Case Report

Round Cell Liposarcoma of Scrotum with Indolent Course in Young Adult

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Myxoid/Round cell liposarcoma accounts for one-half of all liposarcomas and occurs as the second most common subtype. Both myxoid and round cell types share clinical, histological features and are accepted to represent a spectrum of lesions ranging from pure myxoid to near completely round cell liposarcoma. Round cell liposarcoma is highly metastatic and is classified as high grade and poorly differentiated myxoid sarcoma. Typical non-round cell myxoid liposarcoma is less metastatic and has more favorable prognosis. Karyotypic study of myxoid and round cell liposarcomas reveal a characteristic reciprocal translocation t (12;16)(q13;p11) resulting in the fusion of CHOP gene with TLS gene in more than 90% of cases. Most masses within the scrotal sac arise from the testis proper, and less likely from the extratesticular tissue. Liposarcoma represents approximately 20% of malignant extratesticular neoplasms, with the well differentiated subtype being the most common. Myxoid/round cell liposarcoma and round cell liposarcoma are rarely encounter in extratesticular soft tissue. We reported a rare case of round cell liposarcoma (high grade myxoid liposarcoma) of extratesticular tissue. To our knowledge, this is the first case of a large size (> 5cm) round cell liposarcoma arising from soft tissue within the scrotal sac of young adult with indolent course. Simple excision or enucleation are inadequate therapies and wide excision of the hemiscrotum including inguinal soft tissue and nodes is recommended. The role of retroperitoneal lymph node dissection and adjuvant chemotherapy remains controversial.

Keywords: *Round cell liposarcoma, Scrotum, Young adult, Indolent course*

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Liposarcoma is the second most common soft tissue tumor in adults, with an incidence ranging from 9.8 to 16.0%[1,2]. Myxoid/Round cell liposarcoma accounts for one-half of all liposarcomas and occurs as the second most common subtype[3]. This subtype is classified according to its histologic, biologic, cytogenetic, and molecular characteristics. The behavior of each subtype is variable ranging from local recurrence to metastasis. According to the 2002 World Health Organization (WHO) histologic classification of tumors, liposarcoma can be divided into 5 categories: atypical lipomatous tumor/ well differentiated; dedifferentiated; myxoid; pleomorphic; and mixed-type liposarcoma. Round cell liposarcoma and the mixed myxoid and round cell types have recently been subclassified under the heading of myxoid liposarcoma and mixed-type liposarcoma[4]. These distinctions are problematic in routine usage. The Evans classification system is practical and easier to use. This system divides myxoid and round cell liposarcoma into three subgroups depending on the relative-amount of round cell components. Tumors with a round cell component totaling < 10%, 10-25%, and > 25% are defined as myxoid, mixed myxoid and round cell, and round cell liposarcoma, respectively[5]. Both myxoid and round cell types share clinical, histological, and cytogenetic features and are accepted to represent a spectrum of lesions ranging from pure myxoid to near completely round cell liposarcoma. Karyotypic evaluation of both

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myxoid and round cell liposarcoma characteristically reveals the reciprocal translocation t (12;16) (q13;p11) in more than 90% of cases, resulting in the fusion of the CHOP and TLS genes[6]. However, these tumors exhibit a distinctly different clinical behavior. Round cell liposarcoma tends to metastasize and is classified as a poorly differentiated, or high grade sarcoma. Myxoid liposarcoma without a round cell component is considered a low to moderate grade sarcoma and has less metastatic potential and a more favorable prognosis than the high grade round cell type[7].

Masses within the scrotal sac are most commonly located within the testis and less likely in the extratesticular tissue. Paratesticular tumors are most commonly benign (70%) and arise from the spermatic cord. Despite being relatively rare, malignant neoplasms, including sarcomas, do occur. Of these, liposarcoma is encountered about 20% of the time and the most common subtype is a well-differentiated liposarcoma, predominantly lipoma-like[8].

Liposarcoma is primarily a tumor of older adults, with a peak incidence of 40-60 years of age. Most cases arise within the retroperitoneal or intra-abdominal regions. The peak age group of myxoid round cell liposarcomas is the fifth decade and the most preferential site is the lower extremity, especially the medial thigh and popliteal fossa[9]. To the authors knowledge, this is the first case of a large size (> 5cm) round cell liposarcoma (High grade myxoid liposarcoma) arising from the soft tissue within the scrotal sac of a young adult with indolent course.

