Juvenile Xanthogranuloma

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Abstrak

Latar Belakang: Xantogranuloma juvenil adalah bentuk histiocytosis non-sel-Langerhans atau histiocytosis non-X yang paling sering dijumpai. Sering mengenai bayi dan balita.
Laporan kasus: Suatu kasus xantogranuloma juvenil pada anak laki-laki usia 3 bulan telah dilaporkan. Terdapat nodul berwarna merah kecoklatan, kenyal, multipel, bulat dan oval, berbatas tegas, dengan diameter 0,5-2 cm, tersebar di kulit kepala, wajah, badan, ekstremitas dan genitalia. Sebagian mengalami ulserasi. Tidak ada keterlibatan membran mukosa dan sistemik. Hasil pemeriksaan histopatologik ditemukan sel datia Touton yang khas untuk xantogranuloma juvenil.
Conclusion : Dalam beberapa tahun, lesi dapat mengalami regresi spontan dan meninggalkan area berupa pigmentasi atau skar atrofik.

Katakunci — Xantogranuloma juvenil, nodul merah kecoklatan, sel datia Touton, regresi spontan

Abstract

Background: *Juvenile xanthogranuloma is the most common form of non-Langerhans-cells histiocytosis or non-X histiocytosis. Most often affecting infants and young children.*
Case Report: *A case of juvenile xanthogranuloma in a 3-month-old male infant has been reported. There were multiple, discrete, firm, red-brownish, orange nodules, round and oval in shape, well-defined, 0.5–2 cm in diameter, disseminated on his scalp, face, trunk, upper and lower extremities, also genitalia and some of them with ulceration on its surface. No mucous membrane and systemic involvement. Pathology result revealed Touton giant cells that characteristic to juvenile xanthogranuloma although the other diseases might contain these cells such as Hashimoto-Pritzker disease and dermatofibroma.*
Conclusion: *Within few years, the lesions could regression spontaneously and leaving a flat, atrophic scar or an area of altered pigmentation.*

Keywords— ***Juvenile xanthogranuloma, Touton giant cells, regression spontaneously***

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I. INTRODUCTION

Juvenile xanthogranuloma (JXG) is a benign, self-healing, non-Langerhans-cell (LC) histiocytosis or non-X histiocytosis most frequently seen in infants and children. It is characterized by yellowish papulonodular lesions located in the skin and other organs and consisting of an infiltrate of histiocytes with a progressively greater degree of lipidation in the absence of metabolic disorders.[1]

The frequency is unknown, since lesions occur early in life, may be misdiagnosed and spontaneously regress.2 It has observed 117 cases in the past 30 years.1 In childhood, JXG occurs predominantly in males (1.4:1). Multiple cutaneous lesions occur predominantly in males (12:1). Approximately 35% of cases of JXG occur at birth, with as many as 71% of cases occurring in the first year.

The etiology of JXG is unknown.2-4 The red-to-yellowish papulonodular of JXG represent collections of differentiated non–Langerhans cell histiocytes. The consensus is that the cells of origin are dermal dendrocytes. As postulated, JXG may be a granulomatous reaction of histiocytes to an unidentified stimulus(3) or a non specific tissue injury.[2]

There are several clinical forms of JXG. The papular form is characterized by numerous (>100), firm, hemispheric lesions, 2 to 5 mm in diameter, that are a red-brown color at first and quickly turn yellowish. The nodular form is less frequent and occurs as one or few lesions. Such nodules are generally round, 10 to 20 mm in diameter, translucent, red or yellowish, and may show telangiectases on their surface. Giant JXG is used to indicate lesions larger than 2 cm. Mixed form is characterized by the simultaneous presence of both small and large nodules. En plaque form is used to define a group of JXG lesions with a tendency to coalesce into a plaque. Subcutaneous form consists of a solitary deep-seated congenital or perinatal lesion. 1 to 2 cm in diameter usually located on the head.1 Many extracutaneous sites have been reported.2 There are in oral cavity,5 nasal cavity,6 muscle,7 and eye.8 The eye, particularly the uveal tract, is the most frequent site of extracutaneous involvement. Approximately one half of patients with ocular involvement have skin lesions.[2,8]

