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# A Dedifferentiated Liposarcoma of Soft Tissue with Features of Fibrosarcomatous Redifferentiation

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A case of dedifferentiated liposarcoma in a fifty-one year old man is presented. The patient received a wide extirpation for a relatively rapidly growing mass in his right gluteal region. The mass was multinodular and consisted of two clearly distinct elements; well differentiated liposarcoma and non-lipogenic spindle cell sarcoma (fibrosarcoma). This is first proven case of dedifferentiated liposarcoma of the soft tissue in Korean literature, and its histogenesis is discussed along the dedifferentiation-redifferentiation pathway of fibrohistiocytic differentiation.

## INTRODUCTION

The 'dedifferentiated liposarcoma', a term coined by Evans[1] in 1979, was proposed for tumors containing distinct areas of well differentiated liposarcoma and cellular nonlipogenic spindle cell or pleomorphic sarcoma. It is also understood as a tumor characterized by the coexistence of well differentiated and poorly differentiated areas in portions of the same neoplasm or in the primary tumor and the recurrence or metastasis. Although it is roughly estimated as fewer than 5% of all liposarcomas and classified under a subtype of well differentiated liposarcoma[2], its occurrence is very rare and only a single instance of this category in the liver has been reported by one of authors[3] in Korea. Because of the limited evidence on its histogenetic explanation, however, we strongly feel that many cases might be overlooked or misinterpreted during the daily diagnostic pathologic service. Therefore, the purpose of this study is to draw an attention of surgical pathologists and oncologists on this loosely conceptualized neoplasm, and to review and postulate all possible histogenetic explanations.

## CASE HISTORY

A fifty-one year old man was admitted to the orthopedic Surgery Service of Seoul National University Hospital with a painful right gluteal mass of 3 months' duration in November, 1985. On palpation the mass was infant-head sized, rather fixed and tender. No other abnormality was noted on physical examination. Past history was not contributory. He had currently suffered from central chorioretinitis and irritant dermatitis. Other physical checkup results were positive HBsAg and HBeAb, gallstones on sonography, chronic superficial gastritis on endoscopic biopsy and normal liver function test.

Radiographic study of the gluteal region suggested an adhesion of the mass to the underlying bone, and an extirpation of the mass together with adjacent cortical bone removal was done under the clinical impression of soft tissue sarcoma. Postoperative

