GIANT CELL FIBROBLASTOMA IN A 62-YEAR-OLD PATIENT. A CASE REPORT

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Summary

A case of giant cell fibroblastoma in a 62-year-old male is described. The 2x1.5x1.5 cm tumor was excised from the right supraclavicular area. Histologically, it was typical with exceptions that the typical pseudovascular spaces were seen only focally and the neoplastic cells were closely spatially associated with lymphocytes and plasmocytes. This association was suggestive of emperipolesis. The unusual clinicopathologic features caused some diagnostic difficulty.

Key words: dermatofibrosarcoma protuberans - emperipolesis - giant cell fibroblastoma - myxoinflammatory fibroblastic sarcoma - Rosai-Dorfman disease

Súhrn

Obrovskobunkový fibroblastóm u 62-ročného muža. Kazuistika

Obrovskobunkový fibroblastóm je tumor s typickým výskytom v detskom veku. V histologickom obraze sú preň charakteristické pseudovaskulárne priestory vystlané CD34-pozitívnymi nádorovými fibroblastami, zčasti viacjadrovými („floret" typu). Popísaný je prípad u 62-ročného muža, t.j. podľa literatúry u doposiaľ najstaršieho pacienta. Tumor rozmerov 2x1,5x1,5 cm bol excidovaný zo supraklavikulárnej oblasti. Histologicky boli diagnostické pseudovaskulárne štruktúry slabo vyvinuté a prítomné len fokálne. V tumore bola pozorovaná asociácia nádorových buniek s lymfocytmi a plazmocytmi, ktorá tvorila až obraz emperipolézy a tým lézia napodobňovala iné jednotky s emperipolézou, ako sú Rosai-Dorfmanova choroba a myxoinflamatórny fibroblastický sarkóm. Poznanie spomenutých menej obvyklých klinickopatologických rysov lézie môže byť nápomocné pri diagnóze.

Kľúčové slová: dermatofibrosarcoma protuberans – emperipoléza – obrovskobunkový fibroblastóm – myxoinflamatórny fibroblastický sarkóm – Rosai-Dorfmanova choroba

Čes.-slov. Patol., 44, 2008, No. 3, p. 75–78

INTRODUCTION

Giant cell fibroblastoma (GCF) was described by Shmookler and Enzinger in 1982 (**23**). The tumor is located in dermal and subcutaneous tissue, it has a tendency for local recurrence, and sometimes it transforms to dermatofibrosarcoma protuberans (DFSP) (**5, 6, 12, 24**). GCF shares some morphological (**6, 12, 23, 24**), immunophenotypical (**5**) and genetic features with DFSP (**2, 16, 26**), and therefore both lesions are regarded to be variants of one entity (**6, 12**) or, alternatively, GCF is considered to be juvenile form of DFSP (**24**). GCF occurs usually in children whereas patients with DFSP are predominantly adults. Here, we would like to present unusual GCF in 62-year-old male patient. To our knowledge, a case with age higher than 62 years was not reported before. In addition, the present case showed some features that had caused diagnostic difficulty, such as a paucity of diagnostic pseudovascular spaces, an association of multinucleated cells with inflammatory cells mimicking any other tumor with emperipolesis, and areas resembling pattern of myxoid DFSP (**4**).

MATERIALS AND METHODS

The formalin-fixed tissue of the surgically removed specimen was routinely processed and the sections were stained with hematoxylin and eosin, PAS with and without diastase stains, and alcian blue at pH2.5. For immunohistochemistry, the sections were stained with antibody against vimentin (V9), epithelial membrane antigen (EMA, E29), alpha-muscle-specific-actin (HHF-35), alpha-smooth muscle actin (1A4), desmin (D33), S100 protein (polyclonal), HMB45 (HMB45), leukocyte common antigen (LCA), CD68 (KP1), lysozyme (polyclonal), CD31 (JC70A, 1:50, MW), (all from DakoCytomation, Glostrup, Denmark), CD34 (Qbend 10), cytokeratin AE1/AE3 (both from NeoMarkers, Westinghouse, CA, USA), and D2-40 (Signet, Dedham, MA, USA) using the avidin-biotin peroxidase complex technique. Appropriate controls were used. The clinical information was obtained from the patient's physician.

CASE REPORT

The 2x1.5x1.5 cm dermal-subcutaneous tumor was marginally excised from right supraclavicular region in a 62-year-old male patient. Clinician suspected cutaneous cyst, because the cut surface was fibrous and gelatinous and the lesion was slightly protuberant. Two months after the marginal excision a reexcision was performed. After additional four months no signs of recurrence were found. **Histologically**, the dermal/subcutaneous tumor without ulceration was non-encapsulated and, focally, it showed honeycomb and parallel growth patterns of infiltration into subcutaneous fat (**Fig. 1**).