The histopathology of early lesions may show large accumulations of vacuolated cells without significant lipid infiltration intermingled with only a few lympho cytes and eosinophils. When no foamy cells or giant cells are seen, the possibility of JXG is often overlooked. In mature lesions, a granulomatous infiltrate is usually present containing foamy cells, foreign-body giant cells and Touton giant cell as well as macrophages, lymphocytes and eosinophils. The presence of giant cells, most of them Touton giant cell (present in 85% of cases), showing a wreath of nuclei surrounded by foamy cytoplasm and eosinophilic cytoplasmic center is quite typical for JXG.2,9 Under the electron microscope, the histiocytes that characterize the early stage of the disease exhibit pleomorphic nuclei, are rich pseudopods and contain many elongated and irregular dense bodies.1 In older lesions there are predominance of foamy cells, the cytoplasm of which is completely filled with lipid vacuoles, cholesterol clefts and myeloid bodies.1,4 Despite the fat-filled histiocytes in the skin, the levels of lipids in the blood are quite normal.4 Immunohistochemistry shows the lesions to be positive for factor XIIIa, CD68, CD163, fascin, and CD14 but negative for S100 and CD1A. This can be used to differentiate these lesions from Langerhans cell histiocytoses.[2]

Clinically, JXG must be differentiated from Hashimoto-Pritzker disease, dermatofibroma, and giant cell

fibroblastoma. Hashimoto-Pritzker disease (HPD) or congenital self-healing reticulohistiocytosis is the benign self-healing variant of Langerhans cell histiocytosis (LCH).10 It is usually present at birth but may not appear until several days or weeks after delivery. Affected infants have scattered papules and nodules.[9] Typically, the disease is characterized by the eruption of multiple disseminated, elevated, firm, red-brown nodules. These lesions can grow in size and number in the first few weeks of life and some may become quite large.[9,10] Large nodules tend to break down in the center and form crater-shaped ulcers.9 This disorder is characterized by lack of systemic involvement and absence of mucous membrane lesions.[10] The lesions begin to involute within 2 to 3 months and usually have completely regressed within 12 months.[9] The histologic picture unite the many varied form of LCD. The key to diagnosis is identifying the typical LCD cell in the appropriate surroundings. The cell has a distinct folded or lobulated, often kidney-shaped nucleus. Nucleoli are not prominent, and the slightly eosinophilic cytoplasm in unremarkable. In the lesions reveal in the dermis numerous foamy cells, as well as varying number of LC and some eosinophils. Multinucleated giant cells are frequently present. They are mainly of the foreign body type but occasionally have the appearance of Touton giant cell.[9] For years the gold standard has been to employ electron microscopy searching for the typical Birbeck or Langerhans cell granules. S-100 and antigen CD1a positive.[9,11]

Dermatofibroma is nodule that occur anywhere on the body surface, with a propensity for the extremities, usually the lower legs. More common in women, they may occur at any age, but most patients present with the lesions in their early twenties. The cause of the tumor is unknown, although trauma, such as insect bites, has been thought to induce some lesions. Characteristically, a dermato fibroma often presents firm, dome-shaped papule to nodule, a few millimeters to several centimeters in size. Hyperpigmentation is common in the center of the lesion or in a ring around a pale center. The color can vary from red to brown, with some lesions appearing yellow to ivory.[12] They may be multiple. Generalized lesions have been described. Usually asymptomatic and may ulcerate following trauma. Some tumors grow very rapidly over a relatively short period, other remain static for many years. Regression may leave an area of hypopigmentation.[13] Histologic feature reveal rather symmetrical proliferation of spindle cells and ovoid cells, usually with a central cellular or sclerotic focus with spindle-shaped cells around it. There are mononucleated and multinucleated large histiocytes with pale cytoplasm. Cholesterol crystals and lipid may also be deposited, giving a few of the multinucleated cells the appearance of Touton giant cells. Mitotic is present.[12]

Giant cell fibroblastoma (GCF) is rare and benign soft tissue neoplasm that usually occurs in children.[14] This is recurring locally aggressive tumor, often several centimeters in diameter, present as an indurated plaque with firm bosselated protuberant varying from flesh color to reddish brown. The shiny, often thin, epidermis may be focally ulcerated. The lesion occurs most commonly on the trunk but may occur in any area of the skin. Some lesions may grow to become large nodular tumors. Lesions recur incessantly if not excised with very wide margin.[13] Histologically, GCF is a tumor of the dermis with a rather myxoid background containing spindle cells and occasional giant cells, but with characteristic stellate clefts lined by multinucleated giant cells and spindle cells. The mitotic rate is low.[14]

