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Original Article

Dermatofibrosarcoma protuberans: a report of 36 cases in Hong Kong and review of the literature
隆突性皮膚纖維肉瘤：香港 36 例及文獻回顧

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Objective: To report a case series of dermatofibrosarcoma protuberans focusing on the clinical presentation and prognosis of this tumour. ***Patients and Methods:*** A total of 36 patients with confirmed histological diagnosis of dermatofibrosarcoma protuberans were retrieved from the database of Queen Elizabeth Hospital, Hong Kong from 1994 to 2007. Their demographic characteristics, clinical manifestations, management and clinical outcomes were documented and tabulated. ***Results:*** Up to 86% of cases occurred in adults between 30 and 60 years old without gender predilection. Most of them showed delayed presentation with 90% and 60% of cases presenting at least 6 months and 1 year prior to the diagnosis of dermatofibrosarcoma protuberans respectively. Asymptomatic growth was the leading clinical manifestation. The most prevalent sites were trunk followed by extremities and then head and neck region. In our series, all patients received surgical treatment, with clear margin achieved in 25 patients (69.4%) but the margin was involved in the remaining 11 patients (30.6%). Post operative radiotherapy and chemotherapy were offered to 9 patients (25.0%) and 3 patients (8.3%) respectively. Metastases occurred in 5 patients (13.9%). ***Conclusion:*** In spite of its deceptively benign clinical manifestation, dermatofibrosarcoma protuberans should draw the attention of dermatologists for its variability and the extent of excision could be reduced by early detection.

目標：報導一系列隆突性皮膚纖維肉瘤病例，重點為此腫瘤的臨床表現及其預復。**病人及方法：**病例採集自 1994 年至 2007 年間本港伊利沙伯醫院的資料庫。全部 36 例均經組織學確診。對所有病例的人口統計學資料，治理及療效進行紀錄及表列。**結果：**近 86% 病例發生於 30 至 60 歲的成年人，無性別差異。大多數病例呈遲發表現。 90% 病例歷時 6 個月以上建立診斷， 60% 病

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例歷時一年建立診斷。無症狀性生長為最常見的臨床表現。最常見的部位為軀幹，其次為四肢以及頭頸。全數病人均接受手術治療。25 名病人（69.4%）切除完整，11 名病人（30.6%）切緣受累，9 名病人（25.0%）接受手術後放療，3 名病人（8.3%）接受手術後化療，5 名病人（13.9%）出現轉移。**結論：**雖然隆突性皮膚纖維肉瘤的臨床表現貌似良性，皮膚專科醫生應留意其多變性，從而達至早期診斷並縮小其切除範圍。

Keywords: Dermatofibrosarcoma protuberans

關鍵詞：隆突性皮膚纖維肉瘤

Introduction

Dermatofibrosarcoma protuberans (DFSP) is an uncommon low grade sarcoma.[1,2] It usually presents as an asymptomatic erythematous plaque which is initially ignored due to its insidious nature, but eventually get noticed because of its increasing growth and nodularity.[1] We report a case series of DFSP, focusing on the clinical presentation and prognosis of this tumour.

Summary of the case series

A total of 36 patients with confirmed histological diagnosis of DFSP were retrieved from the database of Queen Elizabeth Hospital, Hong Kong from 1994 to 2007. The age at diagnosis ranged from 14 to 72 years old. The mean age was 45 years old and the standard deviation was 12 years. Up to 86% of cases occurred in adults between 30 and 60 years old while childhood onset cases were only found in 5% of cases (Figure 1). There was no gender predilection.

The duration between onset of symptoms to diagnosis of DFSP ranged from 2 months to 16 years, with a median duration of 12 months. Most of them had delay in diagnosis, with 90% of cases presenting at least 6 months and 60% of cases presenting at least 1 year prior to the diagnosis of DFSP (Figure 2). Asymptomatic growth was the commonest manifestation (Figure 3). The size of tumour at diagnosis ranged from 2 x 2 cm to 11 x 18 cm (Figure 4).

The tumour was found on the trunk in 25 out of 36 patients (69.4%), upper extremities in 8 patients (22.2%), lower extremities in 2 patients (5.6%) and head and neck region in 1 patient (2.8%, Figure 5).

Typical histologic features included monomorphous spindle-shaped cells arranging in a storiform pattern on a background of fibrous stroma (Figures 6 and 7). Immunohistochemical studies showed positive result for CD34 and negative results for S100 (Figure 8). Fibrosarcomatous changes rarely arose in DFSP and in this series of 36 patients, fibrosarcomatous changes were found in 3 patients (8.3%).

