A novel COL1A1 exon 14/PDGFB fusion gene in dermatofibrosarcoma protuberans

Dermatofibrosarcoma protuberans (DFSP) is an uncommon neoplasm which appears as a solitary lesion with firm consistency, adhering to the overlying skin but movable over deep underlying tissue and preferentially located on the trunk of young adults. Histopathologically, DFSP appears as a poorly circumscribed neoplasm that diffusely involves the entire dermis and is composed of a dense proliferation of spindle shaped, monomorphous cells with elongated nuclei and giant cytoplasm. The COL1A1-PDGFB fusion gene is the most characteristic cytogenetic anomaly in DFSP [1, 2]. The majority of exons in the α-helix domain of the COL1A1 gene have been reported to be involved in the fusion with exon 2 of the PDGFB gene [3-5]. However, exons 9, 12, 14, 15, 21 and 30 remain unreported.

The diagnosis of DFSP is most often clear, however, it may need to be differentiated from other soft tissue tumours. This study was performed to confirm the diagnosis of DFSP in a 32-year-old male patient who presented with a tumour just below the left breast for more than 10 years. In the year prior to presentation, the tumour grew considerably in size and it developed irregular nodules. Physical examination showed a firm subcutaneous tumour measuring 10 × 12 cm with irregularly elevated nodules containing hyper and hypopigmented areas (figure 1A). Total excision was performed with 3 cm wide margins from the visible tumour. The study was performed with institutional board approval according to the Declaration of Helsinki. Histological findings showed densely packed, monotonous spindle shaped cells arranged in a storiform pattern (figure 1B). CD34 immunohistochemical staining was strongly positive (figure 1C) while factor XIIIa stain was negative (results not shown). RNA was extracted from both formalin fixed paraffin embedded tissues and frozen tissues for analysis by reverse transcriptase polymerase chain reaction (RT-PCR). Agarose gel electrophoresis showed bands from exons 5, 8 and 10 of the COL1A1 gene as shown in figure 1D. Purified PCR products were used for direct sequencing as described previously [6] in both reverse and forward directions. DNA sequencing showed a chimeric gene between the end of exon 14 of the COL1A1 gene and the start of exon 2 of the PGFB gene (figure 1E). This chimeric gene has never been reported before.

Although translocations resulting in in-frame fusion genes between the COL1A1 and PDGFB genes have been implicated in the pathogenesis of DFSP and its juvenile form giant cell fibroblastoma [4], the COL1A1 exonal breakpoint has not been associated with any clinical or histological phenotype. However, in a study of 42 positive cases, exons 7 (12%) and exon 25 (17%) were found to be more frequently expressed than others [5]. In contrast, however, in a study of 23 cases at our centre, we found that 30% of the cases showed involvement of exon 32 (unpublished data). In order to be able to fully examine the significance of each exonal breakpoint in DFSP, it is important to report every new chimeric gene until all uninvolved exons of the have been reported. We report here the first case showing participation of exon 14 of the COL1A1 gene in the chimeric transcript. Further collection of patient data and gene analysis is needed to gain more insight into the significance of each COL1A1 breakpoint in the pathogenesis of DFSP.


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Successful thalidomide treatment of adult solitary perianal Langerhans cell histiocytosis

A 27-year-old male presented with a 1 year history of perianal erosion with a yellow effusion. Later, two soft bean-sized papules were found in the perianal region. Histories of exophthalamos, diabetes insipidus, skeletal lesions, and diseases of the digestive tract were absent. Physical examination revealed no evident abnormality except the skin lesion, which showed red erosion around the anus, was 6 cm in diameter with a distinct boundary, with no obvious infiltration, and a little yellow effusion on the surface. An external hemorrhoid was observed on the anus (figure 1A). Routine blood, urine and stool tests, liver and kidney function tests, free triiodothyronine, free thyroxin, thyroid stimulating hormone, C-reactive protein, tumor associated antigen including AFP and CEA, immune associated antigen including immunoglobulin, complement, ANA, ds-DNA antigen, and RF were all within normal limits. Microscopic examination for fungi in the perianal effusion, rapid plasma reagin, treponema pallidum particle agglutination, HIV1 and 2 antibodies, and HSV IgG and IgM were all negative. Skull computerized tomography, B ultrasound of liver, guts, pancreas, spleen, and chest X-ray were normal. Enteroscopy revealed multiple polyps of colon. A biopsy of the lesion revealed a proliferation of large round histiocytes with bright cytoplasm in the dermis, some of which had indented nuclei. Scattered eosinophils and neutrophils were observed (figure 1C). Immunohistochemistry revealed positive for CD1a and S100 (figures 1D, 1E).

The diagnosis was Langerhans cell histiocytosis (LCH). Both physical and laboratory examinations revealed the skin was the only organ involved.

The patient was treated with thalidomide 150 mg/d orally and 1:10 povidone iodine and ethacridine zinc oxide oil topically. Five months later, the effusion had vanished. The area of the erosion was almost healed (figure 1B) and he had no adverse effects from thalidomide. Thalidomide was gradually decreased to 50 mg/d. He is still followed up for both the lesion and the adverse effects of thalidomide.

LCH is a broad-spectrum disease, and sometimes the skin is the only organ involved. The vulva (women) and anus (men) are frequently involved regions in adults. However, solitary vulvar or perianal lesions are rare. Field et al. [1] reported a solitary perianal lesion of LCH in an adult, while Santillan et al. [2] reported a solitary vulvar lesion in another adult.

Figure 1. A) Shows the clinical appearance of patient before treatment. B) Shows the clinical appearance of patient five months after treatment. C) Shows the histological appearance (H&E, original magnification ×10). D) Shows immunohistochemistry of CD1a is positive (Original magnification ×20). E) Shows immunohistochemistry of S100 is positive (Original magnification ×40).