Unless they occur in the eyes, JXG are harmless growths and disappear eventually over 2 to 3 years.4 Spontaneous regression leaving a flat, atrophic scar or an area of

altered pigmentation.15 Removal is seldom necessary.[4]

II. CASE REPORT

A 3-month-old male infant admitted to the Hospital with red-brownish lumps that scattered over the body since he was 10 days old. Initially, there appeared a small pimple - insect bite like- on his left cheek. The pimple became larger and wider and formed the lump, red and brownish in color. Along with a time, the number of the lump became more and more that involved his head, trunk and extremities. There wasn't difficult to breathing. There wasn't jaundice history. Defecation and urinate were normal. He had not suffer from the same disease yet before. He didn't have the same disease history in his family. Birth history was normal.

In physical examinations were found mild illness, bodyweight 6,8 kg, body height 62 cm, no cyanosis, no edema. Pulse frequency 100x/mnt, body temperature 370C, breathing 28x/mnt. Head, neck, heart, lung, abdomen, extremities, lymph node gland were in normal limits.

In dermatological state were found red-brownish, orange, firm, discrete nodules, round and oval in shape, well-defined, 0.5–2 cm in diameter, disseminated on his scalp, face, trunk, upper and lower extremities, also genitalia and some of them with ulceration on its surface. Mucous membrane was no lesion.

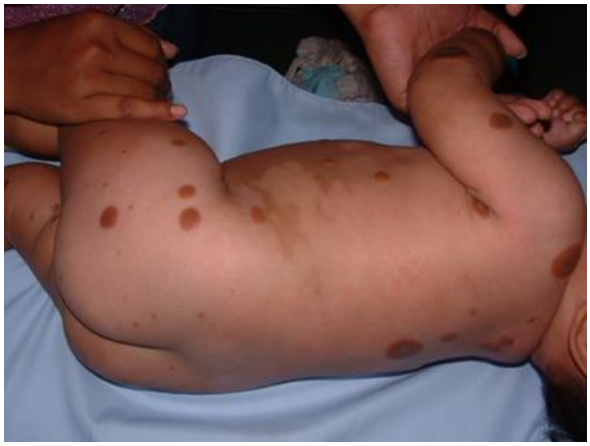

Figure 1. Red-brownish, orange, firm, discrete nodules on his trunk, upper and lower extremities

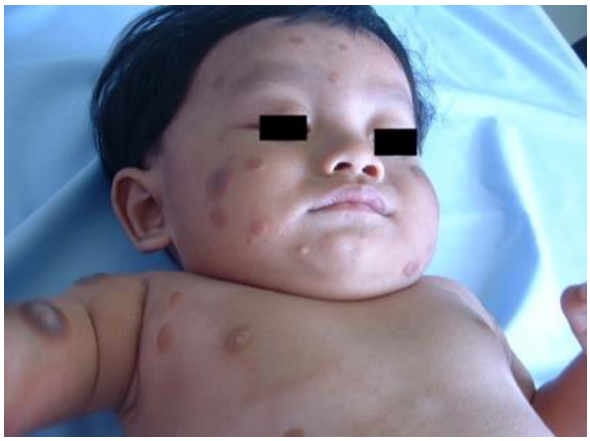

Figure 2. Red-brownish, orange, firm, discrete nodules on his face.

Working diagnosis was Hashimoto-Pritzker disease and differential diagnosis was Juvenile xanthogranuloma, Dermato fibroma, Giant cell fibroblastoma. Routine blood results were Hb 11,1 gr%, Leucocyte 7300/mm2 (5000-10000/ mm2), Diff count 0/1/1/29/65/4 (0-1/1-3/2-6/50-70/20-40/2-8). Urinalisis and defecation were normal limits. Thorax X-ray examination results were in normal limits.

Incisional biopsy result were found beneath epidermis appeared the structure of diffuse pleomorphic cells. There were small, oval and spindle-shape with vesicular nuclei. It was thought histiocyte and the cell infiltrated to deep dermis and subcutaneous tissue. There appeared Touton giant cells. Interpretation was juvenile xanthogranuloma. The diagnosis was

juvenile xanthogranuloma based on histopathology result.

