular-weight anti-cytokeratin antibody AE1, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), and gross cystic disease fluid protein-15 (GCDFFP-15). This suggests that the clear cells are eccrine or apocrine secretory cells in the epidermis. These cells are similar to vacuolated melanocytes but

show negative staining by Fontana-Masson stain. Also, they are not Langerhans cells or histiocytes because of the negative staining for S100 protein or lysozyme. Reduced or absence of melanization in the epidermis of the lesions is noted but the number of basal melanocyte appears normal.

Electron microscopy

The clear cells are non-keratinocyte, non-melanocyte and non-Langerhans in nature, and are larger than the adjacent keratinocytes. They are pale, round or oval, situated mainly in the basal layer and are connected

to the adjacent keratinocytes by small desmosomes. The nuclei are pale and the cytoplasm are abundant and contain a big clump of mucin granules, most of which are disintegrated with fluffy or reticulated contents.

Histogenesis of the epidermal clear cells

Histopathologically, the clear cells are analogous to Toker's clear cells of the nipple.⁶ Toker's clear cells of the nipple are incidental microscopic findings from mastectomy specimens or autopsy material and do not represent a clinical entity. The presence of lesions along the milk lines also supports their relation to Toker's clear cells. Toker also suggested that the clear cells in the nipple might represent abortive mammary differentiation within the basal layer during embryonic or postnatal life. He speculated that the discovery of these benign pagetoid clear cells in the nipple epidermis might provide an anatomical basis for the development of Paget's disease as a primary intraepidermal malignancy. As the clear cells resemble Paget's cells of extramammary Paget's disease, some authors extend the hypothesis of Toker and suggest that the clear cells may represent the benign counterpart potential precursor cells of extramammary Paget's disease.

Clear cell papulosis of the skin: can it be the precursor lesion to Mammary Paget's Disease (MPD) and Extra-Mammary Paget's Disease (EMPD)?

Can these hypopigmented macules represent potential precursor lesions to EMPD and MPD in some patients? Depigmented macules or patches had been reported to be the sole, early clinical manifestation in two patients with EMPD.^{7,8} As EMPD and MPD usually occur in late adulthood, a life-long follow up of patients with clear cell papulosis of the skin is required. Practically, the differential diagnoses of such lesion include early lesions of MPD and EMPD, in addition to chicken pox scars, hypomelanotic tinea versicolor, anetoderma, post-inflammatory hypopigmentation, vitiligo, idiopathic guttate hypomelanosis and papular elastorrhesis.

Prognosis

The ultimate fate is unknown. The lesions tend to increase in number gradually over the first 2 to 3 years after birth. All the reported patients are under 3-4 years of age, and some authors presume it may disappear before adulthood. This condition may be overlooked or misdiagnosed in adults, particularly when the lesions are fewer in number and their milk-line distribution is not readily appreciated clinically. The association between clear cell papulosis and the café-au-lait spots is also unknown.

Learning points:

Clear cell papulosis of the skin is a benign disease with multiple white macules / papules presented in early childhood.

References

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