

CASE REPORT

Retroperitoneal liposarcoma in an adult patient with Down syndrome

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Abstract

Retroperitoneal liposarcoma is a rare solid tumour of mesenchymal origin with an incidence of 2.5 per million population. We report what is, to the best of our knowledge, the first case in the English literature of retroperitoneal liposarcoma in an adult patient with Down syndrome. The tumour was surgically resected with no use of adjuvant chemotherapy or radiation. No recurrence was found at follow-up 2 months postoperatively. Clinicians should consider retroperitoneal liposarcoma in the differential diagnosis of abdominal distention in adult patients with Down syndrome.

Key words: Down syndrome, trisomy 21, liposarcoma

INTRODUCTION

Down syndrome is a chromosomal aberration that occurs in 1 of every 732 live births.¹ About 95% of affected individuals have trisomy of chromosome 21 as a result of meiotic nondisjunction. The remaining 5% have translocations or somatic mosaicism of chromosome 21. Although the overall incidence of cancer among individuals with Down syndrome is not significantly different from that of the general population, a lower incidence of solid tumours has been observed.² It has been hypothesized that tumorigenesis in individuals with Down syndrome may be inhibited in part by the additional dosage of antiangiogenic protein-expressing genes on chromosome 21, including *Collagen 18a*, a disintegrin and metalloprotease with thrombospondin type 1 motifs (*AdamTS-1*), and Down syndrome candidate region-1 (*DSCR1*).^{3,4} We describe the case of a middle-aged adult with Down syndrome who presented with progressive abdominal distention secondary to a massive retroperitoneal liposarcoma. To our knowledge, this solid tumour of mesenchymal origin with an incidence of 2.5 per million population⁵ has not been previously reported in an adult patient with Down syndrome.

CASE REPORT

A 46-year-old man with Down syndrome was admitted to hospital with a 3-week history of constipation, decreased appetite, and progressive abdominal distention with signs of pain. Comorbid disease included an atrial septal defect, Raynaud's syndrome, C1 to C5 cervical spine fusion, and hallux valgus repair. He did not have a habit of smoking or consuming alcohol. Clinical examination revealed a distended abdomen with a large palpable mass. Abdominal ultrasonography revealed a large heterogeneous soft tissue mass of unclear origin in the left mid abdomen. Computed tomography (CT) revealed a well-defined heterogeneous 30 cm fat-containing tumour likely originating in the left mid retroperitoneum (Figures 1 and 2). The patient was admitted for neoadjuvant total parenteral nutrition for malnutrition (serum albumin 18-20 g/L). No significant increase in albumin was observed after 4 weeks, at which time the patient was taken to the operating room. The tumour was excised with *en bloc* resection of the left kidney, spleen, and descending colon. Resection margins were observed to be tumour-free.

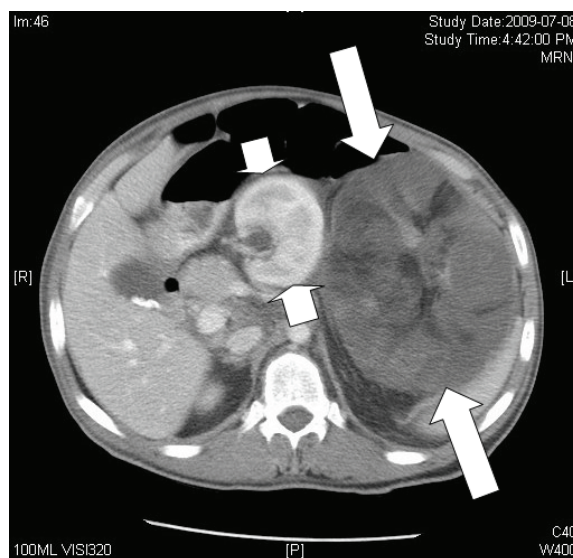


FIG. 1: Enhanced axial CT image at the level of mid abdomen shows a large heterogeneous mass (arrows) displacing the left kidney (arrowheads) anteriorly and medially suggesting retroperitoneal origin.