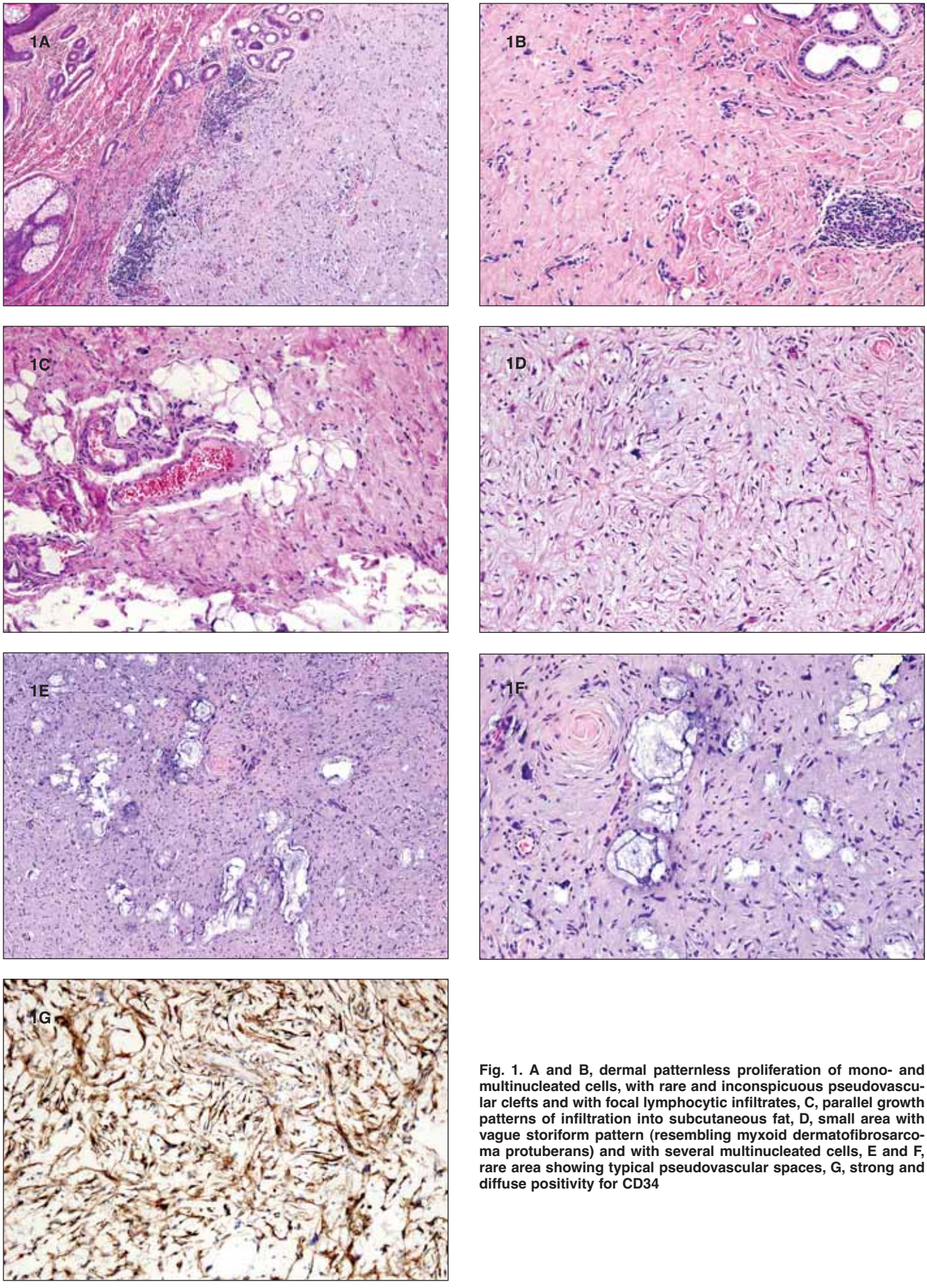

Fig. 1. A and B, dermal patternless proliferation of mono- and multinucleated cells, with rare and inconspicuous pseudovascular clefts and with focal lymphocytic infiltrates, C, parallel growth patterns of infiltration into subcutaneous fat, D, small area with vague storiform pattern (resembling myxoid dermatofibrosarcoma protuberans) and with several multinucleated cells, E and F, rare area showing typical pseudovascular spaces, G, strong and diffuse positivity for CD34

