Clear Cell Papulosis in Hispanic Siblings

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Background: Clear cell papulosis is a rare condition that has been reported in 14 children, all but 1 of whom are of Asian descent. It was first described in 1987 and is thus named because of the presence of clear cells in the epidermis.

Observation: We describe the cases of 3 Hispanic children in the United States with clear cell papulosis. All 3 patients presented with multiple grouped, oval, hypopigmented macules and flat papules in the suprapubic area and trunk. Histopathologic examination revealed characteristic clear cells within the basal layer and Malpighian layer.

Conclusions: Clear cell papulosis is a unique entity with most cases reported in patients of Asian heritage. The characteristic cells have histologic and immunohistochemical similarities to Paget cells and Toker clear cells of the nipple, although the exact relationship to these cells is not clear. The natural history of clear cell papulosis is unknown; thus, continual surveillance for development of extramammary Paget disease is suggested.

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Clear Cell Papulosis (CCP) was first described in 1987 in 2 young brothers from Taiwan. There have been 12 subsequent reports, 1 from Europe and the rest from Asia. Clear cell papulosis is characterized by multiple hypopigmented macules and flat papules distributed most commonly over the lower abdomen and along the milk line. Histologically, diagnostic clear cells are present predominantly in the basal layer and less frequently in the suprabasal layer. We present the first report, to our knowledge, of Hispanic children with CCP in the United States.

REPORT OF CASES

CASE 1 AND CASE 2

An 18-month-old Hispanic boy presented with a 10-month history of asymptomatic white spots in the suprapubic area and axillae. His 6-year-old sister had developed similar white spots on the anterior trunk and pubic area over the past month. Both patients were otherwise healthy. The parents were not consanguineous, and there was no family history of a similar eruption.

Physical examination of the boy revealed multiple (approximately 50) grouped oval to round hypopigmented macules and minimally palpable flat-topped papules ranging in diameter from 1 to 4 mm and located in the suprapubic area and axillae (Figure 1). A few small macules were noted on his lower abdomen. The surfaces of the lesions were flat and smooth. His sister had similar lesions in the suprapubic area and on the lateral aspects of the trunk. Findings from a potassium hydroxide preparation from the macules were negative for organisms. A skin biopsy specimen was obtained from a lesion in the inguinal area and sent for routine histopathologic and immunohistochemical analysis.

Histopathologic analysis revealed scattered enlarged cells with pale eosinophilic cytoplasm and lobulated nuclei within the basal layer and occasionally within the Malpighian layer (Figure 2A). Adjacent keratinocytes showed decreased melanin pigment. The pale cells were strongly positive by immunoperoxidase reaction for high-molecular-weight cytokeratin, carcinoembryonic antigen, and cytokeratin 7 (Figure 2B). They were negative for S100 and CD1a protein. Findings from a mucicarmine stain were negative, but the pale cells were positively periodic acid–Schiff without diastase and negative with diastase.

CASE 3

Ten months after the first 2 patients were seen, a healthy 2-year-old Hispanic boy...
presented with a 1-month history of asymptomatic white spots in the diaper area. Physical examination revealed hypopigmented macules and flat papules in the inguinal and suprapubic area. A few similar lesions were located symmetrically on the abdomen and below the right axilla. Findings from a skin biopsy specimen from the inguinal area showed large cells with clear to slightly eosinophilic cytoplasm in the basal and spinous layers. These cells stained positively for carcinoembryonic antigen, cytokeratin 7, epithelial membrane antigen, and mucicarmine and negatively for CD1a and S100 protein.

Clear cell papulosis has been reported in 13 patients from Asia, including Taiwan, Korea, China, India, and Singapore, and 1 from Italy.1-8 The clinical findings in our patients were quite similar to those in prior reports. The most commonly affected sites are the pubic area, lower abdomen, and anterior trunk, although one of the previous cases had lesions only over the lumbar back and buttocks.3 The lesions seem to follow the milk line. They are hypopigmented macules or barely palpable papules, 1 to 10 mm in diameter, numbering anywhere from a few lesions to around 100. The number of lesions seems to increase gradually over time.3 Clear cell papulosis presents in early childhood, at an age range of 4 months to 5 years in the cases reported, with a single case reported in an adult.3,8 It has been reported in 3 pairs of siblings, including our patients, suggesting a genetic predisposition.1,3

The most characteristic histologic feature of CCP is the presence of clear cells among the basal keratinocytes. The cells are round, with ample clear cytoplasm, and larger than the adjacent keratinocytes. Their nuclei are pale and sometimes grooved. In addition, positive staining for cytokeratin, carcinoembryonic antigen, and epithelial membrane antigen helps establish the diagnosis of CCP. Positive findings for gross cystic fluid disease protein and cytokeratins CAM5.2 and CK 7 has been reported in a few cases but is not mentioned in others.1,3 Because of this staining pattern, the clear cells are thought to be of eccrine or apocrine origin. Because staining for gross cystic fluid disease protein is inconsistent and staining for carcinoembryonic antigen has been demonstrated in all cases reported, an eccrine origin is thought to be more likely. Another study10 demonstrated that the clear cells stain with IKH-4 and CAM5.2 but not with lysozyme, further supporting an eccrine origin. Mucin stains are usually positive in CCP. Among our cases, mucicarmine staining varied from negative to positive, although periodic acid–Schiff staining was weakly positive. In 1 other reported case, findings were negative for mucin, and not all of the reported cases mention mucin staining. Therefore, the relevance of mucin in making this diagnosis is unclear. The large clear cells are differentiated from Langerhans cells and melanocytes by negative staining for S100. They are further differentiated from Langerhans cells with negative staining for CD1a protein. Decreased melanin pigmentation of the basal layer compared with adjacent normal epidermis has been demonstrated in some cases.3,4 The melanocytes appear to be normal, and the reason for the hypopigmentation is unknown.

Similar clear cells have been found in the epidermis of the nipple and were described by Toker in 1970.10 They have been demonstrated in up to 83% of normal nipples at autopsy using immunohistochemical analysis. They are also found in accessory nipples, and thus it is speculated that they are a normal component of the epidermis.
along the milk line. There seems to be a histologic and immunohistochemical similarity between the clear cells of CCP and both Toker cells and Paget cells. All stain positively for cytokeratin, carcinoembryonic antigen, and epithelial membrane antigen and negatively for S100. Clear cells of CCP are positive for cytokeratin 7, which is also positive in Paget cells and Toker cells with a high degree of sensitivity. Toker cells do not stain with mucin stains, whereas Paget cells do. The CCP cells in most reported cases are positive for mucin, but the staining is variable. Because of these histological and immunohistochemical similarities, it has been hypothesized that Toker cells and clear cells of CCP may be a benign counterpart or precursor of primary intraepidermal Paget disease or of extramammary Paget disease, which tends to be distributed along the milk line, with most cases in the groin and axillae. This is also where CCP and Toker cells may be found. It is possible that clear cells of CCP are the link between Toker cells, which are known to be a benign component of nipple epidermis, and Paget cells, which are malignant.

There is no known treatment for CCP. Because the lesions were asymptomatic in both of our patients, no treatment was offered. The prognosis of the disease is unknown because there are no follow-up or long-term reports in the literature. Although there is no definitive evidence that CCP is a precursor of primary intraepidermal Paget disease or extramammary Paget disease, continued surveillance is suggested.

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