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Research Article

Management of Giant Retroperitoneal Liposarcoma With Parathyroid Adenoma

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ABSTRACT

The coexistence of giant retroperitoneal liposarcoma and parathyroid adenoma presents a unique clinical challenge, as highlighted in our case involving a 44-year-old male presenting with nonspecific abdominal symptoms and significant weight loss. Initially suspected to be a benign lipoma, diagnostic imaging revealed a large retroperitoneal mass, which upon surgical excision and subsequent histological analysis was identified as a liposarcoma. The patient's post-operative period was complicated by the incidental discovery of a parathyroid adenoma, further complicating his clinical course. This case underscores the diagnostic and therapeutic complexities associated with retroperitoneal masses, especially when presenting alongside endocrine abnormalities. The management involved multidisciplinary approaches including surgery, histopathological examination, and genetic testing, specifically MDM2 amplification testing which confirmed the diagnosis of liposarcoma. This testing is crucial as it aids in distinguishing between lipoma and liposarcoma, which can often appear similar histologically. Furthermore, the case highlights the importance of considering parathyroid adenoma in patients with unexplained hypercalcemia, especially when presenting with other neoplastic processes. This association, although rare, suggests a potential link between hyperparathyroidism and certain sarcomas, which may warrant further investigation.

INTRODUCTION

Liposarcoma is a rare mesenchymal neoplasm arising from the lipocytes in the soft tissues [1]. They account for about 15% of all cases of sarcoma with an incidence level of 0.3% - 0.4% per 100,000 [2]. Though liposarcoma can occur wherever fat is present, the most commonly observed site is the retroperitoneum [3]. Retroperitoneal liposarcoma can occur in any age group but the incidence is high between 60-70 years of age with equal gender distribution [4]. It often leaves the diagnostician in a dilemma as it has no specific clinical features or any identified predisposing factors. The patient's symptoms are nonspecific, including abdominal pain/fullness, flank pain, early satiety, lower extremity swelling. There could be neurological, musculoskeletal, and obstructive urinary or bowel symptoms which could be the result of local invasion or compression [5].

The growth of the tumor is highly unpredictable, it could be gradual, or rapid or it might remain inert for a long time and have accelerated growth within a short period. USG and CECT are useful to find the extent of the lesion, compression caused by the lesion, and anchoring extension structures which could be the small bowel, Kidneys, Pancreas, and Liver. The prognosis of the disease is poor until treated, surgical excision of the tumor with negative margins is the gold standard for treatment of Retroperitoneal liposarcoma. A mutuation study would be useful to differentiate the diagnosis of liposarcoma following which the plan of management would change. Correlation between liposarcoma and parathyroid adenoma however, is not well established in literature.

CASE REPORT

A 44yrs gentleman visited the General Surgery OPD with complaints of upper abdominal fullness for the past 7 months with

insidious onset which was associated with pain for the last 1 week. There was intermittent pain which was localized to the right hypochrodrial region. The patient also complained of weight loss of 8kg within the last 12 months. The abdomen examination revealed distension, soft with no organomegaly, and no warmth or tenderness. The provisional diagnosis was Retroperitoneal or Intra-abdominal Lipoma was considered. USG of the Abdomen and pelvis revealed a large heterogenous hyperecholic lesion measuring about 12.0 cm x 13.0 cm was appreciated in the retroperitoneum on the left side. The impression from the CECT was that a large capsulated fat density lesion measuring 27.0 cm x 13.6 cm occupied almost the entire abdomen extending into the pelvis and left inguinal region. The lesion is seen to displace the small and large bowel loops towards the right (Figure: 1.1,1.2).

A USG-guided biopsy of the retroperitoneal mass was performed which showed scanty tissue with adipocyte clusters and a lipomatous lesion was considered. Exploratory Laparotomy was performed to excise the tumor which weighed about 7.25kg and measured about 52x34x14cm with the external surface congested. (Figure: 2.1,2.2,2.3).

Post operatively, biopsy of the lesion showed adipocyte tumor with atypical cells and provisional report of liposarcoma was considered. Though the histologic appearance showed predominantly mature adipocytes and was suggestive of lipoma (Figure: 3.1, 3.3, 3.4), molecular studies for MDM2 were advised considering the size and location of the tumor.