Case Report

A 34-year-old Thai man presented with a left scrotal mass of approximately 6 months duration. He complained of only dull pain and no other symptoms. The tumor had progressively enlarged but was not tender. The first clinical impression was that of a hydrocele. Physical examination revealed a well-circumscribed, mobile and soft left scrotal mass with smooth surface. A CT scan of the abdomen was normal. Operative findings showed a well encapsulated, smooth-surfaced mobile mass localized within the scrotum. The mass was not adherent to the testis and was easily removed. A wide excision was performed. Laboratory investigation revealed β-HCG = < 5 mU/ml, Alpha-fetoprotein = 2.2 IU/mL. CXR-PA was within normal limit. CT-SCAN whole abdomen: No ascitis was noted. No significant enlarged lymph node was detected.

Pathologic examination revealed a well-defined tumor mass measuring 8.0 x 6.0 x 4.0 cm. It was multinodular with fibrous encapsulation and had an inhomogeneous grey-white cut surface. The percentage of tan and gelatinous area was approximately 10% of the whole mass (Fig. 1).

Histological examination showed solid sheets and islands of round to oval shaped cells with slightly vacuolated cytoplasm. The round cells showed moderate pleomorphism, high nuclear/cytoplasmic ratio, conspicuous nucleoli, and small amounts of eosinophilic cytoplasm. At the initial sampling, no myxoid areas were seen. Additional tissue sampling from the tan gelatinous area revealed focal areas of univacuolated lipoblasts and a few multivacuolated cells within the background of myxoid stroma and chicken-wire capillary vascular pattern. All slides were examined to identify lipoblasts, round cells, solid and myxoid areas to determine the percentage of round cell component. The round cell component represented approximately 90% of the sampled tumor (Fig. 2A). Extracellular mucin, including pooling of mucin, admixed with a small amount of round cells and lipoblasts was identified and represented about 10% of the tumor (Fig. 2B). Mitotic figures were present at a rate of 3/10 HPFs. Areas of necrosis and hemorrhage were not found. Immunohistochemical staining revealed positivity for S-100 protein (Fig. 3A) and negativity for lymphocyte common antigen (LCA). Ultrastructural study revealed lipoblasts with variably sized lipid droplets as well as primitive cells devoid of lipid droplets (Fig. 3B).

Discussion

Benign and malignant paratesticular soft tissue neoplasms represent 52% of all paratesticular

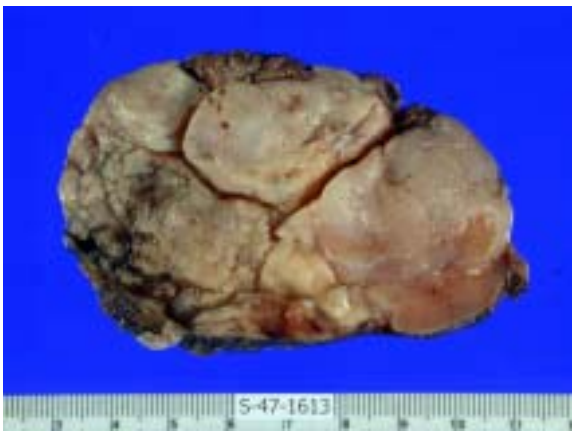

Fig. 1 Multinodular mass with grey-white cut surface and 10% of tan and gelatinous area of the whole mass

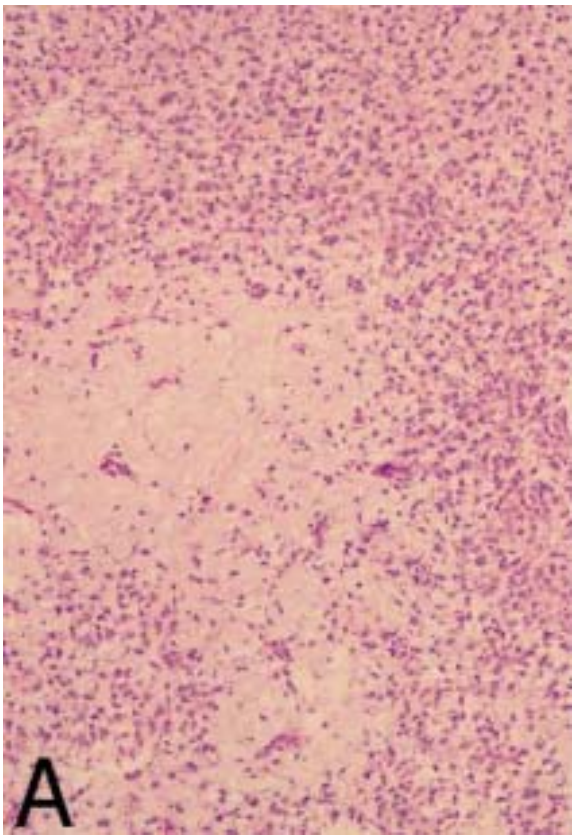

Fig. 2A Solid sheets and islands of round to oval shaped cells with slightly vacuolated cytoplasm within background of myxoid stroma and chicken-wire capillary vascular pattern

