Familial sebaceous hyperplasia: A case report.

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ABSTRACT :

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Familial sebaceous hyperplasia is a rare form of sebaceous hyperplasia and predictive late onset genome dermatoses. There are only 15 cases were reported since 1980. Familial variant is more diffuse and early onset. Some genetic diseases are associated with familial sebaceous hyperplasia such as Muir-Torre syndrome and anhidrotic ectodermal dysplasia. We reported a case presented with leonine facies. The dermoscopic and histologic examination are compatible with sebaceous gland hyperplasia. Her family members have been diagnosed as sebaceous hyperplasia as well. She was treated by isotretinoin. The clinical is significantly improved.

Key words: Sebaceous hyperplasia, familial sebaceous hyperplasia, leonine facies

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บทคัดย่อ:

เพ็ญวิภา ตระกูลวรรณชัย, ธนวัฒน์ คูถิรตระการ, รายงานผู้ป่วย FAMILIAL SEBACEOUS HYPERPLASIA วารสารโรคผิวหนัง 2559; 32: 255-261.

สถาบันโรคผิวหนัง กรมการแพทย์ กระทรวงสาธารณสุข

Familial sebaceous hyperplasia เป็นอาการแสดงที่พบได้น้อยมากของ sebaceous hyperplasia. นับตั้งแต่ปี ค.ศ. 1980 มีรายงานผู้ป่วยเพียง 15 ราย อาการแสดงของ familial sebaceous hyperplasia จะเป็นแบบกระจายตัวเป็นจำนวนมากและเกิดก่อนวัยกลางคน และอาจพบสัมพันธ์กับโรคทางพันธุกรรม เช่น Muir-Torre syndrome, anhidrotic ectodermal dysplasia. ผู้เขียนได้รายงานผู้ป่วยหนึ่งรายที่มีอาการแสดงแบบ leonine facies ผลตรวจโดย dermoscopy และผลทางพยาธิวิทยาเข้าได้กับ sebaceous hyperplasia. สมาชิกในครอบครัวผู้ป่วยได้รับการวินิจฉัยว่าเป็น sebaceous hyperplasia เช่นเดียวกัน ผู้ป่วยได้รับการรักษาด้วย isotretinoin หลังได้รับการรักษาอาการดีขึ้นอย่างชัดเจน

คำสำคัญ: ต่อมไขมันเจริญมากกว่าปกติ, ต่อมไขมันเจริญมากกว่าปกติแบบที่มีบุคคลในครอบครัวมีอาการ-เช่นเดียวกัน, leonine facies

Introduction

Familial sebaceous hyperplasia is a rare manifestation of sebaceous hyperplasia. Normally, sebaceous hyperplasia occurs in middle age and increases with time. While the clinical manifestation of familial sebaceous hyperplasia is more diffuse and early onset. The patient with this clinical presentation are needed to be excluded from Muir-Torre syndrome and hypohidrotic ectodermal dysplasia. However, our patient in this report presented with more diffuse lesions, called leonine facies.

Case report

A 44-year-old female presented with numerous yellowish papules on face for 15 years. The lesions were gradually increased in number and extended to neck and chest wall. Lesions on face turned to thick plaques with deep furrow especially on forehead looked like leonine facies. She did not have another skin lesions. She did not have any medical problem or take any medication regularly. Her first and second younger sisters had same lesions as hers but less severe (Fig. 1). There was no significant medical problem and consanguineous marriage in her family.