The results from MDM2 mutation study was suggestive of Liposaroma (Figure: 4). Immediate post op period was uneventful and he was discharged and since liposarcoma was confirmed, he was planned follow up ultrasounds. 2 month follow up ultrasound showed no abnormality. The next post-operative USG was done 5 months later which suggested possibility of fat containing lesion in left iliac fossa which was suggestive of recurrence so PET-CT was done. PET-CT showed fat with ill-defined stranding (measuring 5.5 x 7.2 x 12 cm) and few small foci of mild FDG uptake (SUVmax ~ 4.11) within the retroperitoneal fat plane in the left lower abdomen and iliac region in continuity with the inguinoscrotal hernia with encasement of left ureter and minimal dilatation of mid ureter (Figure: 5). Parathyroid adenoma (left superior) was also noted (Figure: 6).

Following oncology consult, he was advised resection and stenting of ureter with chemotherapy but patient defaulted on surgical management as he was asymptomatic. He presented a month later with knee and back pain and on further evaluation his PTH levels were high- 160pg/mL (reference range: 15pg/mL - 65pg/mL) and DEXA scan showed osteoporosis. He underwent parathyroidectomy and his post-operative blood report showed ionised calcium was 1.171 mmol/l (reference range: 1.1mmol/l - 1.3mmol/l) and PTH was 31.70 pg/ml (reference range: 15pg/mL - 65pg/mL). He has improved symptomatically post-surgery and will be on continued follow up for the recurrent lesion.

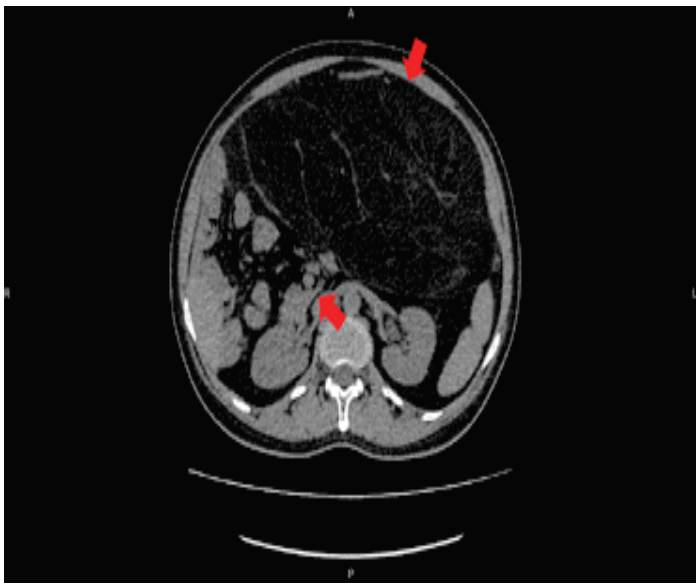

Figure 1.1: CT without Contract

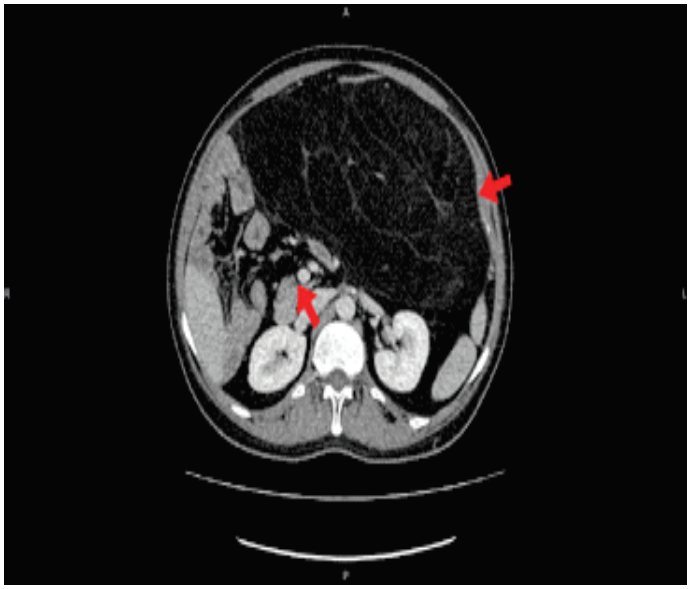

Figure 1.2: CT with Contract

Large retroperitoneal mass displacing the small and large bowels to the right side of the abdomen.

