Retroperitoneal Undifferentiated Sarcoma in a Hemodialysis Patient

Kuan-Chou Chen, Yun-Ho Lin*

Retroperitoneal undifferentiated sarcoma is a soft tissue sarcoma that is highly positive for vimentin but has no reactions to various cell-specific markers in immunohistochemical study. This tumor has never been reported in a hemodialysis patient with chronically immunosuppressed uremic state. We report a case of retroperitoneal undifferentiated sarcoma in a 50-year-old uremic man who presented with intermittent left flank dull pain and painless hematuria. MRI revealed a huge left perirenal mass, and complete resection was achieved. The pathological examination of the tumor cells revealed poorly-differentiated spindle or oval-shaped sarcoma cells, and the immunohistochemical study excluded the diagnosis of rhabdomyosarcoma, leimyosarcoma, liposarcoma, angiomyolipoma, sarcomatoid renal cell carcinoma, and sarcomatoid transitional cell carcinoma. This indicated that the sarcoma did not show any differentiation. The patient had an uneventful postoperative course and is currently well 3 years after operation. We review the clinical picture of this tumor in a hemodialysis patient, elucidate the "undifferentiated" histopathological characteristics by immunohistochemical study and point out the possible connection between sarcoma formation and immunosuppressive status from uremia.

Key words: retroperitoneal sarcoma, undifferentiated sarcoma, hemodialysis, immunohistochemical study

Ten percent of soft tissue sarcomas arise in the retroperitoneal space, and the 5-year survival rates of retroperitoneal sarcoma range between 12% and 70% with wide variability[1]. Complete surgical resection of the primary tumor offers the best chance of cure, but this is often limited by the anatomical location, wide invasion of adjacent structures and late detection of the lesion. More unfavorable outcome is associated with the high clinical stage at presentation, high histological grade, incompletely resected or unresectable primary tumor[2].

Retroperitoneal undifferentiated sarcoma in a hemodialysis patient is extremely rare, and to date this may be the only case reported in the medical literature. With intention to improve the current poor understanding of the histopathological characteristics and clinical strategies for this lesion, we present our experience of managing this lesion in a hemodialysis patient with 2-year survival until now, and elucidate the "undifferentiated" histopathological characteristics by immunohistochemical study.

Case Report

A 50-year-old male patient has been suffering from end stage renal disease due to toxic effect of herbal drugs and has received regular hemodialysis for more than 3 years. Two years after the beginning of hemodialysis, intermittent left flank dull pain and painless hematuria were noticed. In the Urological Outpatient Department, a huge left perirenal mass (19×15×14 cm in size) was noticed on the MRI (Fig 1). Complete resection com-

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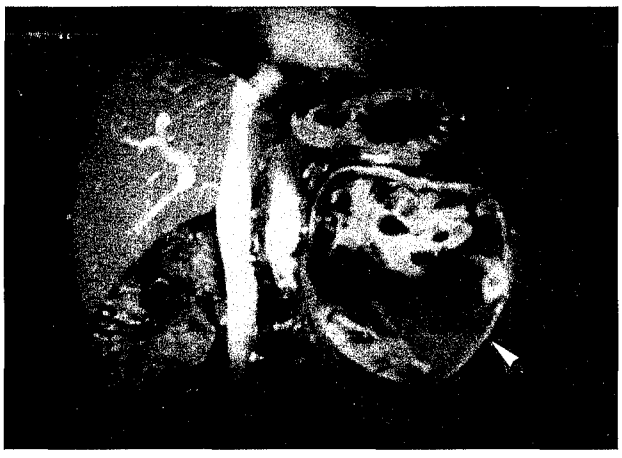

Fig 1. MRI reveals a huge left perirenal mass measuring 19 ×15×14 cm (arrow head).

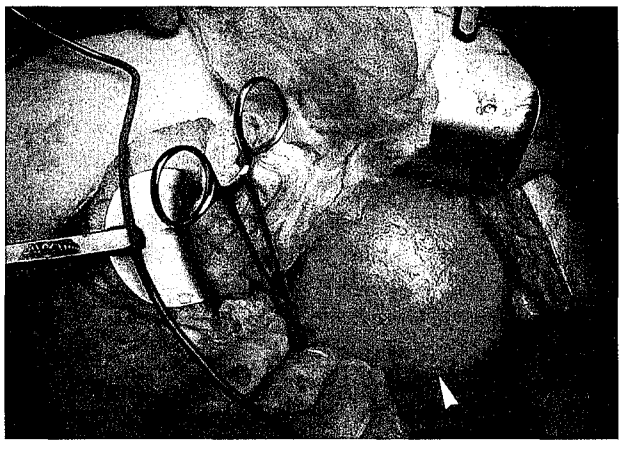

Fig 2. Complete resection of the tumor was achieved, and the solid tumor showed a well-circumscribed appearance. (arrow head).