Pathology

Upon gross examination, the tumour measured 30 cm × 29 cm × 14.5 cm and weighed 7.37 kg. The tumour was well-circumscribed, multilobular, and covered by a thin, intact pseudocapsule. Serial sectioning revealed a macroscopic area of necrosis measuring 13 cm × 12 cm × 7 cm. Histologically, the tumour represented a well-differentiated liposarcoma primarily spindle-cell variant but also included lipoma-like and sclerosing variants (Figures 3 and 4). Focal

areas of necrosis were identified involving areas of well-differentiated liposarcoma. Sampling around the necrotic area demonstrated foci of increased cellularity with scattered pleomorphic cells and a mitotic rate of 3 per 10 high-power fields (Figure 5). This area did not meet the criteria for de-differentiated liposarcoma which is associated with metastatic potential. The tumour was grade II by the FNCLCC sarcoma system.⁶ Venous and lymphatic invasion were identified. The resected left kidney, spleen, and

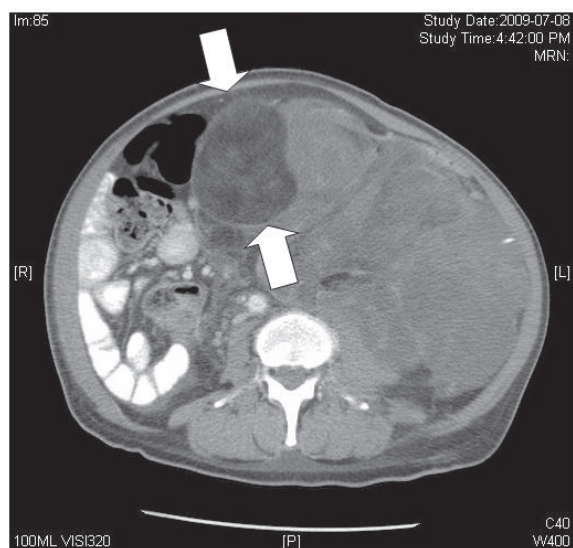


FIG. 2: Enhanced axial CT image slightly more inferior demonstrates fat density within the lesion (arrows) suggesting liposarcoma.

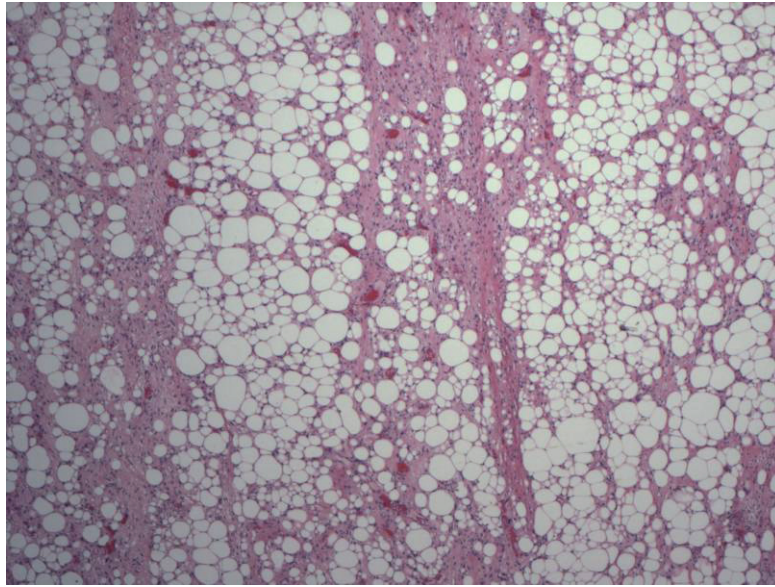


FIG. 3: Microphotograph demonstrating area of well-differentiated liposarcoma, lipoma-like variant [H&E, 20 X]

descending colon were negative for sarcoma involvement.

Post-operative course

Postoperatively, the patient's course in hospital was complicated by cardiac arrest secondary to aberrant conduction common in older patients with Down syndrome. His nutritional status improved rapidly. Adjuvant chemotherapy and radiotherapy were not prescribed. Baseline post-operative CT obtained at 2 months showed no

recurrence of the tumour.