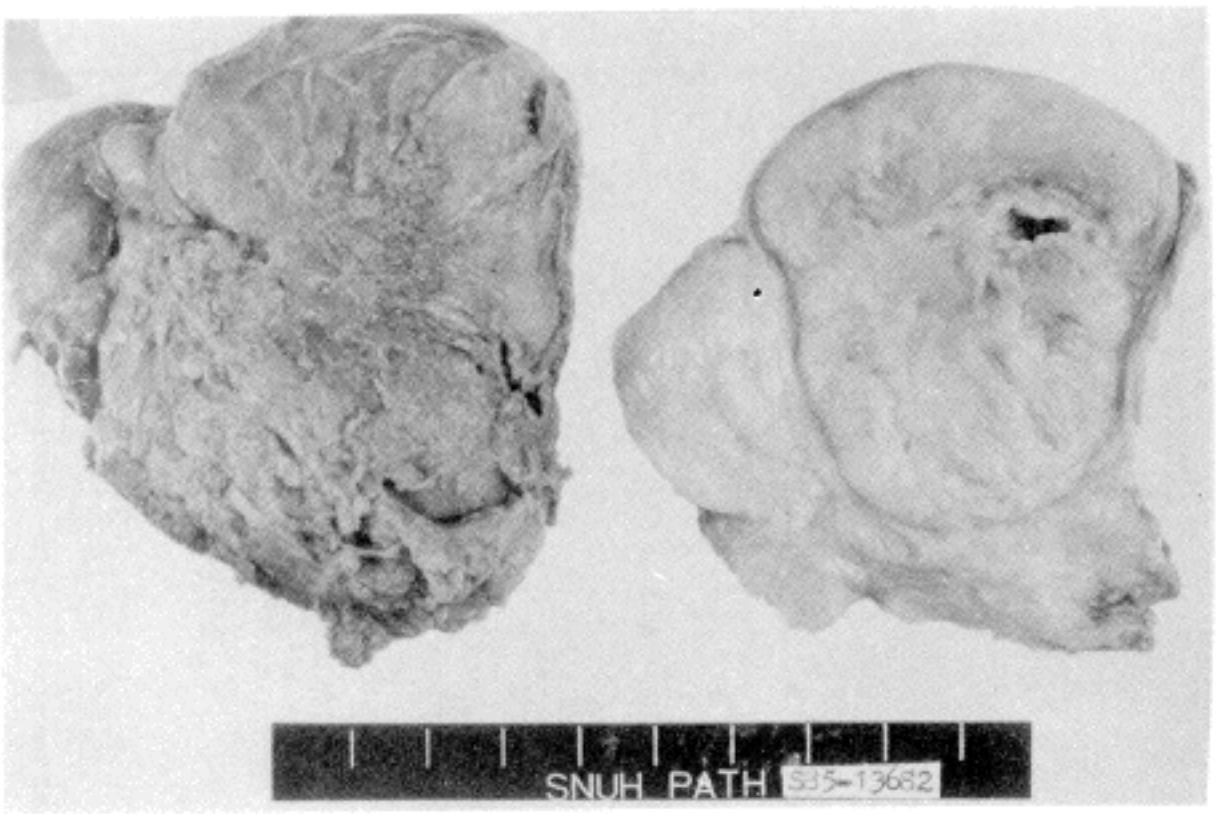


**Fig. 1.** The extirpated multinodular mass. Cut surface is and yellowish trabeculated in the center with a necrotic area, but partly fatty at the periphery.