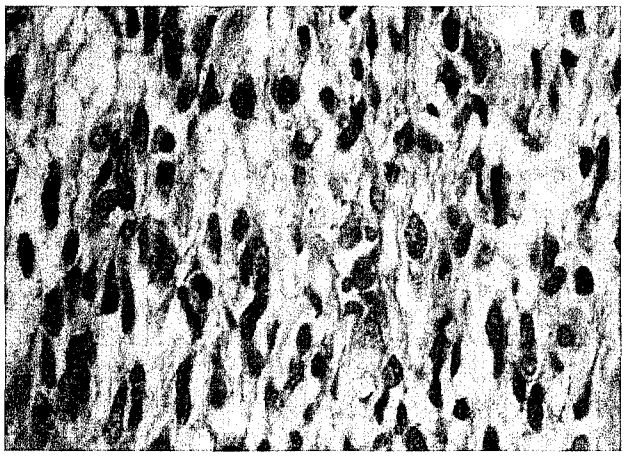

Fig 3. Pathological examination of the tumor cells revealed undifferentiated spindle or oval-shaped sarcoma cells (H&E×400).

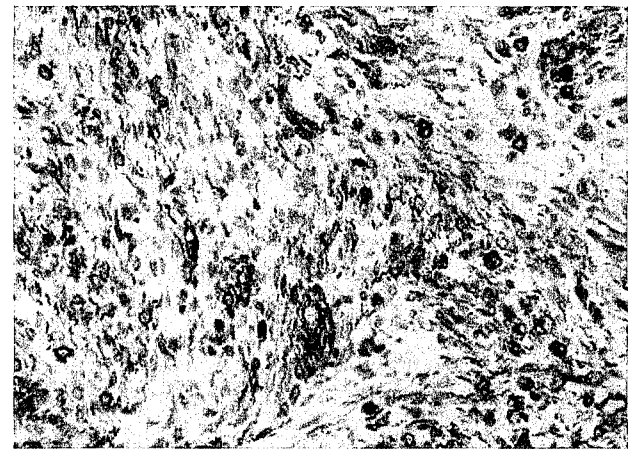

Fig 4. The tumor cells were strongly reactive with vimentin (brown color, ABC method, 400×).

Table1. Immunohistochemical Findings in Retroperitoneal Undifferentiated Sarcoma of a Hemodialysis Patient

Antibody	Primary tumor
Vimentin	++++
Cytokeratin	−
Actin	−
PTAH	−
Myoglobin	−
MyoD1	−
Desmin	−
CD34	−
Fat stain	−
S-100	−
HMB-45	−
EMA	−
PAS	−

bined with nephrectomy was performed on January 15, 2002 and the solid tumor showed a well-circumscribed appearance (Fig 2). The pathological picture of the tumor cells was characterized by undifferentiated spindle or oval-shaped sarcoma cells (Fig 3), and the immunohistochemical findings are summarized in Table 1. Tumor cells were strongly reactive with vimentin (Fig 4), but no immunoreactivity was found for actin, PTAH, myoglobin, MyoD1, desmin, CD34, fat stain, S-100, HMB-45, EMA, PAS, and cytokeratin. The immunohistochemical study excluded the diagnosis of rhab-

domyosarcoma, leimyosarcoma, liposarcoma, angiomyolipoma, sarcomatoid renal cell carcinoma, and sarcomatoid transitional cell carcinoma. The surgical margins were free of tumor and no adjuvant irradiation or chemotherapy was administered. Follow-up abdominal computed tomographies were performed every 3 months in the first post-operative year and then every 6 months in the second year. There were no signs of local recurrence or metastasis 3 years after the operation.

Immunohistochemistry

The immunohistochemical stains were performed under the Nexes IHC (Ventana) automatically with Avidin-Biotin-peroxidase Complex (ABC) method. The I° antibody was anti-mouse or anti-rabbit monoclonal antibody, and the II° antibody was Ventana DAB detection kit (containing anti-mouse and anti-rabbit monoclonal antibodies). Internal or external positive control stains were performed for all negative stains.

Discussion

Retroperitoneal sarcoma comprises only 10% of soft tissue sarcomas[3,4]. Soft tissue sarcoma, a term used to describe a group of malignancies arising in mesodermally derived extraosseus tissues, accounts for 0.7% of all cancers.

Beginning in July 1982, a prospective database for all soft tissue sarcomas was set up at the Memorial Sloan-Kettering Cancer Center (MSKCC), and researchers who have used this database have identified the following particular features of soft tissue sarcoma as important clinical and pathological prognostic factors[5-9]: tumor grade (high versus low), size (less than 5 versus greater than 5 cm), depth of invasion (superficial versus deep), resection of all gross disease, the presence or absence of metastatic disease at presentation, and the expression of the retinoblastoma gene product. In retroperitoneal sarcoma, in addition to tumor size and grade, the ability of the surgeon to resect the tumor completely independently improves survival[6].