The tumor was relatively hypocellular, myxoid and, to a lesser extent, sclerosed. Basic cell type was wavy spindle cell of fibroblastic appearance. Majority of the cells were mononuclear whereas scattered cells showed multinuclear floret-like morphology. The cells were arranged haphazardly in most areas. Approximately 5% of the tumor showed vague storiform cell arrangement similar to that of DFSP (**Fig. 1D**). In 10-15% of the tumor typical angiectoid and cleft-like spaces were seen (**Figs. 1E and F**). Focal lymphoplasmocytic infiltrates were seen through the lesion. Lymphocytes and plasmocytes were often closely associated with multi- and mononucleated cells, sometimes to such extent that the picture was highly suggestive of emperipolesis (i.e., the presence of lymphocyte or plasmocyte in the cytoplasm of the neoplastic cell) (**Fig. 2**). As the neoplastic fibroblasts including multinucleated giant cells contain only small amount of cytoplasm, we were unable to decide with absolute certainty whether this association represents a "true" emperipolesis or only cell to cell "adhesion" between fibroblast and lymphoplasmocytic cell. Mitotic figures were very rare. The reexcision specimen contained only a scar tissue without the tumor cells.

Immunohistochemically, the tumor was strongly positive for CD34 (**Fig. 1G**) and vimentin, and negative for actins, desmin, S100 protein, EMA, pancytokeratin, CD10, CD31, D2-40, lysozyme and CD68. LCA highlighted inflammatory cells (**Fig. 2C**) including those in close association with neoplastic cells.

DISCUSSION

GCF is a fibroblastic tumor of dermal/subcutaneous tissue with tendency for local recurrence (about one half of tumors recur after simple excision) (**6, 23, 24**). Distant metastasis has not been observed. The tumor occurs most often in children or young adults, and predominantly in male patients. In our case, the clinical features were typical except of high age of the patient. In a most extensive series of 87 cases from AFIP files (**6**) the median age was 6 years, and only 10 patients (11.5%) were older than 40 years. To our best knowledge, the oldest reported patient with GCF was a 62-year-old male in this AFIP series (**6**). In our case, the patient was equally 62-year-old. Such (although rare) cases indicate that diagnosis of GCF is to be considered also in higher age.

Histologically, the typical features of GCF are as follows: poor circumscription with honeycomb and/or parallel growth pattern of subcutaneous infiltration; hypocellularity; neoplastic cell population of relatively bland spindle shaped fibroblasts with haphazard cell arrangement; scattered multinucleated large cells of floret type; numerous pseudoangiomatoid tissue clefts and branching spaces; focal lymphoplasmocytic infiltrates (**6, 23, 24**). Immunohistochemically, GCF is usually strongly and diffusely positive for CD34 (**5**). Our case showed all of the abovementioned features with some exceptions. The pseudoangiomatoid spaces were sparse and not prominent. However, they were found with certainty after complete embedding of the lesion. Thus, a complete examination of the tumor may be necessary for the finding of this diagnostically important feature. The neoplastic cells were in some foci spatially closely associated with lymphocytes and plasmocytes to the extent that the picture was highly suggestive of emperipolesis (i.e., the presence of lymphocytes and plasmocytes in the cytoplasm of the tumor cells). Emperipolesis was never described in GCF and therefore this feature caused some diagnostic difficulty in the present case. It is typical for Rosai-Dorfman disease (**20**) but is not entirely specific because it was described also in some other reactive or neoplastic conditions such as low grade myxoinflammatory fibroblastic sarcoma, mesothelial cells in pleuritis, retroperitoneal angiomyolipoma, follicular dendritic cell sarcoma, hematological diseases, and some poorly differentiated malignant tumors (**7-9, 15, 17, 19, 21, 22, 27, 28**). In the present morphological context we had to consider especially a possibility of low-grade myxoinflammatory fibroblastic sarcoma (MIFS) (**10, 11, 13**). This lesion contains fibroblast-like cells with frequent bizarre shape, nuclear atypia and multinucleation. However, it shows, in contrast with GCF, a pseudolobular architecture due to alternating myxoid and fibrous areas. Moreover, the bizarre cells in MIFS are multivacuolated lipoblast-like or they show large viral inclusion-like nucleoli that are much more prominent in comparison with the small nucleoli in floret cells of GCF. Inflammatory cells in MIFS are more numerous and often they form germinal centers not seen in GCF. CD34 can be positive in MIFS and therefore immunohistochemistry does not assist in this differential dia-