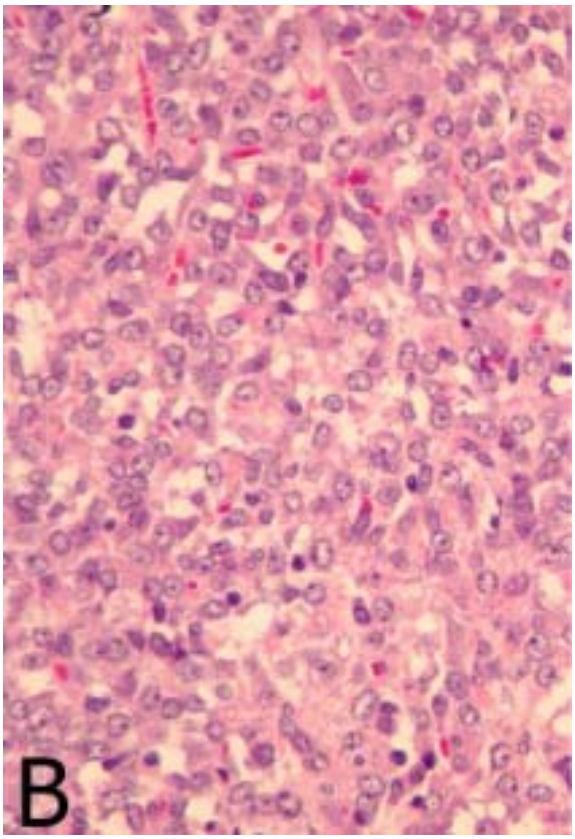

Fig. 2B The round cells shows round to oval shaped nuclei with high nuclear-cytoplasmic ratio, visible nucleoli, and less cytoplasm

tumors reported by the Canadian Reference Center of Cancer Pathology from 1949 to 1987 accounted for about 52 % of all paratesticular tumors[8]. The most common benign tumors include lipoma, adenomatoid tumor and leiomyoma. Malignant tumors of the paratesticular soft tissue are very uncommon. The percentage of various types of paratesticular sarcomas has been previously reported as follows: Leiomyosarcomas (32%), rhabdomyosarcomas (24%), liposarcomas (20%), and malignant fibrous histiocytomas (13%)[10].

Liposarcomas in the paratesticular region can either arise de novo from adipose tissue around testis and spermatic cord or possibly from a pre-existing lipoma[11]. Previously reports of liposarcoma subtypes included well-differentiated, myxoid/round cell and pleomorphic types, with the most frequent subtype being well-differentiated liposarcoma. These typically present in older adults as a large mass in paratesticular region, and tend to recur if incompletely excised.

The preoperative impression of an otherwise asymptomatic tumor mass in the paratesticular region can lead to an initial misdiagnosis of a hydrocele, as was the case in the presented patient. At surgery the tumor mass was large but was easily separated from the testis and there was no evidence of infiltration to surrounding tissue. Grossly, the tumor was rather firm and solid. As round cell liposarcoma is considered a poorly differentiated, high grade sarcoma with an unfavorable prognosis, it is important that all myxoid liposarcomas be extensively sampled in order to detect round cell components. Additionally, in the setting of any small round cell tumor occurring in this region, round cell liposarcoma must be considered in the differential diagnosis along with lymphoma, rhabdomyosarcoma, poorly differentiated (round cell) synovial sarcoma, and other small round cell tumors. Kilpatrick et al. showed a relationship between the rate of metastasis and the percentage of round cell component in myxoid/round cell liposarcoma. Round cell