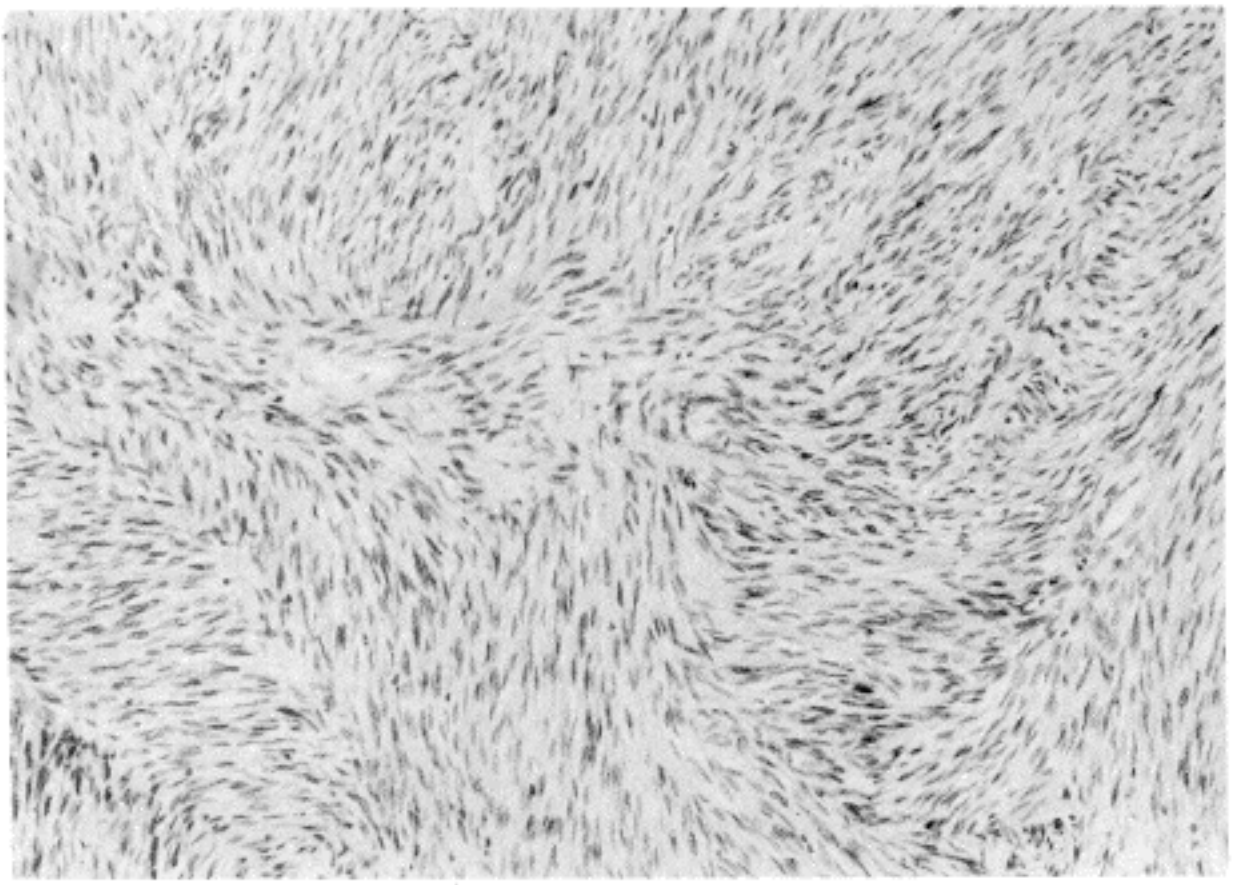

**Fig. 2.** Dedifferentiated area representing non-lipogenic spindle cell sarcoma, focally featuring storiform pattern. (H&E, ×100)

bone scan showed multiple hot spots on the ribs, but he received no further treatment. No recurrence or metastasis has been found yet in postoperative period of 20 months.

## PATHOLOGIC FINDINGS

Grossly the removed tumor was relatively well circumscribed, yellowish white and rubbery firm in consistency. It measured 10×7×5 cm and was focally surrounded by an irregular musculofibrous tissue. On section the mass was multionodular. The largest one measured 6 cm in diameter and showed a whitish coarsely trabeculated cut surface with areas of central necrosis (Fig. 1). Smaller nodules were located at periphery, showing a sharp demarcation from