Magnetic resonance imaging (MRI) may be useful to define the extent of tumour growth and tissue penetration. Torreggiani et al reported the largest series of MRI features in DFSP. If the tumour is large in size, preoperative MRI may assist in determining the size and extent of tumour for appropriate surgical planning. Postoperative MRI studies may be performed to look for tumour recurrence.[3] In our series, MRI was used in 11 out of 36 patients (30.6%) as a method of preoperative assessment to delineate the size and extent of tumour.

DFSP is a locally aggressive tumour with a high recurrence rate. Surgical excision with adequate margins is the main treatment. The high recurrence rate is mainly attributed to inadequate surgical margins. Local recurrence can

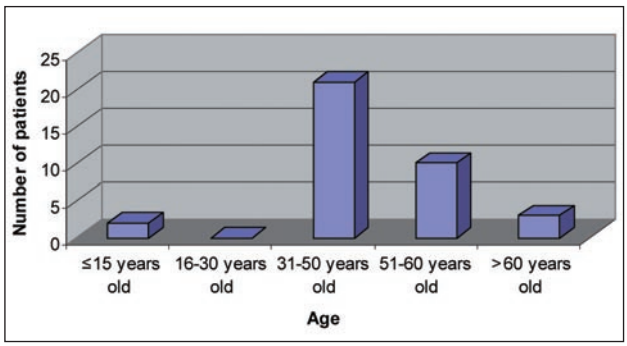

Figure 1. The age distribution at diagnosis of dermatofibrosarcoma protuberans (DFSP).

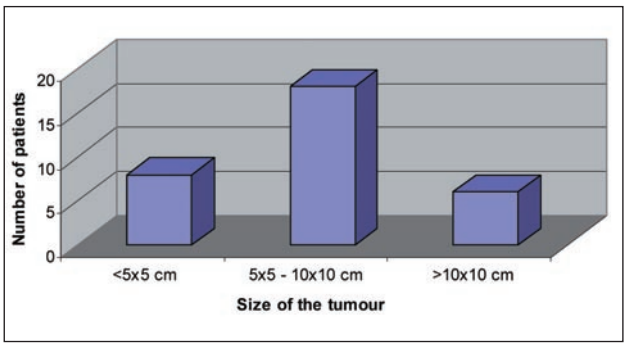

Figure 4. Size of the DFSP on presentation.

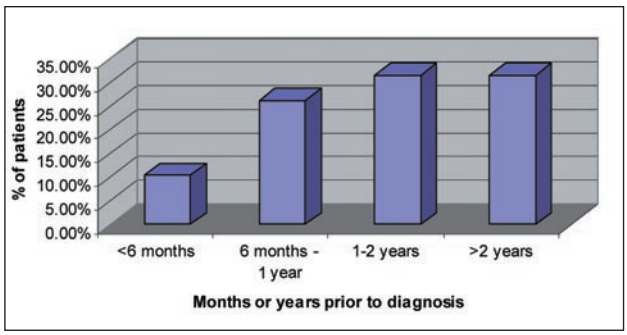

Figure 2. Duration prior to the diagnosis of DFSP.

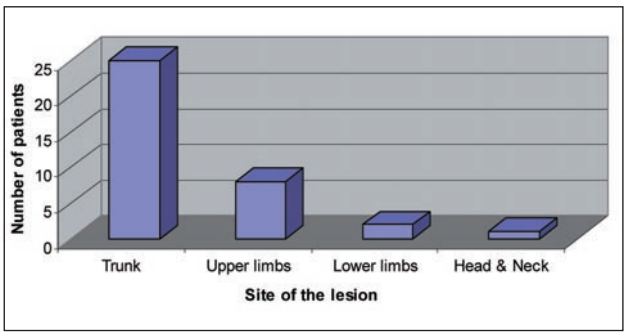

Figure 5. The distribution of the site of DFSP.

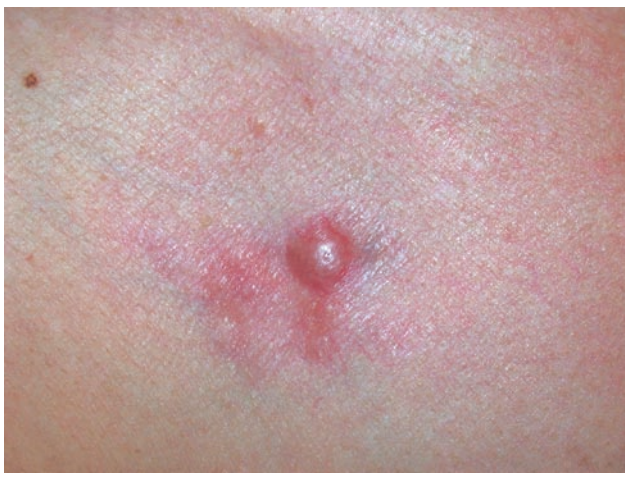

Figure 3. Asymptomatic growth was the commonest manifestation. As demonstrated in one of the subjects in this study, an erythematous keloid like nodule with surrounding ill defined erythematous plaque was a prototypical clinical presentation in this condition.

