A Case of Congenital Self-Healing Reticulohistiocytosis

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Congenital self-healing reticulohistiocytosis (CSHRH) is a rare Langerhans cell disorder usually showing spontaneous resolution within 3-4 months. By electron microscopy, the identification of Birbeck granules and laminated dense bodies in the infiltrated cells is mandatory for the diagnosis of CSHRH. However, in some reported cases, Birbeck granules could not be demonstrated and only cytoplasmic dense bodies were seen. If the lesion is more advanced, Birbeck granules are transformed to lysosomes, i.e., 'unique phagosomes', in which they are degraded.

A 2-month-old Korean girl presented with congenital, numerous red-brown pigmented papules on the left side of trunk and upper extremity without systemic symptoms. A biopsy specimen demonstrated papillary dermis containing epidermotropic infiltrates of histiocytes with abundant eosinophilic cytoplasm. Some had kidney-shaped nuclei and PAS-positive cytoplasmic inclusions. Immunohistochemically, infiltrating cells expressed S-100 protein and ultrastructurally, no Birbeck granules but many dense laminated bodies and unique phagosomes were found. It was ten months since the skin lesions developed that they have started resolving.

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Key Words : Congenital self-healing reticulohistiocytosis, Laminated dense body, Unique phagosome

Congenital self-healing reticulohistiocytosis (CSHRH), first described in 1973 by Hashimoto and Pritzker, is a benign condition usually present at birth[1]. It consists of multiple disseminated papulonodular skin lesions of varying sizes. Occasionally, only solitary nodules are seen[2]. It usually completely regresses within 12 months[3]. Hashimoto noted that the presence of Birbeck granules and laminated dense bodies together in the same cell is highly diagnostic of CSHRH[2] and in most cases of CSHRH, Birbeck granules are identified in only a small percentage of cells. However, two cases of CSHRH without Birbeck granules, only showing laminated dense bodies, were reported in the English literature[4,5].

In Korea, there were 3 reported cases[6-8]. Two of these cases showed Birbeck granules and laminated dense bodies and 1 case showed only Birbeck granules. All the lesions of these cases spontaneously regressed between 1 week and 3 months.

We report a case of CSHRH which has abundant unique phagosomes without Birbeck granules. The skin lesions in our case persisted longer than most of the cases reported previously.

CASE REPORT

A 2-month-old girl presented with numerous red-brown pigmented papules on the left side of the trunk and the left upper extremity which had been present since birth(Fig. 1.). She had no fever and no mucosal lesion. Neither hepatosplenome-

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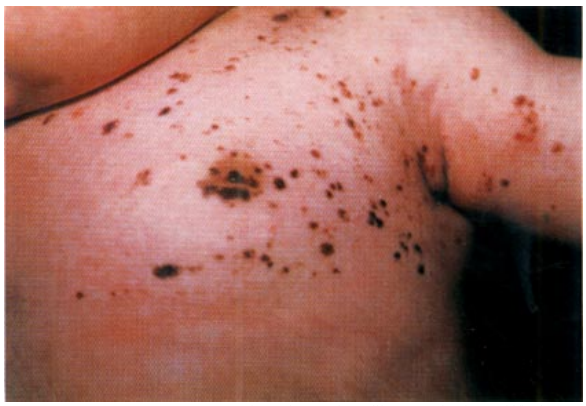

Fig. 1. Numerous red-brown pigmented papules on the left side of trunk and left upper extremity.

galy nor lymph node enlargement was present, and the infant was in otherwise excellent health. Laboratory studies including complete blood cell count, differential count and chest x-ray were normal. On the basis of clinical findings, a diagnosis of incontinentia pigmenti was suspected. We performed an incisional biopsy of the lesion in the shoulder. Hematoxylin and eosin-stained sections of biopsy revealed papillary dermis containing epidermotropic infiltrates(Fig. 2a.). At higher magnification, infiltrates consisted of pale histiocytes with kidney-shaped nuclei, reticulohistiocytes with abundant, eosinophilic, 'ground-glass' cytoplasm, and multinucleated histiocytes(Fig. 2b.). Infiltrating cells surrounded adnexal structures without destroying. Some cells contained Periodic acid-

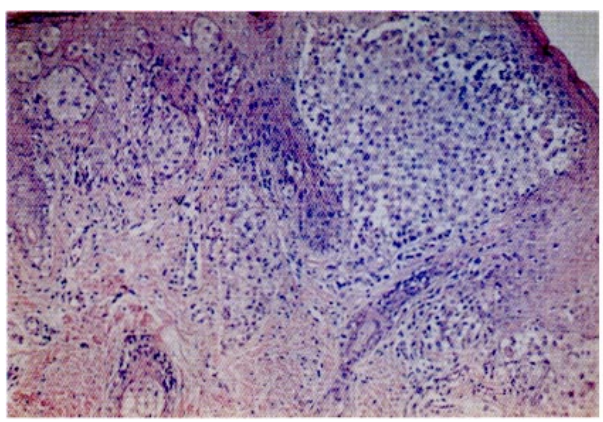

Fig. 2a. The dermal papillae are filled with reticulohistiocytes. (H&E, ×100).