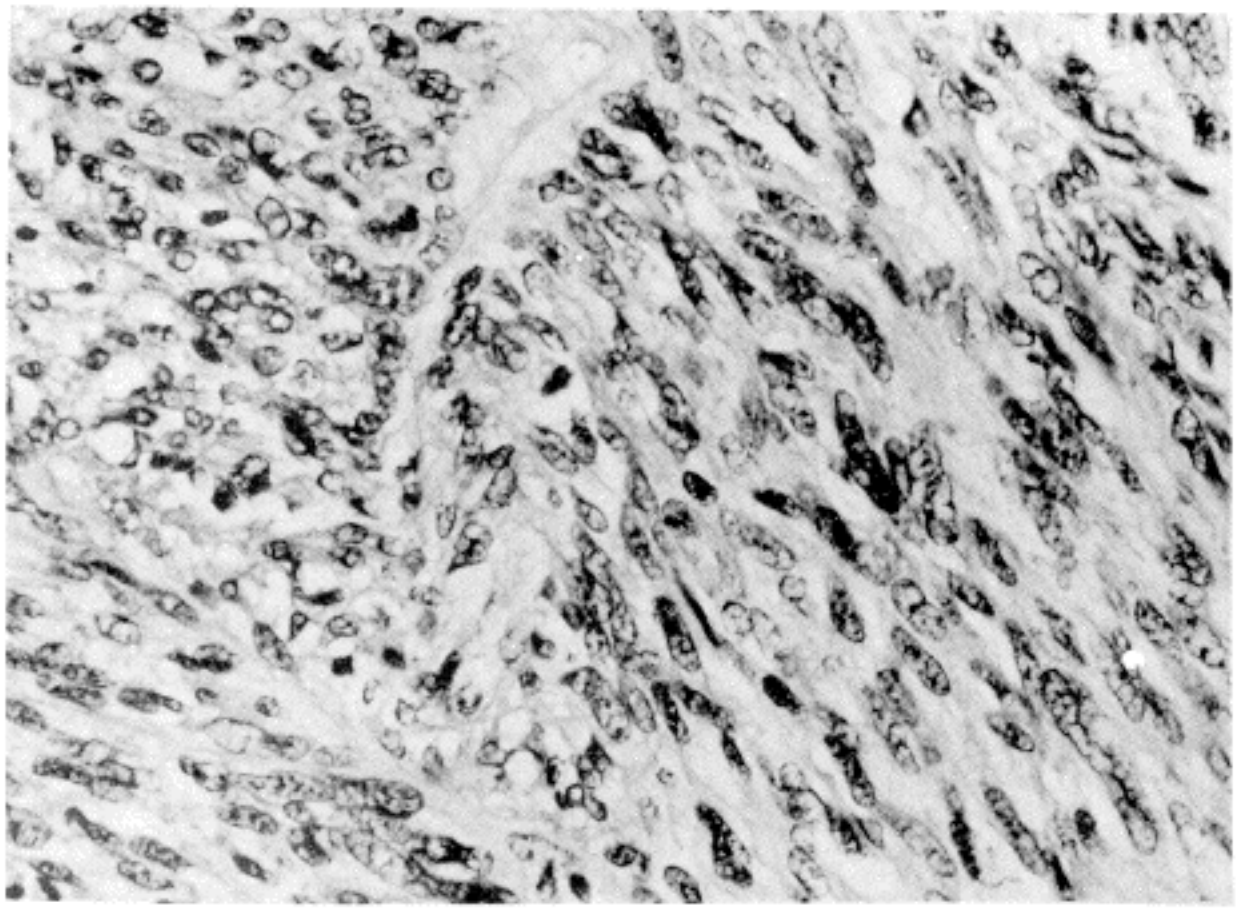

**Fig. 3.** High power view of Fig. 2. Hyperchromatic spindleshaped nuclei show moderate pleomorphism and mitotic figures. (H&E, ×400)

