Benign Cephalic Histiocytosis in Singapore – A Review of 8 Cases
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ABSTRACT

Aim of Study: Benign cephalic histiocytosis (BCH) is a rare, benign, self-healing papular eruption that affects mainly children. The aim of this study was to characterise our Singapore children affected by this condition and to review some of the recent literature on non-Langerhans cell histiocytoses.

Methodology: The case records of all cases of BCH seen between January 1990 and December 1996 in our centre were retrieved and analysed. Further details not available in the case records were obtained via a telephone interview with the patients or their parents.

Results: A total of 8 cases were seen. There was no sex preponderance or ethnic predilection. The average age of onset was 29 months. All patients began with small brownish papules on the face and sometimes the upper trunk, and most of the lesions regressed in less than 84 months.

Conclusion: BCH is a benign non-Langerhans cell histiocytosis in which spontaneous resolution is the rule. A small skin punch biopsy is simple, diagnostic and helpful in its management. The management of BCE is expectant and reassurance is sufficient. However the regression and resolution of the lesions may take up to several years.

Keywords: brownish papules, non-Langerhans cell histiocytosis, benign, self-healing

INTRODUCTION

Benign cephalic histiocytosis (BCH) is a rare, benign, and self-healing papular eruption that is classified as a non-X histiocytosis. It was first reported by Gianotti et al in 1971(1). Since then about 25 cases have been reported in the literature worldwide. The etiology and pathophysiology of this condition is still poorly understood except for the fact that it is a benign histiocytic proliferation. It is uncommon and therefore easily mistaken for other more common skin diseases seen in children.

METHODS AND MATERIALS

This study covers all cases of BCH seen between January 1990 and December 1996 in our centre. Patients’ case records were retrieved and the following data were noted: age of onset, sex, ethnic group, morphology of lesions, site of involvement and progression of disease.

RESULTS

A total of 8 cases were seen during this period of study. The age of onset ranged from 3 months to 6 years (average of 29 months). There was an equal number of boys and girls affected, with 4 Chinese, 3 Indians and one Malay (Table I) seen.

The typical morphology of the lesions observed were that of yellow to brown glistening papules 2 mm to 4 mm in diameter (Fig 1). These papules first erupted on the face in all our patients. Subsequent extension to the trunk was seen in 3 patients with patient no. 1 experiencing further extension to the lower limbs.

The diagnosis of BCH was confirmed by skin biopsy in 5 patients. In the remaining patients, permission was not granted by the parents for skin biopsy.

Routine haematoxylin and eosin staining of skin biopsy specimens showed a collection of histiocytic cells in the upper and mid dermis forming a slightly dome-shaped papule (Fig 2). The histiocytic cells contained pink cytoplasm and oval to slightly indented nuclei with inconspicuous nucleoli. Non-specific infiltrates of eosinophils, neutrophils and lymphocytes may be present. The overlying epidermis may be slightly atrophic, especially in the larger lesions.

Three patients (patient nos. 8, 3, 9) had total clearance of all lesions by 9, 26 and 78 months respectively. Patient nos. 5, 1, and 2 had a good degree of clearance of lesions by 27, 77 and 84 months respectively. Only 1 patient (no. 6) still had persistent lesions while one (patient no. 4) was lost to follow-up subsequently.