There is little evidence to suggest a definite etiologic factor for the development of retroperitoneal sarcomas. Prior radiation exposure, trauma, and environmental exposure to asbestos and herbicides have been implicated[10], but no immunologic etiologies have been suggested. Since the chronically immunosuppressed uremic state followed by hemodialysis may contribute to the development of malignancy[11], this report would suggest the possible connection between sarcoma formation and immunosuppression from uremia.

Complete surgical resection of the primary tumors offers the best chance for cure. Many sarcomas have a pseudocapsule that often is mistaken as the appropriate limit of resection. However, the pseudocapsule is formed by expansion of the tumor and compression of adjacent tissues, and tumor cells frequently invade beyond it. Therefore, tissue surrounding the capsule should be resected[12]. If a tumor has been resected completely and all surgical margins are negative, postoperative radiation or chemotherapy is not necessary[13]. In our case, the tumor was dissected along the capsule easily, and all surgical margins were found to be free of tumor during intraoperative frozen biopsies, so the wider tissue resection was omitted, and no further adjuvant therapy was administered.

Patients should be followed closely at 3-month intervals for 1 year and 4 to 6-month intervals for 2 years. If there has been no recurrence after 3 years, a yearly follow-up visit probably is appropriate. The ultimate role of radiation therapy and chemotherapy for the postoperative residual tumor or metastasis disease remains to be defined[6]. A local recurrence without distal metastasis should be treated surgically, since an operation is the only effective palliative treatment.

The most common retroperitoneal sarcomas are liposarcomas, leiomyosarcomas and malignant fibrous histiocytomas[10]. Although sarcomas initially reflect the immunohistochemical appearance of their cells of origin, undifferentiation often makes distinction of histological types difficult[4].

Generally, immunohistochemistry using various cell-specific markers reveals that undifferentiated sarcoma is highly positive for vimentin[14], and a few case reports have demonstrated that tumor cells were reactive to cytokeratin and S-100 protein. In our case, vimentin was positive, whereas cytokeratin and S-100 were negative.

The myogenic phenotype at the immunohistological level (actin, PTAH, desmin myoglobin, MyoD1 stains), the lipoblastic differentiation marker (oil red stain), the angiomyolipoma marker (HMB-45), the lymphoid and myeloid haemopoietic differentiation marker (CD34 protein), and the renal cell carcinoma marker (epithelial membrane antigen) were also negative in our case. This indicated that the sarcoma did not show any differentiation.

Malignant fibrous histiocytomas (MFH) can no longer be regarded as a definable entity, as reflected in the latest World Health Organization classification of soft tissue tumors[15], and is now viewed as a synonym for undifferentiated pleomorphic sarcoma. It has become a

diagnosis of exclusion to be reserved for tumors showing no other line of differentiation. Even in MFH, there were some degrees of positive immunoreactivity for each antibody[16], but in our case, the immunohistochemical features were completely negative, and the morphological appearance was atypically identical to the MFH, and so we defined the tumor as "undifferentiated" sarcoma.

Uremia is associated with immune system dysregulation due to multiple defects of the immune system[17,18]. Daichou et al reported that lymphopenia was detected in uremic patients with a significant reduction in CD4+ helper T cells and an increase in CD8+ suppressor T cells[19]. These conditions significantly decreased the CD4 / CD8 ratio. Some reports have provided evidence of a low proportion of B cells in uremic patients[20,21], which might partly account for the altered antibody response in uremia. The cytotoxicity of natural killer (NK) cells among uremic patients was found to range from decreased to increased, as compared with normal individuals[22,19]. These findings are relevant to several clinical observations such as the increased incidence of the reduced mixed lymphocyte reaction and malignancy in HD patients[11,23]. Considerable insight into the regulation of T cell and NK cell activations with the formation of sarcoma in our patient will be the goal of future research.

In conclusion, this report suggests a possible connection between sarcoma formation and immunosuppression from uremia. Complete surgical resection of the primary undifferentiated sarcoma in a hemodialysis patient offers the best chance for cure. Using various cell-specific markers, immunohistochemistry initially may fail to reflect the cell origin of undifferentiated sarcoma.

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一位血液透析病患的後腹腔未分化肉瘤

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後腹腔未分化肉瘤，其特性為在免疫組織化學染色下，無法染出特異之細胞分化指標，只能染出高強度之肉瘤指標“Vimentin”。文獻上這類腫瘤從未發表發生在具有慢性免疫力低下的血液透析病人身上。我們報告一位50歲的尿毒症病患，患有後腹腔未分化肉瘤。其細胞病理特性為未分化的紡錘狀或卵圓形的肉瘤細胞，而其免疫組織化學反應排除橫紋肌肉瘤、平滑肌肉瘤、脂肪肉瘤、過誤瘤、類肉瘤性的腎細胞癌及類肉瘤性的移行性上皮細胞瘤。手術後經過3年，病人之預後良好，且無腫瘤再發之跡象。我們闡述未分化肉瘤之病理及影像特徵，並點出肉瘤形成與尿毒症之間的可能關連性。

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