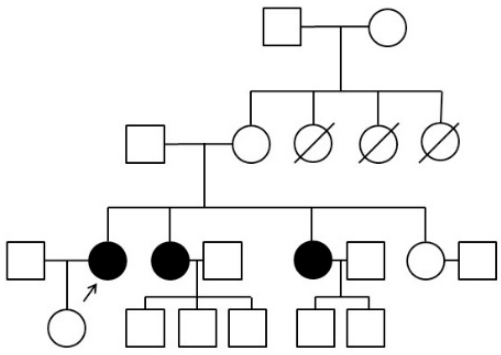

Figure 1 Family pedigree of the patient

Physical examination revealed numerous yellowish dome-shaped papules with central umbilication, confluent to thick plaques with deep furrows, except periorbital and perioral areas (Fig. 2a). Hair, nails and teeth were normal. Dermoscopic examination showed multiple yellow white globules and thin non-arborizing blood vessels (Fig. 2b). Skin biopsy was obtained from the face. Histopathologic examination showed multiple enlarged mature sebaceous gland in dermis (Fig. 3a, Fig. 3b). Immunohistochemistry staining for MutS protein homolog 2 (MSH-2) and MutL homolog 1 colon cancer nonpolyposis type 2 (MLH-1) revealed no loss of nuclear staining (Fig. 3c, Fig. 3d). Colonoscopic examination was normal. The patient was diagnosed as diffuse familial sebaceous hyperplasia.

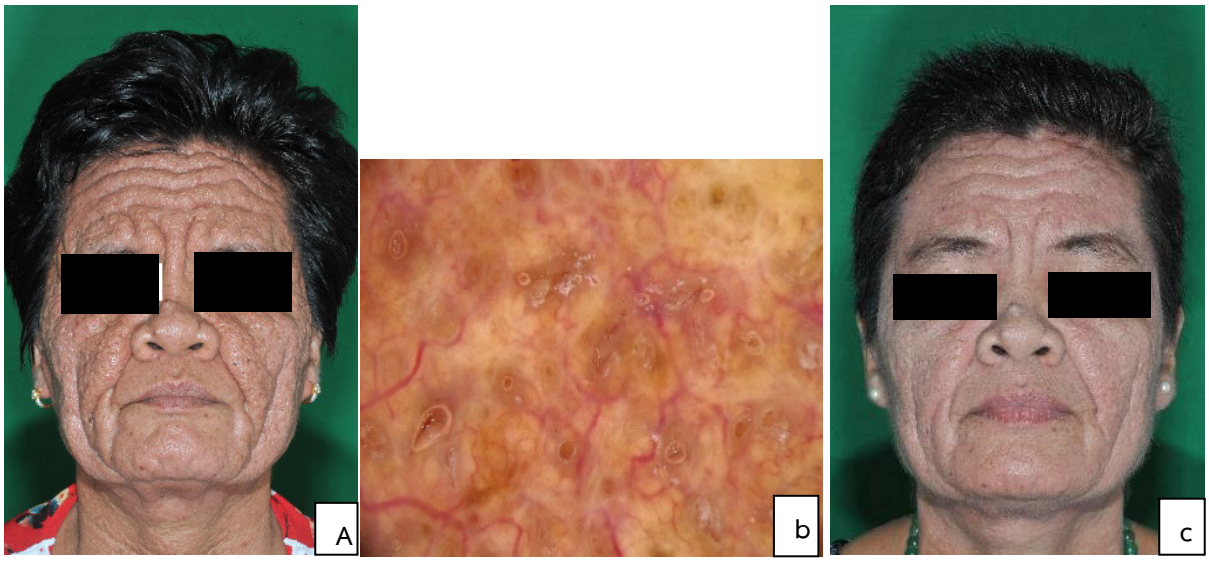

Figure 2 (a) numerous yellowish dome-shaped papules with central umbilication on the face, neck, chest wall some confluent to thickened plaques with deep furrows on the forehead and both cheeks (b)dermoscopic examination showed multiple yellow white globules and thin non-arborizing blood vessels (c) after 12 weeks of Isotretinoin treatment