Fig 1
Table I – Summary of the 8 cases of BCH

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age of onset (mths)</th>
<th>Sex</th>
<th>Race</th>
<th>Morphology</th>
<th>Initial site</th>
<th>Extension</th>
<th>Skin biopsy</th>
<th>Present outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>Male</td>
<td>Malay</td>
<td>Brownish papules</td>
<td>Face</td>
<td>Chest, legs</td>
<td>BCH</td>
<td>60% – 70% clearance by 77 months</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>Male</td>
<td>Chinese</td>
<td>Yellowish papules</td>
<td>Face</td>
<td>Trunk</td>
<td>BCH</td>
<td>Lesions much flatter by 84 months</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>Female</td>
<td>Chinese</td>
<td>Brownish papules</td>
<td>Face</td>
<td>None</td>
<td>Not done</td>
<td>All lesions cleared by 26 months</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>Female</td>
<td>Indian</td>
<td>Brownish papules</td>
<td>Face</td>
<td>None</td>
<td>BCH</td>
<td>Uncontrollable</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>Female</td>
<td>Indian</td>
<td>Brownish papules</td>
<td>Face</td>
<td>None</td>
<td>Not keen</td>
<td>80% – 90% clearance by 27 months</td>
</tr>
<tr>
<td>6</td>
<td>66</td>
<td>Female</td>
<td>Chinese</td>
<td>Brownish papules</td>
<td>Face</td>
<td>Neck, chest</td>
<td>BCH</td>
<td>Still present (for 12 months)</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>Male</td>
<td>Chinese</td>
<td>Yellowish papules</td>
<td>Face</td>
<td>None</td>
<td>BCH</td>
<td>All lesions cleared by 78 months</td>
</tr>
<tr>
<td>8</td>
<td>39</td>
<td>Male</td>
<td>Chinese</td>
<td>Yellowish papules</td>
<td>Face</td>
<td>None</td>
<td>Failed attempt</td>
<td>All lesions cleared by 9 months</td>
</tr>
</tbody>
</table>

Table II – Clinical, histopathologic and ultrastructural features of BCH, JXG and GEH in comparison

<table>
<thead>
<tr>
<th>Disease</th>
<th>Benign cephalic histiocytosis</th>
<th>Juvenile xanthogranuloma</th>
<th>Generalised eruptive histiocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions</td>
<td>Macules, papules</td>
<td>Papulonodular</td>
<td>Papules</td>
</tr>
<tr>
<td>Localisations</td>
<td>Head, upper trunk, shoulders</td>
<td>Disseminated</td>
<td>Trunk and proximal part of extremities</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Visceral involvement</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Non-X, nonlipid S100-negative histiocytic infiltrate</td>
<td>Touton giant cells, foam cells, inflammatory infiltrate</td>
<td>Non-X, nonlipid, S100-negative histiocytic infiltrate</td>
</tr>
<tr>
<td>Electron microscopy</td>
<td>Coated vessels, 5% – 30% with comma-shaped bodies</td>
<td>Fatty droplets without limiting membrane; cholesterol clefts; occasionally comma-shaped bodies</td>
<td>Many dense and many regularly laminated bodies; occasionally comma-shaped bodies</td>
</tr>
<tr>
<td>Course</td>
<td>Self-healing</td>
<td>Self-healing</td>
<td>Self-healing</td>
</tr>
</tbody>
</table>

DISCUSSION

BCH characteristically begins as an eruption of flat-top papules 2 mm to 3 mm in diameter, with colour ranging from yellow to brown to skin colour[1]. These are usually asymptomatic and present at age ranging from 2 months to 34 months (average of 10 months), with a male to female ratio of 2.12:1[2]. In our series, the average age of onset was older, at 29 months, with an equal sex incidence.

The initial site of presentation commonly involves the face — forehead, eyelids and cheeks. Subsequent sites include the ears, neck and scalp. More than half of the patients have lesions on parts of the body other than the head, neck and shoulders and extension to the buttocks and thighs have been reported[3,4]. The palms and soles are spared. Mucosal or visceral involvement has not been reported so far and the general health of patients is unaffected.

The lesions begin to regress after a variable length of time ranging from 8 to 48 months[5], and complete resolution may take up to 54 to 72 months[6], leaving behind post-inflammatory pigmented macules.