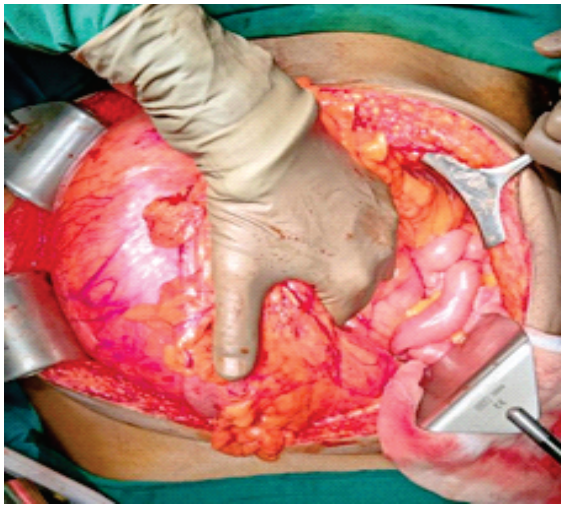

Figure 2.1: The Tumor is retracted to visualize the lateralized bowel

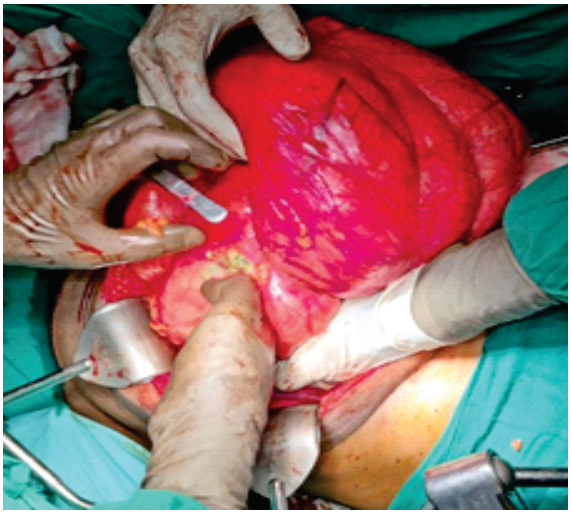

Figure 2.2: Complete extraction of the tumor from the peritoneal cavity

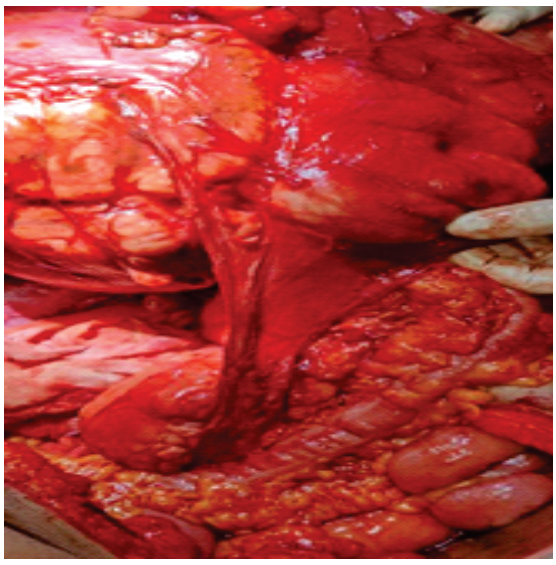

Figure 2.3: Adhesion of the tumor to the peritoneum and bowel

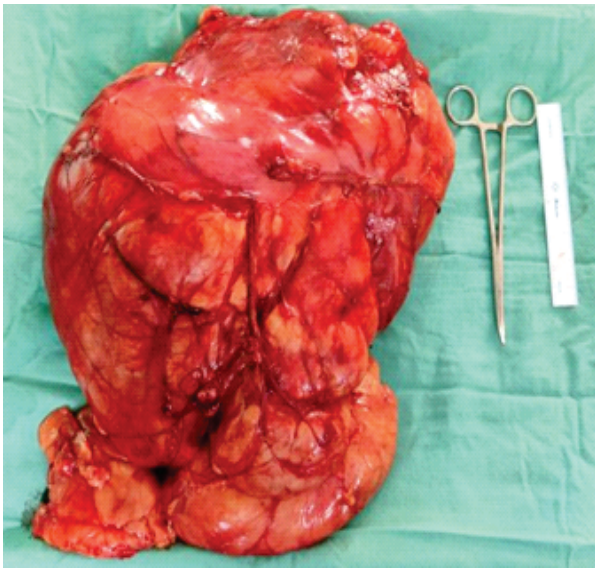

Figure 2.4: The Tumor measures 52x34x14cm, weighing 7.25 kg.