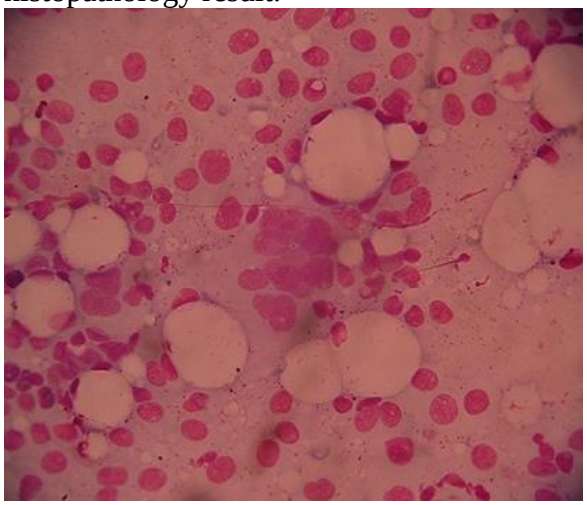

Figure 3. Touton giant cells

III. DISCUSSION

Juvenile xanthogranuloma is benign, self-limited dermatologic disorder of infants, which the frequency is unknown. Clinically, it was difficult to be differentiated from HPD, dermato fibroma and GCF. They appeared in infant with multiple, firm, red-brown and yellow nodules, a few millimeters and centimeters in diameter (table. 1).

TABLE. 1 DIFFERENTIATION OF CLINICAL FINDINGS

Juvenile xanthogranuloma	Hashimoto-Pritzker disease	Dermatofibroma	Giant cell fibroblastoma
Non-Langerhans cell histiocytosis	Langerhans cell histiocytosis	Benign fibrohistiocytic tumor	Fibrohistiocytic tumor with intermediate malignant behavior
Benign, self-healing	Benign, self-healing	May regression	Recurrent
Infant	Infant	Any age, early twenties	Children
Multiple, generalized	Multiple, disseminated	Multiple, generalized, usually lower legs	Any area of the skin, mainly trunk
Firm, red-brown, yellow nodules	Firm, elevated, red-brown nodules	Firm, dome-shaped, red-brown, yellow	Indurated plaque with firm bosselated
		nodules	protuberant vary flesh-color anf reddish brown
A few millimeters and centimeters in diameter	A few millimeters and centimeters in diameter	A few millimeters and centimeters in diameter	A few millimeters and centimeters in diameter
Do not tend to ulcerate	Large nodule tend to break down in center and form ulcers	Ulcerate following trauma	Ulcerated
Extracutaneous involvement	Absent extracutaneous involvement	Absent	Absent

- Working diagnosis was Hashimoto-Pritzker disease. It based on :
- Infant
- Multiple, disseminated
- Firm, elevated, red-brown nodules
- A few millimeters and centimeters in diameter
- Ulcerate
- Absent extracutaneous involvement

After histopathology result, the diagnosis was juvenile xanthogranuloma. Finding of Touton giant cells may exclude the other diseases. Although in HPD and dermatofibroma also is found Touton giant cell, but 85% Touton giant cells is seen in JXG. (Table. 2)

TABLE. 2 DIFFERENTIATION OF PATHOLOGY FEATURES

Juvenile xanthogranuloma	Hashimoto-Pritzker disease	Dermatofibroma	Giant cell fibroblastoma
Touton giant cells (85%) Foamy cells Foreign-body giant cells	Cell with a distinct folded or lobulated, often kidney-shaped nucleus Numerous foamy	Proliferation spindle cells and ovoid cells Touton giant cells (+), if cholesterol crystal and lipid is deposited	Myxoid background containing spindle cells and occasional giant cells Characteristic

	cells Mainly foreign-body giant cells Occasionally Touton giant cells	stellate clefts line by multinucleated giant cells and spindle cells

The ultra structure examination can be used to accurate diagnosis (Table.3). Juvenile xanthogranuloma has S100 protein and CD1a negative. Factor XIIIa negative and doesn't contain Birbeck's granules. Hashimoto-Pritzker disease has S100 protein, CD1a and Birbeck's granules positive and factor XIIIa negative.

In this patient, the lesions were multiple and generalized that involved head, trunk and extremities. It is impossible to be excised. Within 1 to 5 years, the lesions can disappear spontaneously and leaving a flat, atrophic scar or an area of altered pigmentation.

TABLE. 3 DIFFERENTIATION OF ULTRASTRUCTURE EXAMINATION

	JXG	HPD	Dermatofibroma
S100	-	+	-
CD1a	-	+	-
CD68	+	-	+
Lysozyme	+	-	++
α1-antitrypsine	+	-	++
Factor XIIIa	+	-	+
Birbeck's granules	-	+	-

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