Light microscopy of lesion stained with haematoxylin and eosin reveals a well-circumscribed lichenoid infiltrate of histiocytic cells in the upper and middle dermis. Recently, some authors described 3 possible distinct patterns of histiocytic proliferation namely "papillary dermal", "diffuse" and "lichenoid"[7]. In the papillary pattern, pleomorphic histiocytic cells with large, non-foamy eosinophilic cytoplasm and hyperchromatic, sometimes indented nuclei with huge nucleoli can be seen. In the diffuse pattern, round and regular histiocytic cells are noted to have scanty cytoplasm loosely proliferated among collagen bundles intermingled with sparse lymphocytes. In the lichenoid pattern, small histiocytic cells are seen admixed with small lymphocytes and several foamy cells. Histologically, BCH shows features overlapping with generalised eruptive histiocytosis (GEH) and juvenile xanthogranuloma (JXG). Therefore these authors believe that perhaps BCH is a localised form of GEH or an aborted phase of JXG. In immunochemistry studies, the histiocytic cells in BCH are positive for OKM1 and LeuM3 while negative for S100 and OKT6[8] (the latter two being markers for Langerhan cells).

Under electron-microscopy, BCH was first described as a "histiocytosis with intracytoplasmic worm-like bodies" due to the presence of coated vesicles and comma-shaped bodies[9,7]. Numerous coated vesicles measuring about 100 nm in diameter with bristle coats on their cytoplasmic surfaces can be found in the histiocytic cells, sometimes along desmosome-like junctions. Caputo and Gianotti[10] suggested that these vesicles are involved in the formation of the intercellular junctions, a specific feature not observed in other types of histiocytoses. BCH is also characterised by worm-like bodies or comma-shaped bodies found in 5% – 30% of the histiocytic cells, and these consist of 2 electron-dense membranes 60 nm in thickness separated 80 nm apart. Their functions are poorly understood. The absence of Birbeck granules in BCH is typical of non-Langerhans cell histiocytoses.

Some of the important clinical differential diagnoses to be considered would include plane warts,
Langerhans cell histiocytosis, urticaria pigmentosa, micronodular form of JXG and GEH. For example, patient no. 6 was diagnosed as having facial plane warts by the primary health physician. Sometimes it can be difficult to differentiate plane warts from BCH lesions but the diagnosis can be easily confirmed by histology. Langerhans cell histiocytosis may present with papular eruptions on the scalp and trunk but the lesions are usually more florid and pleomorphic with papules, scaling, crusting and petechiae. Moreover, there may be other systemic symptoms such as fever, malaise and failure to thrive. An early diagnosis here is essential as it may involve multiple organs including the eyes and bones. Langerhans cell histiocytes stain positively for S100 and OKT69,10, and ultrastructurally Birbeck granules are present. Lesions of urticaria pigmentosa would immediately urticate on rubbing (positive Darier’s sign). Histology will show a mast cell infiltrate that stains metachromatically with toluidine blue and Giemsa.

In 1986, in a single largest series of BCH cases ever reported, Gianotti and Caputo16 concluded that combination of clinical, histopathologic and ultrastructural features can distinguish JXG and GEH from BCH (Table II). The lesions in the micronodular form of JXG are always papulonodular and may be disseminated over the entire body, with occasional ocular involvement. Multinucleated Touton’s giant cells and foam cells are seen under light microscopy, and lipid droplets can be seen ultrastructurally11. GEH occurs mainly in adults12-14 but is occasionally seen in children15-17. It differs from BCH in that there may be mucosal involvement, and ultrastructurally there is absence of coated vesicles, comma-shaped bodies and desmosome-like junctions.

Nevertheless there are authorities who believe that BCH and GEH are different variants of the same disease17,18 specifically BCH, being a localised form of GEH16. Likewise JXG and BCH are also believed to be the same disease19 because the initial stages of JXG may reveal presence of coated vesicles and comma-shaped bodies and absence of foamy cells in the histiocytes20-22. It could be that BCH is an aborted form of JXG20,23.

The usual benign course of non-Langerhans cell histiocytoses such as BCH is indicative of a reactive process rather than a neoplastic process. However, the trigger factor remains unknown in BCH. Superantigens24 introduced through focal injuries (such as insect bites, folliculitis or trauma) have been implicated.

CONCLUSION
In conclusion, BCH is a benign non-Langerhans cell histiocytosis in which spontaneous resolution is the rule. A small skin punch biopsy is both simple and diagnostic. The management of BCH is expectant and reassurance is sufficient. However the regression and resolution of the lesions may take up to several years.

REFERENCES