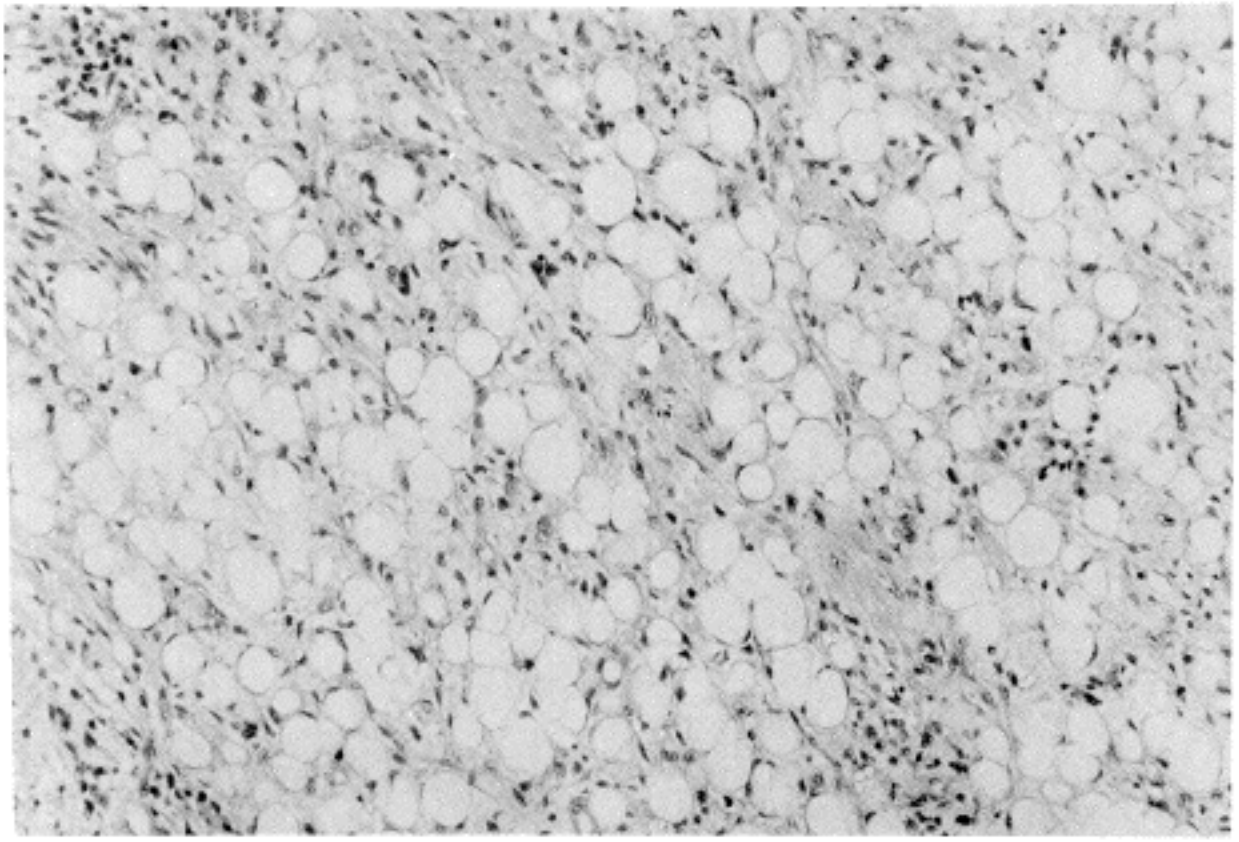

**Fig. 4.** Area showing features of well differentiated liposarcoma. (H&E, ×100)

the main mass by thin septa, and creamy yellow greasy cut surface. The outer margin of the small nodules was not distinct.

Two grossly distinguishable portions showed quite different histologic features as well. The central white trabeculated portion of the mass was composed of compactly arranged bundles of spindle cells. Each cellular bundle ran in irregular directions, often featuring herring-bone and storiform-like appearance (Fig. 2). The individual cell had elongated fusiform or cigar-shaped vesicular nuclei and rather abundant fibrillary cytoplasm with indistinct border. Mitotic figures were abundant, but cellular pleomorphism or giant cell formation was

