Indeterminate cell histiocytosis is a very rare proliferative disorder of histiocytes which displays both langerhans cell histiocytosis and non langerhans cell histiocytosis immunophenotypic features. The majority of the patients develop multiple lesions which are clinically indistinguishable from generalized eruptive histiocytosis. We report a 14-year-old girl with multiple papules on the face, scalp and trunk.

Keywords: indeterminate cell histiocytosis, langerhans cell histiocytosis, proliferative disorder

INTRODUCTION

The histiocytoses represent a group of proliferative disorders that are grouped into langerhans cell (LCH) and non langerhans cell histiocytosis (Non-LCH). Clinical and pathological evaluations are essential for differential diagnosis of these entities. Indeterminate cell histiocytosis is extremely rare and has no apparent sexual predilection. The disorder occurs in adults, adolescents and infants, and a congenital form has also been reported. The pathogenesis of indeterminate cell histiocytosis is unknown. However, it has most recently been speculated that indeterminate cells are dendritic cells en route from the skin to the regional lymph nodes. Therefore, indeterminate cell histiocytosis may represent a group of proliferating cells which have lost their capability to move as veiled cells from the skin through the lymphatics. The question has also been raised as to whether this disorder is actually a separate entity or represents various macrophage disorders identified at various time points in the inflammatory response. While most cases of indeterminate cell histiocytosis have involved the trunk and extremities, the isolated disease of the face and neck has been described. Both a generalized form and a solitary form have been documented. Ulceration can occur. As lesions age, they become brown to yellow. The course may wax and wane, although most patients experience partial or complete regression of lesions. Mucous membrane involvement has not been observed. However, ocular involvement has been described, and visceral involvement and death have been reported in two instances. The histologic picture is quite variable. Most commonly, a monomorphous infiltrate of mononuclear cells intermingled with some giant cells and foamy cells is found.

The immunophenotype of indeterminate cell histiocytosis demonstrates characteristics of both LCH and non-LCH. Lesional cells show expression of S100, CD la, HAM56, CD68, Mac387, lysozyme, ai-antitrypsin, HLA-DR, CD11c, CD14b and factor XIIIa. The ultrastructural features of the histiocytes in indeterminate cell histiocytosis are similar to those seen in Langerhans cells except that no Birbeck granules are found. We herein report a 14-year-old girl with multiple erythematous papules who was finally diagnosed with indeterminate cell histiocytosis.
CASE REPORT

A 14-year-old girl presented with an 18-month history of progressive developing small, scattered lesions on the face, scalp and trunk. Eighteen months ago, some macular and popular lesions appeared on the patient’s face; then, the lesions slowly but progressively developed elsewhere on the body. These lesions were neither painful nor itchy. Her personal history revealed that she was treated with prednisolone (20 mg/daily) and azathioprine (50 mg/daily) for 4-months one year ago. Lesions completely disappeared but recurred after she discontinued drugs. Family history was negative.

On physical examination, multiple brown to reddish and slightly elevated papules were observed on her face (frontal, temporal, periauricular) and scalp along with 2-3 papules on her trunk, ranging from 2-10 mm in diameter. The lesions showed a remarkable tendency to coalesce (Figure 1, 2).

Laboratory examination revealed normal routine hematology, urinalysis, serum biochemistry, erythrocyte sedimentation rate and serum lipid.

Chest X-ray and abdominal ultrasound did not show any abnormalities.

Biopsies of the lesion showed uniform infiltration of histiocytes and few lymphocytes and macrophage in the superficial and mid dermis without epidermotropism or atypia (Figure 3). Immunohistochemistry studies revealed neoplastic cells expressing markers characteristic of both Langerhans cells (CD1a, S-100) and focal monocytes/macrophages (CD68) (Figure 4).

DISCUSSION

Clinically, among non-X histiocytoses, the most likely diagnosis of our patient was generalized eruptive histiocytosis, established by exclusion of other non-X histiocytoses. Benign cephalic...
Indeterminate cell histiocytosis was ruled out because of the age of the patient. Lipidic histiocytosis (papular xanthoma, xanthoma disseminatum and juvenile xanthogranuloma) were excluded in view of the colour of the lesions and the absence of foamy cells. Multicentric reticulohistiocytosis usually starts in the fourth to sixth decades of life, but the absence of arthropathy and acral lesions, together with the lack of giant cells with ground-glass cytoplasm on biopsy, dismissed this possibility. When IHC was performed and S100, CD1a, CD68 were found to be positive, our diagnosis changed to indeterminate cell histiocytosis.

Indeterminate Cell Histiocytosis (ICH) is a rare disorder in which histiocytic cells proliferate, expressing markers of both X- and non-X histiocytosis. Nevertheless, it is not totally clear if both types of markers are co-expressed by the same cells in this disorder or on the contrary, the histiocytosis is made of two phenotypically different types of cells. Fernandez-Flores et al, reported a 74-year-old male who presented multiple yellowish papules on his chest, back and both arms. Their results with the double stain for CD1a and CD68 demonstrated that most of the histiocytes expressed either one marker or the other. Nevertheless, some of the histiocytes of the infiltrate co-expressed both markers. Although CD1a was mainly expressed by the cells at the top of the dermis, some cells of the deep dermis kept expressing this marker. The cells expressing both markers were mostly found in the top part of the dermis. Rezk et al, reported the clinical, morphologic, immunophenotypic, and ultrastructural features of 5 ICT cases. Four of the 5 patients were female, and 4 of 5 were older than 68 years. They suggest that ICT seems to be a rare neoplasm that can occur de novo or in association with a B-cell lymphoma, possibly as a result of B-cell dedifferentiation caused by relatively unknown mechanisms. Our patient was evaluated carefully for this possibility but all laboratory investigations were within normal ranges. In addition, the spontaneous resolution does not support an underlying disease. Wang et al, presented an otherwise healthy 36-year-old woman in whom asymptomatic generalized papules and nodules appeared on all four extremities, the trunk, and cheeks in the previous 6 months. Manente et al, reported a 64-year-old woman with a 3-year history of multiple reddish-brown, slightly yellowish papules on her face and neck. The lesions were painless and nonpruritic and varied from 1 to 5 mm in diameter. Histological and immunohistochemical examination of cutaneous biopsies revealed a diagnosis of indeterminate cell histiocytosis. Sidoroff et al, reported an otherwise healthy 50-year-old woman with a
6-month history of more than 100 generalized, non-confluent, reddish-brown, partially yellow-colored papules; her diagnosis was indeterminate cell histiocytosis. There are also considerable similar reported cases.

In conclusion, we report a new case of ICH, a rare non-X histiocytosis, with some clinical and histological peculiarities. Although most of the patients undergo spontaneous involution, careful follow-up of all patients with indeterminate cell histiocytosis is recommended because visceral involvement and leukemia can occur.

REFERENCES