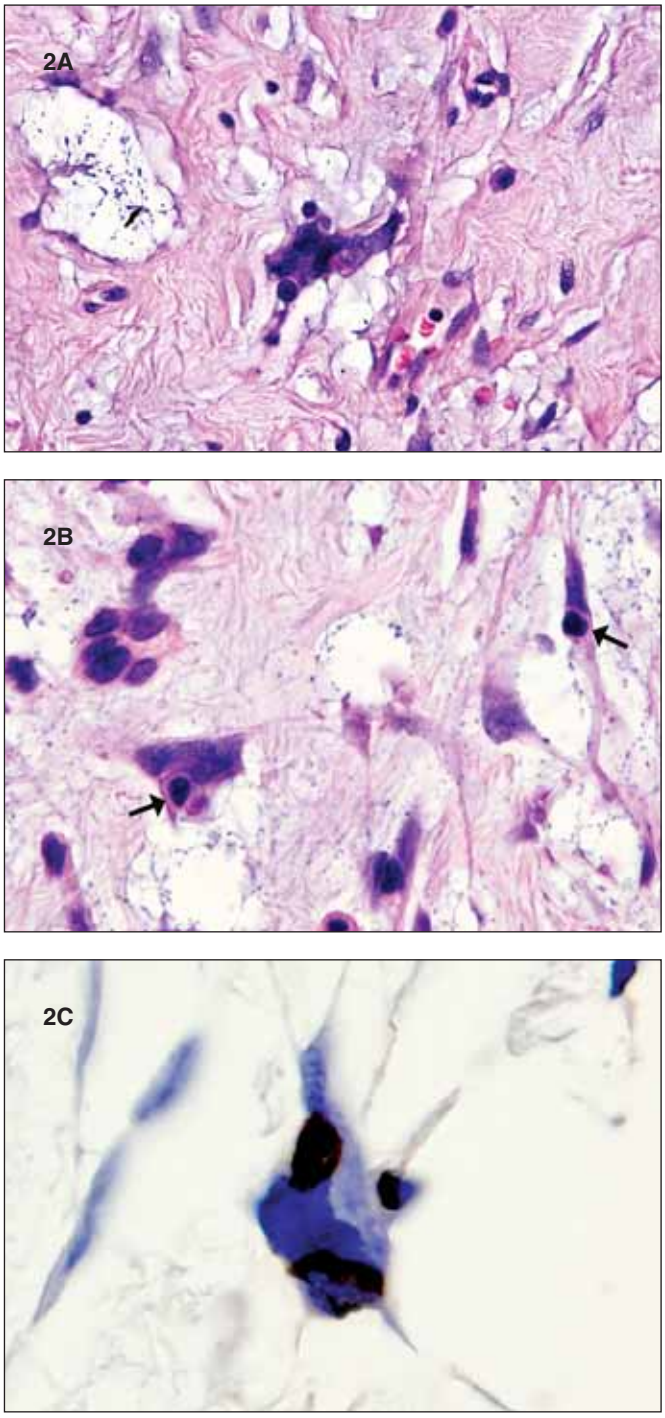

Fig. 2. A and B, close association between neoplastic and lymphoplasmocytic cells (arrows in B) is suggestive of emperipolesis, C, LCA immunostain highlights lymphoplasmocytic cells

gnosis. Rosai-Dorfman disease (**20**) can occur in soft tissue (**14**) or skin (**1, 8, 15, 19**). It contains, in addition to spindle cells, histiocytic cells with polygonal cell shape and with more abundant granular or foamy cytoplasm. Typically, these cells express S100 protein and some of the histiocytic markers such as CD68, lysozyme, alpha-1-antitrypsin and alpha-1-chymotrypsin (**1, 8, 14, 15, 19, 20**). CD34 was described to be negative in Rosai-Dorfman disease (**18**). Clinicopathologic features of another lesions with emperipolesis (**9, 17, 21, 22, 27, 28**) are so different from GCF that they can hardly cause any diagnostic difficulty.

A small focus of vague storiform cell arrangement in the present case resembled the pattern of myxoid DFSP (**4**), and therefore composite GCF-DFSP (**6, 12**) was considered in the differential diagnosis. Multinucleated cells in the storiform area altered the monotonous/monomorphic appearance that is typical for DFSP (**3, 25**), and for this reason we did not classify this (too pleomorphic) pattern as DFSP. The resemblance may be nevertheless interpreted as a feature reflecting close histogenetic relationship between GCF and DFSP (**2, 5, 6, 16, 24, 26**). This relationship is also supported, besides the known morphologic and immunophenotypic overlap, by recent molecular findings such as COL1A1-PDGFB gene fusion transcripts resulting from the t(17;22)(q22;q13) translocation in both GCF and DFSP (**2, 16, 26**).

In conclusion, we described the case of GCF in an unusually high-aged patient. Morphologically, the lesion showed some atypical features such as paucity of diagnostic pseudovascular spaces and close association between neoplastic cells and lymphoplasmocytes suggesting possible emperipolesis. These clinicopathologic features caused diagnostic difficulty and their awareness can help in diagnosis of similar cases in future.

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