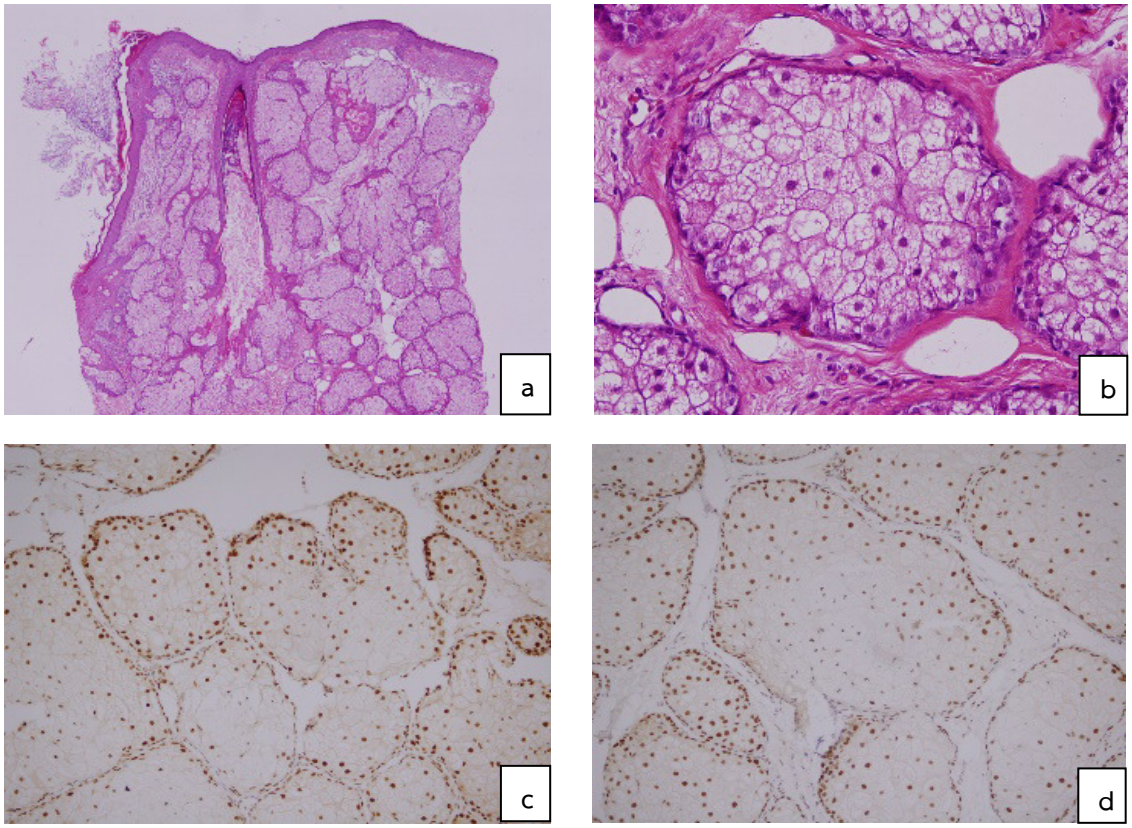

Figure 3 (a) Histopathology at 4x magnification shows differentiated enlarged mature sebaceous gland in dermis. (b) Histopathology at 40x magnification shows one or two layers of undifferentiated basaloid cells at the periphery of sebaceous lobules. (c) MLH-1 immunohistochemistry staining at 40x magnification (d) MSH-2 immunohistochemistry staining at 40x magnification

Table 1 Summary of reported case

Authors, year	Age of onset	Sex	Nationality	Therapy
Dupre, Bonafé, and Lamon (1980)[11]	26	Male	French	Acne therapy; no response
	puberty	Male	French	N/A
Boonchai and Leenutaphong (1997)[12]	15	Male	Thai	Isotretinoin 40 mg/day
	18	Female	Thai	Isotretinoin 20 mg/day
	35	Male	Thai	Isotretinoin
Grimalt, Ferrando, and Mascaro (1997)[13]	20	Female	Spanish	Isotretinoin 1 mg/kg/day
	41 (at visit)	Female	Spanish	Isotretinoin 1 mg/kg/day
	20	Male	Spanish	Isotretinoin 1 mg/kg/day

Authors, year	Age of onset	Sex	Nationality	Therapy
Weisshaar, Schramm, and Gollnick (1999)[14]	Puberty	Male	German	Isotretinoin 0.5 mg/kg/day
	16	Male	German	Isotretinoin 0.5 mg/kg/day
	Puberty	Female	German	Isotretinoin 0.5 mg/kg/day
	25	Female	German	Isotretinoin 0.5 mg/kg/day
Wang W, Qui Y, and Zhang F (2016)[15]	16	Female	Chinese	Isotretinoin 1 mg/kg/day
You-Chen, Yu-Pin, Chuan-I, Chin-Yi and Chia-Yi (2016)[2]	35	Female	Indonesian	Isotretinoin 0.2 mg/kg/day
	26	Female	Indonesian	Isotretinoin 0.2 mg/kg/day

Discussion:

Familial sebaceous hyperplasia is an uncommon form of sebaceous hyperplasia. The first case was reported by Dupre A. in 1980.[1] There were not many cases of familial sebaceous hyperplasia in literatures (Table1).[2] Sebaceous hyperplasia is benign proliferation and enlargement of sebaceous lobules. It is classified as a hamartoma due to significantly larger size of sebaceous gland than normal. Sebaceous hyperplasia is usually found in middle age, however it may occur at any age. The characteristic feature is yellowish or skin-colored papules with central umbilication. It usually presents on the face and non-facial area such as vulva, scrotum and chest wall. Dermoscopic examination shows yellowish papules with central crater and peripheral telangiectasia. Histological study shows increasing in well differentiated sebaceous lobules in the dermis. The peripheral area of sebaceous lobules consist of one or two layers of basaloid germinative cells.[3] The pathogenesis of sebaceous hyperplasia is still unclear. Heparan sulphate, which is found on the cell surface and extracellular matrix, can induce enlarging of sebaceous glands.[4] Recently, mutation in KRAS, HRAS, EFGR gene are found in lesions of sebaceous hyperplasia. EGFR-RAS-MPK pathway may play a role in pathogenesis.[5] Hormonal effect such as androgen, thyroid-stimulating hormone, insulin and hydrocortisone can induce sebaceous proliferation. Extrinsic factors such as UV radiation and some medications such as cyclosporine, highly active antiretroviral therapy (HAART) are associated with sebaceous hyperplasia. Chronic renal failure has been also reported in association with eruptive sebaceous hyperplasia.[3,6]

Table2 The Mayo Muir-Torre syndrome risk score algorithm. A score of 2 or more has a sensitivity of 100% and specificity of 81% for predicting a mismatch repair gene mutation in Muir-Torre syndrome.[9]

Variable	Score
Age at sebaceous neoplasm diagnosis (years)	
60 or older	0
Younger than 60	1
Total number of sebaceous neoplasms	
1	0
2 or more	2
Personal history of any Lynch-related cancer	
No	0
Yes	1
Family history of any Lynch-related cancer	
No	0
Yes	1

Previous reports suggest that familial sebaceous hyperplasia is autosomal dominant inheritance with incomplete penetrance.[2] There is no sex predilection. This disease occurs at earlier age than sebaceous hyperplasia in general population. Family members must have the same presentation but vary in severity. Histopathology is the same as sebaceous hyperplasia which shows mature sebaceous glands in dermis.[2,3] Some genetic diseases such as Muir-Torre syndrome and hypohidrotic ectodermal dysplasia also have history of familial sebaceous hyperplasia.[7,8] All of these conditions are needed to be excluded before making the diagnosis. Muir-Torre syndrome is the disease of sebaceous neoplasm, keratoacanthoma and internal organ malignancy (the most common is colorectal cancer). If Muir-Torre syndrome is suspected, skin biopsy and malignancy screening are needed. The Mayo Muir-Torre syndrome risk scoring system may be used to identify patients who presented with abnormal sebaceous gland before further investigations (Table2).[9] As far as we know, isotretinoin is the mainstay of treatment for familial sebaceous hyperplasia due to it's ability to diminish the size and function of sebaceous glands. Treatment shows effectiveness within 3-6 weeks. Perifollicular stroma turns to fibrosis after 12 weeks of the treatment. The initial dose is 0.5- 1 mg/kg per day. After that it should be tapered minimum effective dose. Previous study

revealed minimal maintenance dose is more than 0.1 mg/kg/day. If the patients discontinue using the medication, the lesions will recur. Therefore, lifelong treatment may be needed.[2,10] In our case, we used isotretinoin 20 mg per day (0.4 mg/kg/day) and the symptoms were improved after 12 weeks of treatment (Fig. 2c). After lowering isotretinoin dosage, the lesions recurred. So we continued on the same dosage and the patient could tolerate to the side effect.

In conclusion, we reported a case of 44-year-old female presented with leonine facies and yellowish papules on the neck and chest wall. Her sisters have similar clinical presentation. The final diagnosis is familial sebaceous hyperplasia. Isotretinoin 20 mg orally once daily has been prescribed with satisfactory clinical improvement.

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