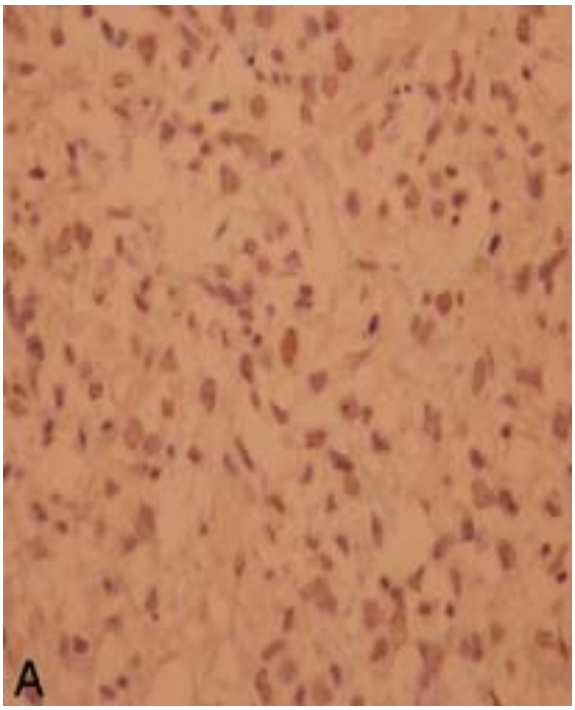

Fig. 3A The immunohistochemistry study for S-100 protein is positive in nucleus of tumor cells

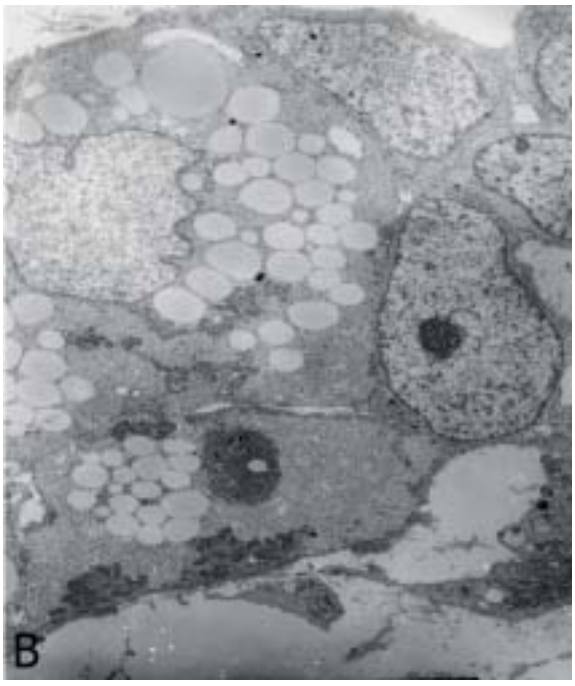

Fig. 3B Ultrastructural study reveals lipoblasts with variably sized of lipid droplets within cytoplasm. The adjacent primitive cell is devoid of lipid vacuoles

components of 0-5, 5-10, > 25% correlated with the likelihood of metastasis of 23%, 35%, and 58%, respectively. Overall, patients with myxoid/round cell liposarcomas metastasized at a rate of 35%, with a tumor related mortality of 31%[11] In tumors with a small round cell appearance in the 40-60 year old age group, the most likely entities for consideration in the differential diagnosis include lymphoma and round cell liposarcoma. In such a tumor with a great preponderance of round cells, immunohistochemistry can be useful in separating these two entities. While lymphoma would be exhibit positivity for leukocyte common antigen and negativity for S-100, round cell liposarcoma would be expected to show the opposite result with LCA negativity and S-100 positivity. If indicated, ultrastructural examination can confirm the lipogenic differentiation of the cells.

Soft tissue sarcomas often locally recur after incomplete excision. Risk factors for local recurrence in this region include large size, inguinal location, and close or positive margin after resection[8]. Factors associated with significantly poor prognosis are age > 45 years, round cell component > 25%, and the presence of spontaneous necrosis[12]. Catton et al. suggested that simple excision or enucleation is inadequate and recommends wide excision of the hemiscrotum including inguinal soft tissue and nodes[13]. The roles of retroperitoneal lymph node dissection and adjuvant chemotherapy remain controversial.

The majority of reported cases of scrotal liposarcoma are well differentiated liposarcoma with low grade behavior. The presented patients prognosis would appropriately be considered less favorable given the high grade histology of this tumor. Favorable prognostic factors in the presented patient include younger age, absence of spontaneous necrosis, relative superficial location of the tumor and ease of complete excision. These may help to explain the indolent course in the presented patient with a histologically high grade sarcoma. The surgeon plans to do left a hemiscrotectomy and groin node dissection after the pathological diagnosis.