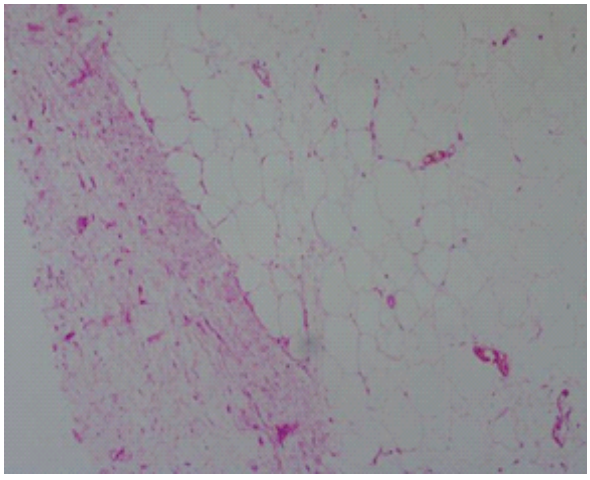

Figure 3.1: Well circumsided neoplasm comprises of predominantly mature adiadipocytes. (H&E 10x) contains congested blood vessels. (H&E 20x)

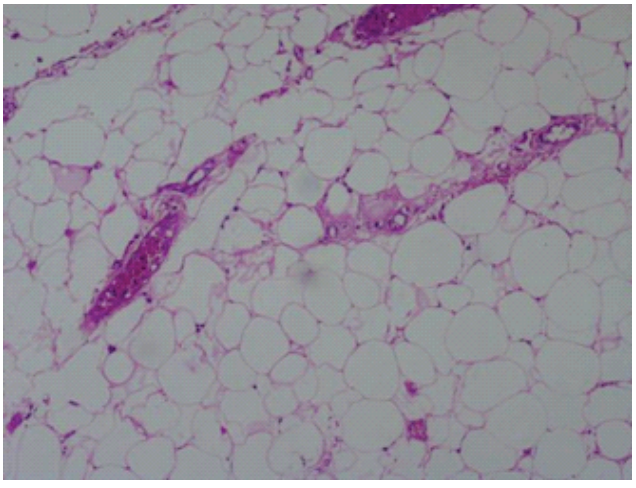

Figure 3.2: Mature adipocytes comprising of reduced cytoplasm and peripherally pulled small nuclei. It also contains congested blood vessels. (H&E 20x)

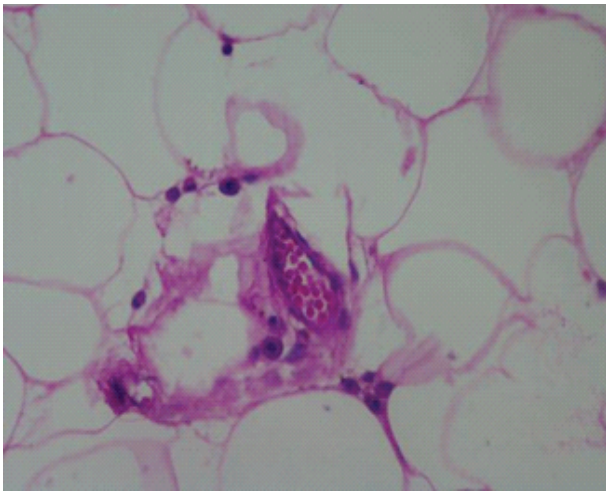

Figure 3.3: Adipocytes with scattered long cells with abundant granular eosinophilic cytoplasm and hyperchromatic nuclei. (H&E 40x)

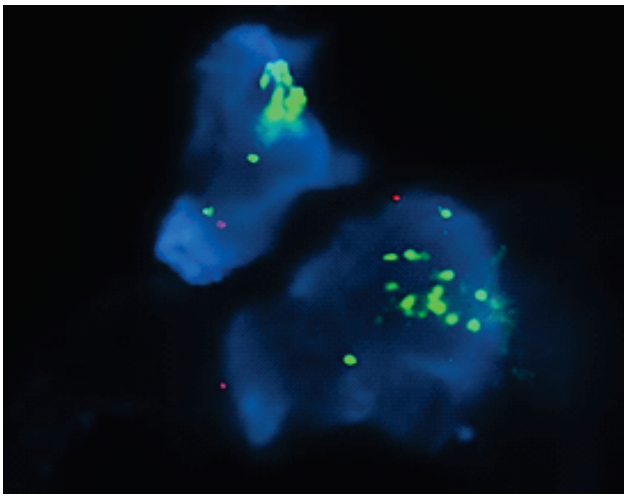

Figure 4: Standard cytogenetic identification of ring and giant rod chromosomes strongly support the diagnosis well-differentiated liposarcoma/atypical lipomatous tumor. (Fluorescence in situ Hybridization,FISH).