DISCUSSION

Large epidemiological studies on cancer incidence have revealed a curious distribution of tumour types among individuals with Down syndrome. While it has been well established that the risk of leukemia in children with Down syndrome is about 20-fold higher than observed in the general population, the risk of solid

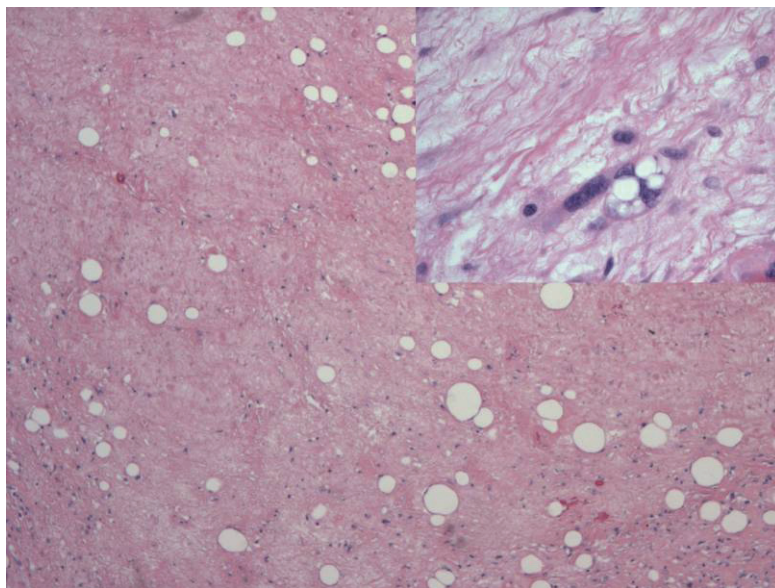


FIG. 4: Microphotograph demonstrating area of well-differentiated liposarcoma, sclerosing variant [H&E, 20 X]. Inset: Microphotograph demonstrating atypical lipoblasts [H&E, 400 X].

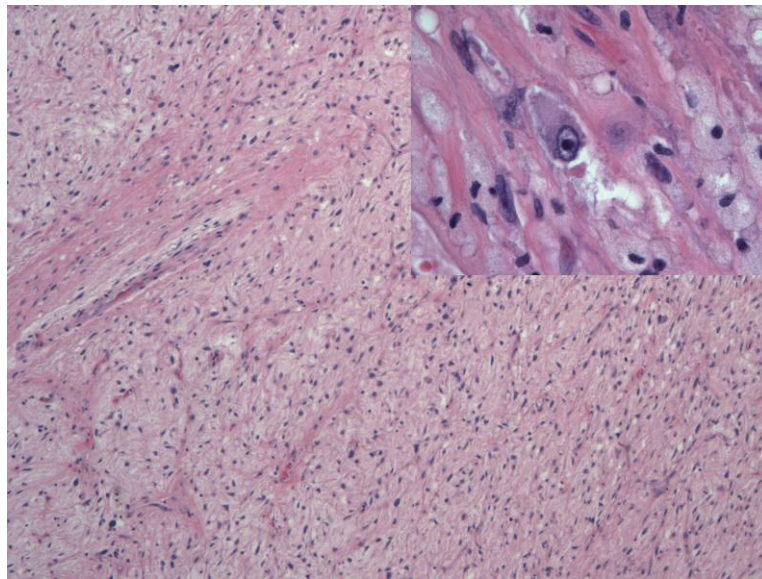


FIG. 5: Microphotograph demonstrating a non-lipomatous area qualifying as focus of cellular liposarcoma [H&E, 40 X]. Inset: Microphotograph demonstrating pleomorphic cells within the non-lipomatous areas [H&E, 400 X].