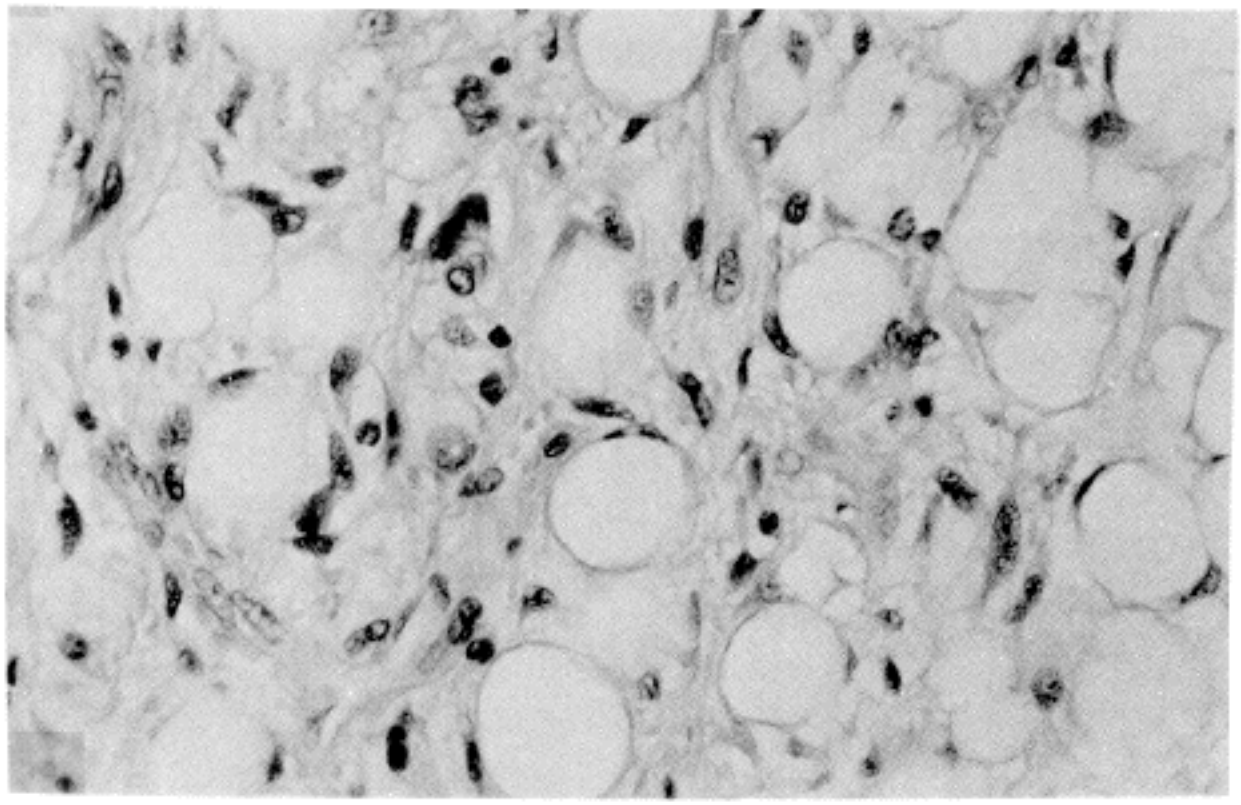

**Fig. 5.** Varying-sized atypical fat cells and lipoblasts having eccentric hyperchromatic nuclei. A multivacuolated fat cell is intermixed (arrow). (H&E, ×100)

not remarkable (Fig. 3). These features were mostly corresponding to those of fibrosarcoma.

The peripherally located yellow nodules showed islands and nests of fat cells within loose myxoid stroma (Fig. 4). The fat cells looked innocent at a glance but had excessive variation in size and shape. On close examination, there were many scattered lipoblasts having eccentrically located hyperchromatic large bizarre nuclei inbetween the cellular elements (Fig. 5). Multivacuolated cells were seldom seen. Numerous atypical cells were also found within the adjacent myxoid stroma, showing large ovoid vesicular nuclei and eosinophilic cytoplasm. They were infiltrating into the adjacent skeletal muscle. Another prominent features were abundant lymphoid and vascular reaction in the stroma. The lymphocytes were seen in aggregates or individually within the stroma and fat cell nests, mimicking inflammatory process as in inflammatory variant of liposarcoma. Numerous capillaries were proliferating in plexiform pattern between the myxoid stroma, lymphoid aggregates and fat cells, reminiscent of myxoid liposarcoma.

In summary, the whole tumor was composed of clearly distinguishable areas of fairly well differentiated liposarcoma and nonlipogenic spindle cell sarcoma.

## DISCUSSION

In 1979 Evans[1] reviewed fifty five cases of liposarcoma with reclassification and suggested the 'dedifferentiated liposarcoma' in eight cases, in which were two distinct areas of well-differentiated liposarcoma and cellular spindle cell or pleomorphic sarcoma without recognizable lipogenesis. The dedifferentiated area resembled most often malignant fibrous histiocytoma in storiform pattern, accompanied by large pleomorphic cells and inflammatory infiltrates. Others were more likely fibrosarcoma or showed only nuclear palisading, myxoid foci and tumor necrosis. They occurred in the retroperitoneum in seven and spermatic cord in one. All the cases recurred after median period of 29 months. The dedifferentiated component was present only in recurrent tumors in two cases, and conversely completely disappeared in another two