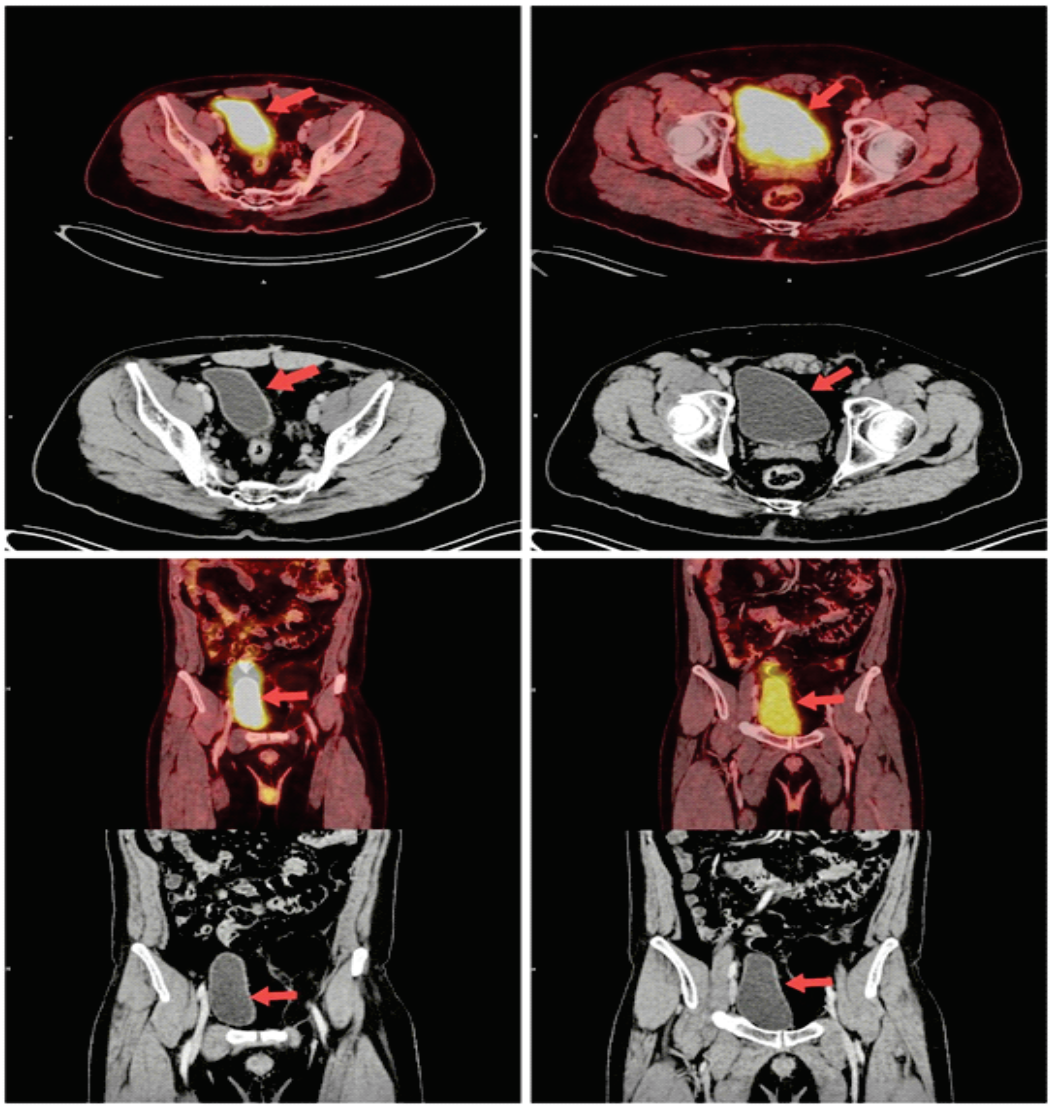

Figure 5: PET-CT- Fat with ill-defined stranding (measuring 5.5 x 7.2 x 12 cm) and few small foci of mild FDG uptake (SUVmax ~ 4.11) within the retroperitoneal fat plane in the left lower abdomen and iliac region in continuity with the inguinoscrotal hernia with encasement of left ureter and minimal dilatation of mid ureter. The lesion is abutting the abdominal wall laterally left perinephric and Gerota's fascia superiorly.