tumours among individuals with Down syndrome appears markedly lower across all age groups.⁷ A study of 2421 children with Down syndrome in Massachusetts, USA, found no cases of solid tumours.⁸ A study from the Danish Cytogenetic Register found only 24 cases of solid tumours among 2814 individuals with Down syndrome while 47.8 cases were expected.⁷ The most common solid tumours that have been reported in adults with Down syndrome are germ cell tumours, lymphoma, and retinoblastoma.^{9,10} Cancers of the lung, breast, digestive tract, and skin have been reported rarely.¹¹ Individuals with Down syndrome may have lower risk for some cancers by reduced exposure to environmental insults including alcohol, cigarette smoke, and ultraviolet light. However, trisomic 21 fibroblasts and their related extracellular matrix components may confer increased resistance to tumours with well-developed stroma¹² in conjunction with angiogenesis inhibitors.^{3,4,13}

A search of MEDLINE (1950 to August Week 3 2010) and Embase (1980 to 2010 Week 33) uncovered no reports of retroperitoneal liposarcoma in an adult patient with Down syndrome. In the paediatric population with Down syndrome, there are few reported cases of fat-containing retroperitoneal masses in children. One case of lipoma¹⁴ and two cases of teratoma^{15,16} are reported.

Liposarcoma accounts for at least 20% of soft-tissue sarcomas in adults with frequent occurrence

in the extremities and retroperitoneum.¹⁷ Liposarcomas of the retroperitoneum tend to occur in adults in their 4th to 6th decades of life with a male predominance. The expandable potential space of the retroperitoneum allows tumours to remain clinically asymptomatic until they achieve considerable size. Common presentations include a palpable abdominal mass, abdominal distention or abdominal discomfort of several months duration.¹⁸ Because of limitations in language comprehension and expression, persons with Down syndrome may not effectively communicate discomfort, pain, or other symptoms.

Five histological categories of liposarcoma are recognized by the World Health Organization (WHO): well-differentiated, dedifferentiated, myxoid, round-cell, and pleomorphic liposarcomas. Well-differentiated liposarcoma is the most commonly encountered subtype in the retroperitoneum and is further classified into lipoma-like, sclerosing, and inflammatory variants. In contrast, pleomorphic liposarcoma is the least common subtype.¹⁹ Mixed histology of well-differentiated and pleomorphic components, as was observed in this case, is also rare.²⁰

In examining the sonographic features of histologically-verified retroperitoneal liposarcomas, Ishida²¹ *et al.* reported that a pattern of multiple, evenly distributed, fine echogenic lines in a tumour is suggestive of

well-differentiated liposarcoma. On CT scan, Lahat²² *et al.* noted that the absence of focal nodular/water density is highly suggestive of well-differentiated liposarcoma while its presence demonstrated high sensitivity (97.8%) but relatively low specificity (51.5%) as a marker of dedifferentiated liposarcoma. Magnetic resonance imaging (MRI) may also be used to differentiate the histological subtypes of retroperitoneal liposarcoma.²³

Primary treatment consists of complete surgical resection of the tumour. In one study by Singer¹⁹ *et al.* of patients with retroperitoneal liposarcoma, surgical resection offered overall disease-specific survival of 73% at 3 years. Complete resection of liposarcomas >10 cm may require resection of surrounding structures in up to 50% of cases, most commonly the kidney and colon.^{5,24} The use of chemotherapy is ineffective as adjuvant treatment for retroperitoneal liposarcoma.²⁵ The use of adjuvant radiotherapy remains controversial as the radiation doses and fields are associated with substantial gastrointestinal morbidity with no clear survival benefit.²⁴ Retroperitoneal liposarcomas frequently recur within 6 months to 2 years of initial surgical resection. In evaluating the growth rates of recurrent retroperitoneal liposarcoma on follow-up CT scans, Kim¹⁸ *et al.* reported a mean tumour volume doubling time of 98 days (range, 46–151 days; median, 104 days). It is suggested that patients undergo CT or MRI surveillance for tumour recurrence every 3 to 6 months during the first 2 years after operation and every 6 months for 3 years thereafter.

Although many solid tumours are rare in patients with Down syndrome, clinicians should consider retroperitoneal liposarcoma in the differential diagnosis of abdominal distention in adult patients with Down syndrome. Awareness of the possibility of this diagnosis may heighten attention to symptom development with timely clinical evaluation and management.

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