It can be seen from this case that upon encountering a large, painless, cystic or solid mass in the paratesticular scrotal region, included in the differential diagnosis should be rare primary mesenchymal tumors including sarcomas. With this differential diagnosis in mind, the appropriate approach to pathologic examination as well as patient management is facilitated.

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มะเร็งไขมันชนิดเซลล์กลมของถุงอัณฑะในผู้ป่วยอายุน้อยที่มีการดำเนินโรคไม่รุนแรง

วรนุช ธนากิจ, Scott D Nelson, **สุเทพ อุดมแสวงทรัพย์**

มะเร็งไขมันชนิดmyxoid/round cell พบเกิดขึ้นประมาณครึ่งหนึ่งของมะเร็งเนื้อเยื่ออ่อน และเป็นชนิดที่พบบ่อยเป็นลำดับที่2ในกลุ่มมะเร็งไขมัน มะเร็งไขมันทั้งชนิด myxoid และ round cell พบว่ามีลักษณะร่วมกันทั้งทางคลินิก, ฮิสโตโลจี, และ ส่วนประกอบทางโครโมโซมและยังได้รับ การยอมรับว่าเป็น spectrum ของโรคที่มีการดำเนินโรคต่อเนื่องโดยเริ่มจากพบแต่ชนิด myxoid ไปสู่ชนิดที่มีแต่ round cell มะเร็งไขมันชนิดround cell พบการแพร่กระจายสูง และถูกจัดอยู่ ในกลุ่มมะเร็งเกรดสูงและมีพัฒนาการที่ไม่ดี ส่วนมะเร็งไขมันกลุ่มที่ไม่มีส่วนประกอบของround cell ซึ่ง ได้แก่ชนิด myxoid พบการแพร่ กระจายของมะเร็งเกิดขึ้นน้อยและมีการพยากรณ์โรคที่ดี กว่า จากการศึกษาส่วนประกอบทางโครโมโซมพบว่าทั้งชนิด myxoid และ round cell พบการเกิด reciprocal translocation มากกว่า 90% ที่ t (12;16) (q13;p11) ส่งผลทำให้เกิด fusion ของจีน CHOP กับTLS ก้อนที่เกิดขึ้นในถุงอัณฑะโดยส่วนใหญ่เกิดขึ้นจากองค์ประกอบของลูกอัณฑะ พบน้อยมากที่จะเกิดขึ้นจากส่วนของเนื้อเยื่อในถุงอัณฑะ และพบการเกิดมะเร็งไขมันที่เกิดจากเนื้อเยื่อในถุงอัณฑะได้ประมาณ 20% ,ชนิดที่มีพัฒนาการดี (well differentiate) เกิดขึ้นได้บ่อยที่สุด ส่วนชนิด myxoid/round cell และ ชนิด round cell พบเกิดขึ้นแต่น้อยมาก คณะผู้วิจัยได้เสนอรายงานผู้ป่วยมะเร็งไขมันชนิด round cell ซึ่งถูกจัดเป็นมะเร็งเกรดสูงที่เกิดจากเนื้อเยื่อในถุงอัณฑะ ซึ่งพบได้น้อยมากจากการค้นคว้าพบว่ารายงานผู้ป่วยฉบับนี้เป็นรายงานแรกซึ่งผู้ป่วยมีอายุน้อยแต่เกิดก้อน มะเร็งไขมันจากเนื้อเยื่อในถุงอัณฑะชนิด round cell โดยก้อนมีขนาดใหญ่ (> 5 ซม.) แต่กลับมีการดำเนินโรคที่ไม่รุนแรง วิธีการรักษามะเร็งไขมันในถุงอัณฑะชนิดนี้พบว่าทั้งการผ่าตัดทั้งชนิด simple excision หรือการเลาะเอาแต่ก้อนออกเป็นวิธีการรักษาที่มีรายงานว่ายังไม่เพียงพอ แต่ให้ทำผ่าตัดชนิด wide excision ของ hemiscrotum โดยการผ่าตัดนี้จะครอบคลุมเนื้อเยื่ออ่อน และต่อมน้ำเหลืองบริเวณขาหนีบด้วย ส่วนการผ่าตัดเลาะเอาต่อมน้ำเหลืองใน retroperitoneum และการให้ยาเคมีบำบัดยังคงมีข้อขัดแย้งกันอยู่ในปัจจุบัน