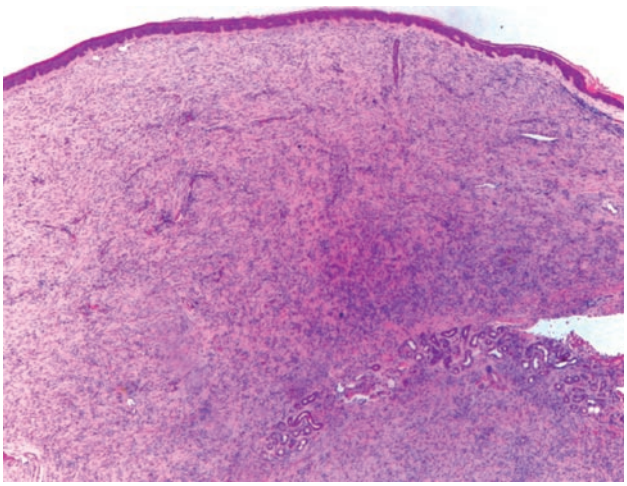

Figure 6. Illustrative histopathological findings of skin biopsy from one of the DFSP subjects showing an ill-defined tumour mass arranged in a storiform pattern in the dermis. (H&E stain, original magnification x 10)

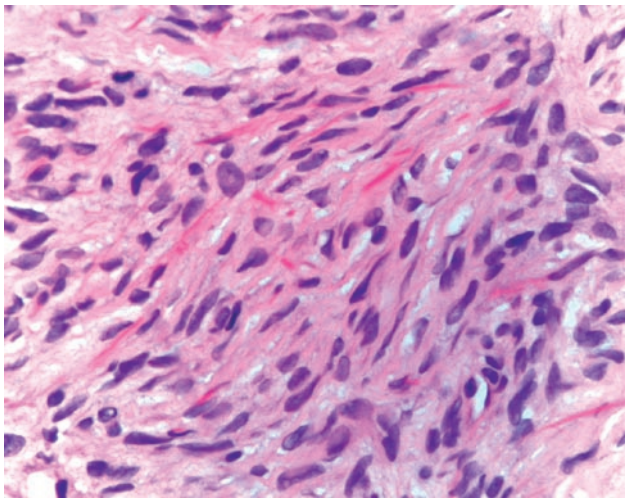

Figure 7. Higher power view of Figure 6, showing that the cellular proliferation is composed of densely packed, monomorphous, plump spindle cells arranged in a storiform pattern. (H&E stain, original magnification x 400)

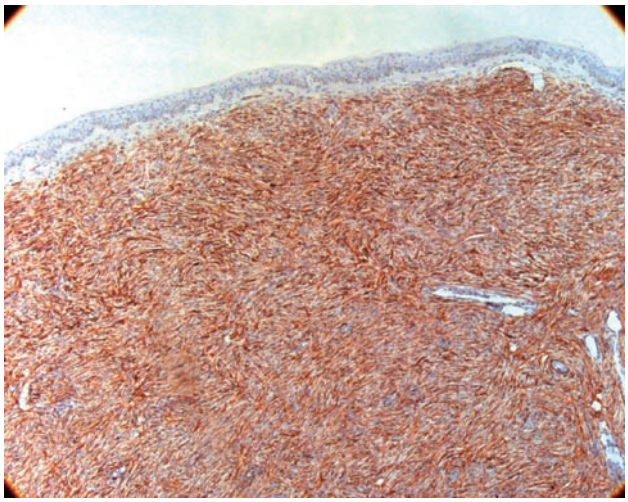

Figure 8. Illustrative immunohistochemical study demonstrating CD34 positivity of the cellular proliferation. (Original magnification x 20)

be managed by reoperation with wider margin. Radiotherapy can minimize the extent of surgical excision in the event of positive margin. It is commonly used as an adjuvant therapy for large tumours or tumours with doubtful surgical margin clearance. Chemotherapy may be indicated in metastasic cases.[4]

In our series, all the patients received surgical excision of the tumour. Clear margin was achieved in 25 out of 36 patients (69.4%) but the margin was involved in the remaining 11 patients (30.6%). Post operative radiotherapy and chemotherapy were offered to 9 patients (25.0%) and 3 patients (8.3%) respectively.