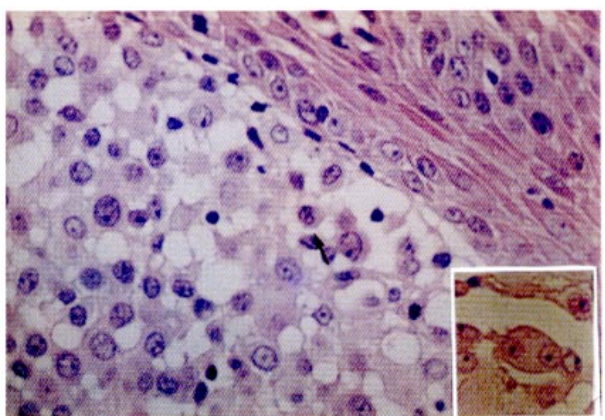

Fig. 2b. The infiltration consists of pale histiocytes with kidney-shaped nucleus(arrow), reticulohistiocytes with abundant eosinophilic cytoplasm and multinucleated histiocytes(inlet). (H&E, ×400).

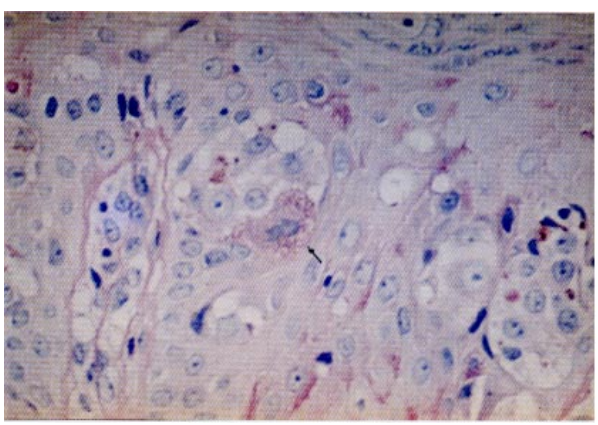

Fig. 2c. PAS-positive materials(arrow) in the cytoplasm of infiltrating cells. (PAS, ×400).

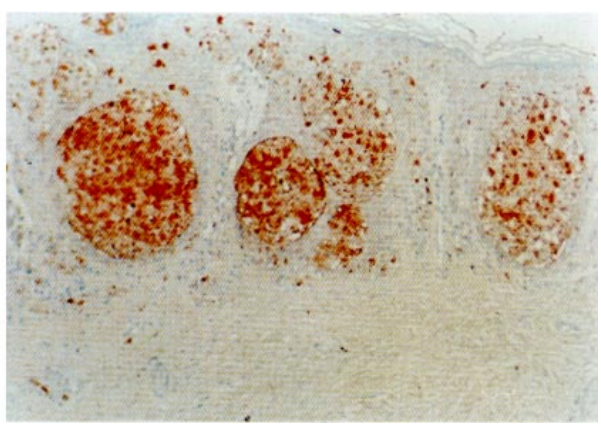

Fig. 2d. The infiltrating cells react strongly to S-100. (S-100, ×100).

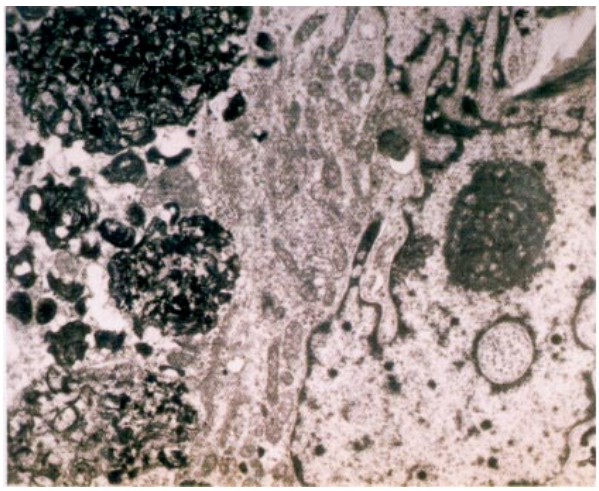

Fig. 3a. The infiltrating cells show indented nucleus and numerous dense bodies in the cytoplasm. (EM, × 10,400).