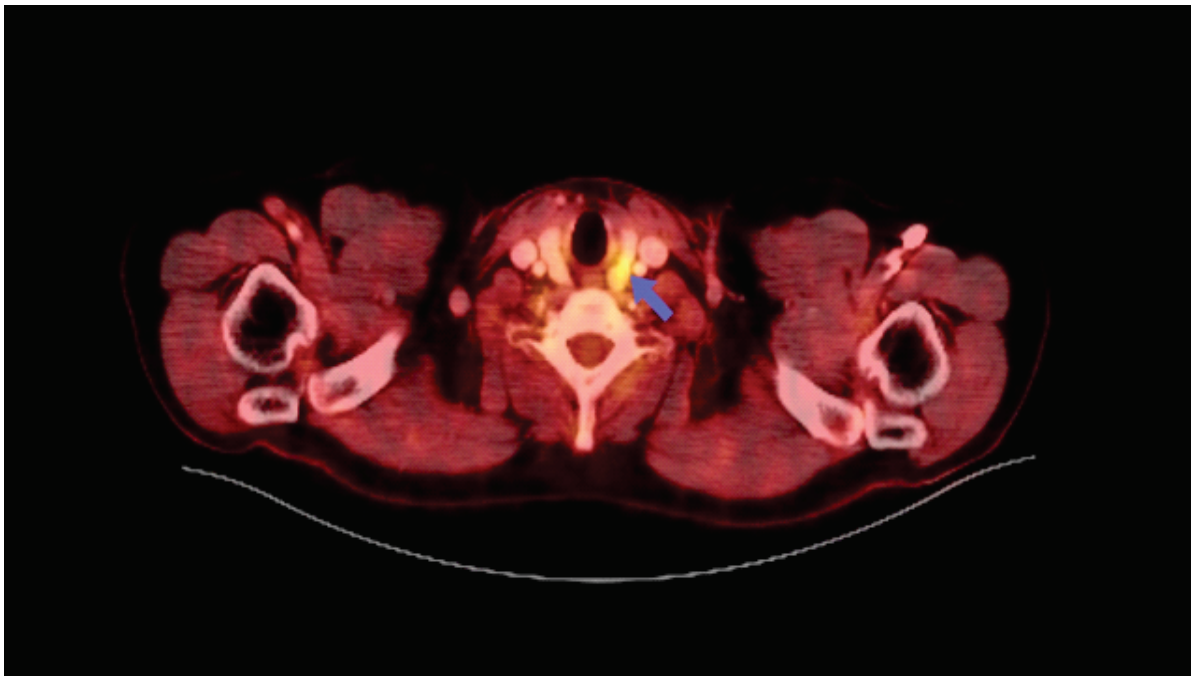

Figure 6: PET-CT Neck showing the FGD uptake in the left superior parathyroid gland.

DISCUSSION

There are a wide spectrum of rare tumours that arise from retroperitoneum that includes both benign and malignant tumours. Presenting symptoms and imaging studies are nonspecific and histological diagnosis is confirmatory. Soft tissue sarcomas are a rare type of malignancy and retroperitoneal sarcomas constitute 10-15% of all soft tissue sarcomas. The malignant tendency of soft tissue tumours is less than 1% in adults. The prognosis is more dependant on tumor margins and grading rather than tumour size. 75% of liposarcoma cases develop in the deep muscle layers, 20% develop in the retroperitoneum while the rest develop between the groin, in the spermatic cord and miscellaneous sites such as subcutis, parenchymal sites [6]. The lesion in the extremities takes several months to years before the patient seeks medical attention. The symptoms of liposarcoma in the retroperitoneum present the same as the intra-abdominal mass. The clinical manifestations vary from vague abdominal pain or mass to mass effect based on tumour growth. The CT images show fat density mass with mottled or streaky zones of higher density corresponding to the fibrous or sclerotic zones because the nature of the lesion has a significant component of mature fat [7,8]. Pelvic MRI (Magnetic resonance imaging) is used for ruling out vascular or muscular invasion, satellite lesions and recurrences [9]. Some possible differential diagnosis includes tumours arising from retroperitoneal visceral structures like renal or adrenal, pancreas etc, a lymphoma or a metastatic lesion. The gold standard of treatment is complete surgical excision and there is no evidence of survival benefits of adding adjuvant chemotherapy or radiotherapy [10,11]. While these tumours are insensitive to chemotherapy and/or radio therapy, adjuvant radiotherapy for lesions >5 cm with positive surgical margins have shown reduced recurrence rate but no increase in survival. Hence, complete surgical resection with free margins is the most important prognostic factor. Extensive resection for tumours that are found to be in contact with various adjacent organs tends to increase the overall morbidity [9,10,11,12,13].