recurrent tumors. Two cases showed metastasis to lung and/or brain in which dedifferentiated component of the primary tumor prevailed. Similar experiences were subsequently shared by Snover et al[4] who reviewed thirteen sarcomas with recurrences which were originally classified as liposarcoma. Seven of them showed multiple sarcomatous patterns including malignant fibrous histiocytoma, hemangiopericytoma, malignant schwannoma and unclassified spindle cell sarcoma as well as various subtypes of liposarcoma. Those tumors containing pleomorphic component were accounted for more aggressive behavior than well differentiated and pure myxoid liposarcoma.

Hashimto et al[5] observed a S-100 protein distribution in various liposarcomas and myxoid malignant fibrous histiocytomas. None of myxoid malignant fibrous histiocytomas and the tumor cells in non-lipogenic areas of six dedifferentiated liposarcomas contained S-100 protein.

Both macroscopic and histologic features of our case virtually meet the diagnostic criteria of dedifferentiated liposarcoma, originally designated by Evans[1], but its histogenetic explanation remains not clearly justified only with previously proposed dedifferentiation pathway in such a case like ours that the non-lipogenic element of the main mass may stand in the same level of differentiated liposarcoma of the peripheral nodular masses. The term of dedifferentiation may be feasible in cases with admixture of malignant fibrous histiocytoma or more primitive sarcomas of uncomitted pleuripotential cell origin to differentiated liposarcoma. Therefore, an additional step of redifferentiation pathway toward fibrogenic tumor from the precursor fibrohistiocytic line may be required rather than a simplified explanation of dedifferentiation of liposarcoma; in another word, the fibrosarcomatous element is the one end of the formerly differentiated mesenchymal counterpart of the coexisiting differentiated liposarcoma which has partly underwent once a dedifferentiated process. This possibility may be partly explained by Brooks[6] who proposed a new model of mesenchymal differentiation by immunohistochemical analysis of six dedifferentiated sarcomas using $\alpha$1-antichymotrypsin. In each case the dedifferentiated component resembled malignant fibrous histiocytoma and expressed $\alpha$1-antichymotrypsin. He suggested that malignant fibrous histiocytoma is a final common pathway for some types of sarcomas and is the result of progression or transformation, that is, selection of the predominant histologic type by less differentiated tumor cells. He termed this loss of one cell specific marker and gain of another the "antigenic shift phenomenon". By these hypotheses he suggested an intermediate precursor, primitive 'fibrohistioblast', in sequence of mesenchymal differentiation. This concept should also be confirmed by successive proof by tumor cell culture in this context.

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## ═ 국문초록 ═

### 역분화성 지방육종
—1증례 보고—

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'역분화성 지방육종'은 1979년 *Evans*가 제의한 이래, 한 종양내에서 혹은 일차성 종양과 재발성 또는 전이성 종양에서 분화가 좋은 지방육종과 분화가 나쁘고 지방을 생산하지 않는 육종이 공존하는 경우을 칭한다. 본 예는 51세 남자로 3개월전부터 눈에 띄게 자라난 우둔근 종괴를 주소로 내원하였고, 적출된 종괴는 경계가 좋은 10×7×5 *cm* 크기의 다결절성 종양으로서 구분이 잘되는 회백색 섬유성 조직과 황색의 지방성 조직으로 이루어져 있었다. 현미경적 관찰에서 회백색 조직은 섬유육종과 유사한 밀집된 방추세포의 불규칙한 배열을 보였고 지방성 조직은 분화가 좋은 지방 육종의 소견을 보였다. 수술후 특별한 처치없이 20개월 동안 추적 검색되고 있으나 국소 재발이나 전이는 없다. 국내에서 아직 조직학적으로 확인된 바 없는 연조직 기원 역분화성 지방육종의 1예를 간단한 문헌고찰과 함께 보고하였으며, 섬유육종성 증식상의 재분화과정의 가능성을 제안하였다.