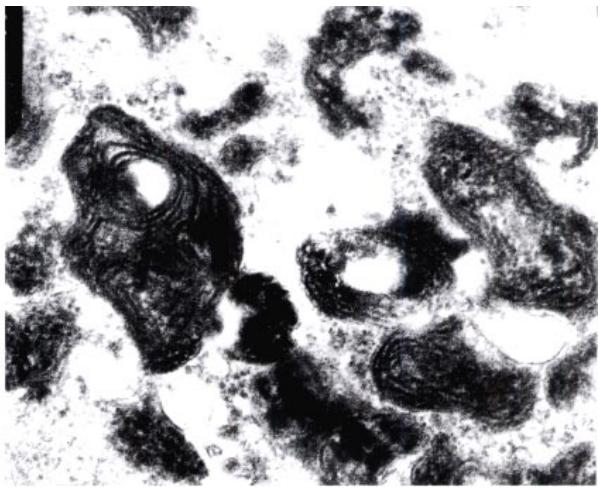

Fig. 3b. Numerous unique phagosomes, which have lamellar structure inside. (EM, ×59,500).

Schiff(PAS)-positive material in the cytoplasm(Fig. 2c.). The infiltrating cells were strongly reactive to S-100(Fig. 2d). Increased reticulin fibers surrounding tumor islands were not prominent. Ultrastructually, the infiltrating cells had elongated, convoluted nuclei and numerous dense bodies in the cytoplasm(Fig. 3a). At higher magnification of the dense bodies, they showed laminations and there were "unique phagosomes", i.e., rounded, membrane-limited bodies that disclosed lamellar structure(Fig. 3b). In spite of an intensive search, no well-formed Birbeck granules were seen; only some vesicular structures were found. According to these results, we diagnosed this case as CSHRH. It was 10 months since the skin lesions developed before they have started resolving. Now as a 1-year-old girl, she has residual skin lesions, decreasing in size and number, without systemic symptoms and developmental abnormalities.

DISCUSSION

Since Hashimoto and Pritzker first reported a case of CSHRH, over 40 cases[9,10] have been described. According to Hashimoto et al.[6,11], diagnostic criteria for CSHRH consist of the following: (1) congenital or perinatal occurrence of multiple dermal nodular lesions that are brownish pink or dusky red and have a generalized distribution; (2) dermal infiltration of large histiocytic cells with eosinophilic cytoplasm and with diastase-resistant inclusions that are positively stained with PAS reagent; (3) eosinophils that are usually admixed, with increased reticulum fibers surrounding large tumor cells, and an epidermis that is usually infiltrated and often ulcerated; and (4) ultrastructurally, 10% to 25% of large tumor cells that are Langerhans cells with Birbeck granules, most of these Langerhans cells containing, in addition, myelin-figured dense inclusions. In our case, the lesions were present at the time of birth in a healthy baby without systemic symptom. They were presented as brownish dusky colored multiple papules and histologically, histiocytic cells with eosinophilic cytoplasm infiltrated the papillary dermis with PAS-positive inclusions, but no eosinophilic infiltration or proliferating reticulin fiber was found. On the electron microscopic exam, there were no Birbeck granules but numerous laminated dense bodies and "unique phagosomes" in the cytoplasm of the infiltrating cells. Dense bodies having myelin-like concentric lamination, were thought to have originated from degenerated mitochondria by Hashimoto[12] and to herald cell death and subsequent resolution. In contrast to Hashimoto's theory, Schaumburg-Lever et al.[4] suggested that Birbeck granules be transformed or give rise to laminated dense bodies. Thus the laminated dense bodies are lysosomes containing partially degraded Birbeck granules. So cells which have dense bodies are Langerhans cells and not indeterminate cells since the latter do not contain Birbeck granules. Also they suggested that

the possibility that intact Birbeck granules in the dermal infiltrate can be found depends on the age of the individual lesion. If the lesion is more advanced, i.e., is resolving, all Birbeck granules have been transformed and are no longer visible. There were two reported cases of CSHRH without showing Birbeck granules. In those two cases[4,5], the lesions completely resolved in 1 month after biopsy, but our case has just started resolving 8 months after biopsy. We suppose that the specimen we examined for electron microscopy is too small to show various stages or there is a somewhat special process generating dense bodies without relation to disease evolution in CSHRH.

The most alarming feature of CSHRH is its close pathologic resemblance to classical histiocytosis X. It is practically indistinguishable from histiocytosis X on routine microscopy. Absence of systemic involvement should always raise the possibility of CSHRH. Immunohistochemically, CSHRH cells generally show the phenotype of Langerhans cells and strong positive staining for S-100 protein, as in the case of classical histiocytosis X. Important differences between CSHRH and classical histiocytosis X can be seen on electron microscopy[2]. Most significant is the relative paucity of Birbeck granules, which are present in only a small percentage of the CSHRH cells (5-40%) but are evident in over 50% of cells in Letterer-Siwe disease. Regular laminated dense bodies are more commonly seen in CSHRH. Indeterminate cell histiocytosis can have the same features as CSHRH in clinical and pathological aspect, but no Birbeck granules or dense bodies are found in the electron microscopic examination. A constant and characteristic feature of CSHRH is its tendency towards spontaneous regression[13]. From our references, skin lesions disappear absolutely before 3 months old, and usually before 10 months. Our patient's skin lesions showed no change until 10 months of age and then gradually resolved; we suggest that long-term follow-up is necessary.

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