Atypical lipomatous neoplasm (ALN) or well-differentiated liposarcoma (WDL) is the most common form of liposarcoma encountered in late adult life. The lesion in the extremities takes several months to years before the patient seeks medical attention. Rare cases have less well-defined borders when compared to lipoma. The cytogenic and molecular finding of liposarcoma is characterized by giant marker and ring chromosomes which contain amplified sequences of 12q13-15 and sites of several genes such as MDM2, GLI, SAS, CDK4, and HMGIC. MDM2 (12q13-15) and HMGA2 (12q15) are consistently amplified, resulting in liposarcoma. CDK4 located at 12q13 and TSPAN31 located at 12q13-q14 belong to a separate amplicon that co-amplifies MDM2 and HMGIC. Amplification of MDM2 and CDK4 results in downstream signaling which results in inhibiting apoptosis and increasing cell proliferation. Immunostaining CDK4 and MDM2 is used for differentiating ALN/WDL from other lipomatous lesions. MDM2 amplification evaluated by FISH is a highly sensitive and specific means of diagnosing ALN/WDL with needle biopsy specimen [14,15]. Most often these are tumors in which the degree of atypia falls short of a threshold level for the diagnosis of malignancy. The situation in which molecular testing for MDM2 is highly recommended are lipomatous tumors with equivocal cytologic atypia, recurrent lipomas, deep lipomas without

atypia that exceeds 15cm and retroperitoneal or intra-abdominal [16,17].

The outcomes of this disease may not be as expected as any other disease since recurrence rate is high. The recurrence rate of liposarcoma is 40 - 50%, the lesion either develop locally or distant metastatic sites. The prognosis of this disease is poor. the patient should be in regular follow up as the possibility of recurrence is high. CT can be done once a year and PET-CT if there are any new lesion. Ultrasound may used for screening but does give accurate imaging of the extent and metastasis of the lesion.

The diagnosis of parathyroid adenoma was incidental on PET CT follow up in this patient. Upon Review of further literature there have been previous cases of hyperparathyroidism associated with various sarcomas, the most common type being osteosarcoma [18,19]. Some cases reported initial diagnosis of hyperparathyroidism with development of sarcoma subsequently. Human cohort studies conducted however did not provide conclusive evidence to the increase of incidence of hyperparathyroidism in sarcoma patients [20].

CONCLUSION

A sarcomatous lesion in the retroperitoneum is rare but the most commonly observed is Liposarcoma. The chances of misdiagnosing a liposarcoma as lipoma is very high as they have similar histopathological features. A MDM2 mutation study has to be done to confirm the diagnosis. Based on the results from the mutation study the treatment regimen and the follow-up can be decided. Follow up of this patient led to the diagnosis and management of parathyroid adenoma. It is always better to do a mutation study (MDM2) for any suspected case of liposarcoma as the biopsy report may be similar to lipoma. As the characteristic and nature of the disease may differ, the results from the mutation study may influence the treatment and the follow-up.

While some case reports did suggest a rare association of hyperparathyroidism and sarcomas, retrospective case studies haven't shown an obvious association between them and further studies are required to establish a clear link between these two pathologies.

ETHICS APPROVAL

All necessary approval including ethical approval has been taken from the Institutional Human Ethics Committee before conducting this study.

CONFLICT OF INTERESTS

Authors declared that there is no conflict of interest.