Metastasis occurred in 5 out of 36 patients (13.9%). Lung was the most common site of metastasis and was found in 4 (11.1%). The other sites of metastases were bone in 2 patients (5.6%), brain in 1 patient (2.8%) and lymph node in 1 patient (2.8%).

Two out of 36 patients (5.6%) succumbed. One patient succumbed 9 months after diagnosis due to terminal metastatic diseases with lung, brain, bone and lymphatic secondaries. Another one died 3 years after diagnosis due to co-existing carcinoma of duodenum with repeated episodes of gastrointestinal bleeding. Both of them had multiple sites of metastases including lung, bone, lymph node and fibrosarcomatous histological changes.

Discussion

DFSP is a low grade sarcoma of uncommon occurrence.[1,2] The incidence of DFSP is estimated at 0.8 case per million people per year, occurring most commonly in adults between 20 and 50 years of age.[5] It comprises approximately 5-6% of soft tissue tumours in children.[6] The line of differentiation remains obscured, and fibroblastic, histiocystic, neural or perineural origin have been suggested.[7] From the literature, majority of the cases shows chromosomal translocation between 17 and 22 with fusion between collagen type 1α1 gene (COLIAI) and platelet derived growth factor PDGF β-chain gene, which lead to deregulation of the wild type PDGF β-chain expression and uncontrolled receptor activation and cell growth.[1,2,7]

Clinically, DFSP usually presents as an asymptomatic erythematous plaque or nodule which is initially ignored due to its insidious nature.[1] Our findings showed the most patients had delay in diagnosis, with 90% of cases presenting at least 6 months and 60% of cases presenting at least 1 year prior to the diagnosis of DFSP. This might be due to the insidious and slow growing nature of the lesion. The clinical differential diagnoses include benign or malignant tumours and cutaneous infection. Malignant tumours include cutaneous lymphoma, nodular type of basal cell carcinoma, atypical fibroxanthoma and cutaneous metastases. Benign tumours include keloid, haemangioma, lymphocytoma cutis and dermatofibroma. Infective causes include cutaneous mycobacterium or atypical mycobacterium infection.

Epidemiological studies have showed that the disease usually occurs in patients at early adulthood to middle age and it is rare in childhood. Similar findings were showed in our series, with adults between 30 and 60 years old accounted for 86% of cases while childhood cases comprised only 5% of the cases. The most prevalent site is the trunk, followed by extremities and then head and neck region.[1,8]

Surgical excision is the mainstay of treatment and the key of success is clear surgical margin. Wide local excision with at least 2-3 cm margin including the fascia is suggested.[1,9] Simple excision without wide margin results in a recurrence rate up to 50-60%. However, even with wide excision margin, recurrence is common and can occur in about 20% of cases. Besides a high recurrence rate, the tumour also has a propensity for local invasion.[10] In our series, the margin was involved in 11 out of 36 patients (30.6%) which required further wide excision in order to achieve clear margin.

If available, Mohs micrographic surgery is theoretically a better option to achieve clear margin and hence reduces the local recurrence rate. According to previous studies utilizing Mohs micrographic surgery, the local recurrence rate can be reduced to 1.6%, as compared to simple excision, which has a local recurrence rate up to 60%.[11]

Metastases occurred in 5 out of 36 patients (13.9%). Lung was the most common site of metastases of DFSP reported in the literature and our study had similar findings.[1] Metastasis is rare, occurring in 1-4% of patients, and is usually preceded by multiple local recurrences according to the literature.[12]

The prognosis of DFSP is usually good with five year survival rate up to 99% but there is a high rate of local recurrence due to its infiltrative nature.[1,9] Most of the recurrences occur within 3 years of excision.[13] Radiotherapy may be used to control local recurrence and is commonly used as an adjuvant therapy for large tumours or when there is doubt on the surgical margin.

In our series, 2 out of 36 patients (5.6%) succumbed. It is interesting to note that both cases have fibrosarcomatous change on histology, which is one of the poor prognostic factors reported in the literature. Fibrosarcomatous change in DFSP is a form of tumour progression that carries an increased risk of metastasis, probably related to p53 mutations and increased proliferative activity.[14] Other poor prognostic factors include multiple lesions, recurrent tumour, advanced age, histological features of high mitotic index and increased cellularity.[9] Lifelong follow-up is necessary, with more frequent examinations during the first 3 years when the risk of recurrence is higher.

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