was no evidence of a local factor that could have lead to the condition.

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Ulcerated Giant Juvenile Xanthogranuloma Accompanied by Hyperlipidaemia

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Sir,
Juvenile xanthogranuloma (JXG) is a tumour frequently seen in childhood and is one of the most common non-Langerhans' cell histiocytoses. It is believed that JXG occurs without any metabolic disorder such as hyperlipidaemia. The macronodular form of JXG has a high tendency to ulcerate. We recently studied a rare case of ulcerated giant JXG accompanied by hypercholesterolaemia.

CASE REPORT

A 4-month-old female infant was taken in for examination of three, gradually enlarging nodules on her scalp and umbilicus. Two months earlier, two pea-sized dome-shaped nodules with yellow to pale red hues were initially noticed on the left temporal and umbilicus regions. One month later, a new dome-shaped nodule, yellow in colour, was found on the left frontal region of the scalp. Two nodules on the temporal and umbilicus became eroded and bled. The baby was delivered normally at term, and physical and mental development was normal. No particular diseases, such as diabetes mellitus, hypertension, hyperlipidaemia or malignant tumour, were found in the patient's or the family past medical history.

Physical examination revealed that this baby suffered from three discrete nodules on the left temporal, left frontal region of the scalp and umbilicus. Each nodule showed different clinical features. The largest one was on the umbilicus and showed a sessile, exophytic, round tumour, measuring $15 \times 15 \times 8$ mm, with a red–brown hue and partial ulceration. The temporal nodule was an ulcerated, dome-shaped tumour, measuring 12 mm in diameter, with a central excoriation covered by a black crust and a brownish yellow halo. The frontal one was a yellowish dome-shaped tumour measuring 8 mm in diameter. The mucous membranes were unaffected. Ophthalmologic examination was normal. The infant had no adenopathy or organomegaly.

The laboratory investigations revealed hyperlipidaemia: serum cholesterol 368 mg/dl (normal upper limit 220 mg/dl), serum triglyceride 136 mg/dl (normal upper limit 160 mg/dl), serum HDL-C 51 mg/dl (normal 40–70 mg/dl), estimated serum LDL-C 344 mg/dl (normal upper limit 130 mg/dl), serum ß-lipoprotein 884 mg/dl (normal upper limit 628 mg/dl). Endocrine functions (GH, ACTH, TSH, cortisol, free T_3 and T_4), erythrocyte sedimentation rate, full blood count, liver and renal function tests were all within the normal range. Chest and abdominal X-rays were normal. Abdominal ultrasound, computed tomography and magnetic resonance imaging showed no internal lesions.

A skin biopsy was taken from the eroded larger nodule on the temple. Hematoxylin and eosin-stained sections revealed a dense, diffuse infiltration composed of monotonous histiocytes intermixed with lymphocytes throughout the dermis. The histiocytes were distributed more compactly from the middle to deep dermis. Many discrete adipocytes were found in this lesion. The majority of the histiocytes had slightly lobulated nuclei and vacuolated cytoplasm. Neither giant cells nor foam cells

were found. The epidermis overlying the granuloma was atrophic and hydropic degeneration was remarkable with lymphocytic invasion. Immunohistochemical studies were carried out on formalin-fixed paraffin sections of the skin sample with an indirect immunoperoxidase method. The majority of the tumour cells infiltrated were positive for CD68 and a few for lysozyme. The tumour cells had no labelling for CD1a, S100 protein, CD34 or CEA. Ultrastructural study revealed no Birbeck granules in the tumour cells.

The patient was treated with antibiotic ointment. All the tumours reached maximum size one year from onset. The frontal, temporal and umbilical lesions reached $16 \times 16 \times 5$ mm, $22 \times 22 \times 8$ mm and $35 \times 35 \times 18$ mm, respectively. At that time, the frontal nodule rapidly began to regress and became a brownish-yellow atrophic plaque at 15 months from onset. The remaining two nodules accompanied by lasting ulcerations showed only slight regression and exhibited a dermatofibroma-like appearance.

DISCUSSION

Typical JXG shows a dense, diffuse infiltration of spindle or epitheloid cells, including obvious foamy histiocytes, Touton giant cells and, occasionally, mitoses. In rare cases, these foamy cells and giant cells may be absent or inconspicuous. The tumour cells in the present case had a characteristic of $CD68^+$/lysozyme$^+$/$S100^-$/$CD1a^-$/$CD34^-$/CEA^-/Birbeck granule$^-$ phenotype. We therefore diagnosed them as a vacuolated type of JXG with inconspicuous foam cells and giant cells.

In this case, hypercholesterolaemia was discovered several months after birth. Yamada et al. (1) reported adult xanthogranuloma accompanied by hypercholesterolaemia, but we could find no reports that JXG is complicated by a metabolic disorder such as hyperlipidaemia. It is believed that JXG is a reactive granulomatous response of histiocytes to an unknown stimulus. We therefore believe that the hyperlipidaemia seen in this case may be coincidental to the JXG rather than associated with it. However, the hypercholesterolaemia might affect the tumour growth.

Gianotti (2) distinguished two forms of JXG: a micronodular form and a macronodular form. In the micronodular form, multiple 2–5 mm diameter papules are seen on the upper part of the body. They grow large and become orange or brownish nodules before beginning to involute at approximately 1–1.5 years of age. Ocular involvement is the most common extracutaneous manifestation in this form. In the macronodular form, fewer nodules, which are 10–20 mm in diameter, are seen on the head and trunk. According to Webster et al. (3), patients with the macronodular type of tumour may have mucosal involvement and systemic lesions on the lungs, liver, spleen, testes, ovaries, colon, kidneys, pericardium, and bone. The nodular lesions of the skin tend to flatten out and disappear within 3 years.

About 17 cases of a macronodular form have been reported by Seo et al. and other groups (4–13). Among them, ulcerations were seen in 8 of 17 cases (47%). In 4 of 14 cases (29%), foam cells and giant cells were inconspicuous or absent. Shapiro et al. (14) reported ulceration in 6/17 (35%) of JXG cases with such a histologic feature. Tahan et al. (15) encountered ulceration in 5/34 cases (15%) with similar histologic in 4 of the cases (12%). The epidermotropism of lymphocytic cells were seen in 9 of 32 cases (28%). However, there is no obvious relation between histologic features and ulceration. These findings suggest that the macronodular form of JXG has a high tendency to ulcerate. Although the mechanism of ulceration is not clear, they may occur due to continual rubbing of the lesions.

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