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REFERENCE

1. Lin ZC, Chang XZ, Huang XF, et al.: Giant liposarcoma of the esophagus: A case report. World J Gastroenterol. 2015, 7:9827-32. 10.3748/wjg.v21.i33.9827.
2. Mettlin C, Priore R, Rao U, Gamble D, Lane W, Murphy P: Results of the national soft-tissue sarcoma registry. J Surg Oncol. 1982, 19:224-7. 10.1002/jso.2930190410
3. Das Gupta TK:Tumors and tumor-like conditions of the adipose tissue. Curr Probl Surg. 1970, 1:60.
4. Chouairy CJ, Abdul-Karim FW, MacLennan GT: Retroperitoneal liposarcoma. J Urol. 2007, 177:1145. 10.1016/j.juro.2006.12.006
5. Vijay A, Ram L:Retroperitoneal liposarcoma: a comprehensive review. Am J Clin Oncol. 2015, 38:213-9. 10.1097/COC.0b013e31829b5667
6. Weiss SW, Rao VK: Well-differentiated liposarcoma (atypical lipoma) of deep soft tissue of the extremities, retroperitoneum, and miscellaneous sites. A follow-up study of 92 cases with analysis of the incidence of "dedifferentiation". Am J Surg Pathol. 1992, 16:1051-8. 10.1097/00000478-199211000-00003
7. Arkun R, Memis A, Akalin T, Ustun EE, Sabah D, Kandiloglu G:Liposarcoma of soft tissue: MRI findings with pathologic correlation. Skeletal Radiol. 1997, 26:167-72. 10.1007/s002560050214
8. Ehara S, Rosenberg AE, Kattapuram SV: Atypical lipomas, liposarcomas, and other fat-containing sarcomas. CT analysis of fat element. Clin Imaging. 1995, 19:50-3. 10.1016/0899-7071(93)00023-r
9. Gronchi A, Miah AB, Dei Tos AP, et al.: Electronic address: clinicalguidelines@esmo.org. Soft tissue and visceral sarcomas: Esmo-Euracan-Genturis Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021, 32:1348-1365. 10.1016/j.annonc.2021.07.006. Epub 2021 Jul 22
10. Caizzone A, Saladino E, Fleres F, et al.: Giant retroperitoneal liposarcoma: Case report and review of the literature. Int J Surg Case Rep. 2015, 9:23-26. 10.1016/j.ijscr.2015.02.019
11. Pisters PWT, O'Sullivan B: Retroperitoneal sarcomas: combined modality treatment approaches. Curr Opin Oncol. 2002, 14:400-05. 10.1097/00001622-200207000-00006
12. Lewis JJ, Leung D, Woodruff JM, Brennan MF: Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated and followed at a single institution. Ann Surg. 1998, 228:355-65. 10.1097/00000658-199809000-00008
13. Weaver J, Downs-Kelly E, Goldblum JR, et al.: Fluorescence in situ hybridization for MDM2 gene amplification as a diagnostic tool in lipomatous neoplasms. Mod Pathol. 2008, 21:943-9. 10.1038/modpathol.2008.84
14. Sirvent N, Coindre JM, Maire G, et al.: Detection of MDM2-CDK4 amplification by fluorescence in situ hybridization in 200 paraffin-embedded tumor samples: utility in diagnosing adipocytic lesions and comparison with immunohistochemistry and real-time PCR. Am J Surg

Pathol.2007,31:1476-89. 10.1097/PAS.0b013e3180581fff

15. Zhang H, Erickson-Johnson M, Wang X, et al.: Molecular testing for lipomatous tumors: critical analysis and test recommendations based on the analysis of 405 extremity-based tumors. Am J Surg Pathol. 2010, 34:1304-11. 10.1097/PAS.0b013e3181e92d0b
16. Bill KLJ, Seligson ND, Hays JL, et al.:Degree of MDM2 Amplification Affects Clinical Outcomes in Dedifferentiated Liposarcoma. Oncologist. 2019, 24:989-996. 10.1634/theoncologist.2019-0047
17. Weaver J, Goldblum JR, Turner S, et al.: Detection of MDM2 gene amplification or protein expression distinguishes sclerosing mesenteritis and retroperitoneal fibrosis from inflammatory well-differentiated liposarcoma. Mod Pathol. 2009, 22:66-70. 10.1038/modpathol.2008.153
18. Herrmann SA, Stanborough R, Chrisinger JSA, et al.: Undifferentiated Pleomorphic Sarcoma and Hyperparathyroidism in an Adolescent Male: A Case Report and Review of Hyperparathyroidism-associated Sarcomas J Am Acad Orthop Surg Glob Res Rev. 2020, 10:19-00125. 10.5435/JAAOSGlobal-D-19-00125.
19. Zengin, Burak Alper; Bahçecioğlu, Adile Begüm1; Erdoğan, Murat Faik1:Primary hyperparathyroidism and sarcoma: A case report and literature review.Journal of Cancer Research and Therapeutics 19(7): p 2082-2085, Oct-Dec. 2023, 10.4103/jcrt.jcrt_2141_21
20. Jimenez C, Yang Y, Kim HW, et al.:Primary hyperparathyroidism and osteosarcoma: examination of a large cohort identifies three cases of fibroblastic osteosarcoma.J Bone Miner Res. 2005, 20:1562-8. 10.1359/JBMR.050507