A large retroperitoneal lipoblastoma as an incidental finding: a case report

Elena Gerhard-Hartmann 1,2*, Verena Wiegering 3, Clemens Benoit 4, Thomas Meyer 5, Andreas Rosenwald 1,2, Katja Maurus 1,2 and Karen Ernestus 1,2

Abstract
Background: Lipoblastoma is a rare benign mesenchymal neoplasm of infancy that most commonly occurs on the extremities and trunk but can arise at variable sites of the body. Retroperitoneal lipoblastomas are particularly rare but can grow to enormous size, and preoperative diagnosis is difficult with diverse, mostly malignant differential diagnoses that would lead to aggressive therapy. Since lipoblastoma is a benign tumor that has an excellent prognosis after resection, correct diagnosis is crucial.

Case presentation: A case of a large retroperitoneal tumor of a 24-month old infant that was clinically suspicious of a malignant tumor is presented. Due to proximity to the right kidney, clinically most probably a nephroblastoma or clear cell sarcoma of the kidney was suspected. Radiological findings were ambiguous. Therefore, the mass was biopsied, and histology revealed an adipocytic lesion. Although mostly composed of mature adipocytes, in view of the age of the patient, the differential diagnosis of a (maturing) lipoblastoma was raised, which was supported by molecular analysis demonstrating a HAS2-PLAG1 fusion. The tumor was completely resected, and further histopathological workup led to the final diagnosis of a 13 cm large retroperitoneal maturing lipoblastoma. The child recovered promptly from surgery and showed no evidence of recurrence so far.

Conclusion: Although rare, lipoblastoma should be included in the differential diagnoses of retroperitoneal tumors in infants and children, and molecular diagnostic approaches could be a helpful diagnostic adjunct in challenging cases.

Keywords: Retroperitoneal tumor, Pediatric, Lipoblastoma, PLAG1 rearrangement, Case report
lipoblastomas may show a particular prominent myxoid appearance, which, together with the previously described vasculature, leads to morphological similarities to myxoid liposarcoma, which is an important differential diagnosis but is exceptionally rare in this age group [8]. On the other hand, in their large series of 59 lipoblastomas, Coffin et al. reported in 76% an extensive maturation towards mature adipose tissue [2], which may obscure the diagnosis, particularly in small biopsies: the lesion may be misclassified as lipoma or completely missed due to histologic similarity to orthotopic adipose tissue. On the molecular level, lipoblastomas typically show a rearrangement of the chromosomal region 8q11–13, which results most commonly in a fusion of the pleomorphic adenoma gene 1 (PLAG1) with diverse partners, most commonly HAS2 (8q24.1) and COL1A2 (7q22) [9, 10].

We here report a case of a large retroperitoneal lipoblastoma of a 2-year-old infant that was difficult to diagnose preoperatively, in order to remind that this tumor – albeit very rare in this location – can be an important benign differential diagnosis.

Case presentation
A 24-month-old girl presented on a routine physical exam with a mass lesion in the right abdomen, which was not tender when palpated. There were no congenital abnormalities, and the development of the child was normal without evidence of any disease so far. The laboratory parameters (including hemoglobin, NSE, alpha-fetoprotein and beta-HCG as well as urine catecholamines) were normal.

Abdominal ultrasound showed a relative homogenous retroperitoneal mass adjacent to the liver and right kidney that measured up to 12.3 cm. MRI revealed a heterogeneous myxoid signal pattern (Fig. 1 a-e). A connection to the right kidney could not be safely excluded. Thus, clinically a malignant tumor, most probably a nephroblastoma or clear cell sarcoma of the kidney, was suspected. In Germany, nephroblastoma would be treated after unambiguous diagnostic imaging according to SIOP2001/GPOH protocol with preoperative chemotherapy without biopsy. However, since the radiological picture was not entirely clear, it was decided to perform a biopsy before systemic treatment. Computer tomography (CT) during biopsy revealed a fat-isodense nature of the mass (Fig. 1 f).

We received fragmented biopsies that are histologically composed of mostly mature adipocytes of slightly variable size with only very focal myxoid stroma, but with some small, slightly curved blood vessels. Although many histologic aspects of the biopsy resemble orthotopic fat tissue, since the tissue reliably stems from the tumor, the diagnosis of a benign lipomatous tumor was rendered, and considering the age of the patient most likely a lipoblastoma was suggested. To corroborate this diagnosis, we performed anchored multiplex PCR based targeted RNA sequencing using the Archer FusionPlex Sarcoma Panel and identified a HAS2-PLAG1 fusion (HAS2: Exon 1, NM_005328.2; PLAG1: Exon 3, NM_002655.2). There was no evidence for a rearrangement of the DDIT3 gene and thus no hint for a myxoid liposarcoma. Thus, the diagnosis of lipoblastoma was made, and surgical resection of the

Fig. 1 Axial abdominal magnetic resonance imaging (MRI) (a-e) and computer tomography (CT) (f) scan shows a right retroperitoneal mass with similar signal intensity to subcutaneous fat on T2-(a) and T1-(b) weighted images as well as on the CT scan. There is no diffusion restriction on the diffusion weighted images (c) and no significant contrast enhancement (e, axial T1-weighted fat suppressed image after intravenous contrast administration). The mass shows a capsule without local infiltration, but cranial displacement of the right kidney with signs of congestion (d, coronal fat-saturated T2–weighted MRI), which gradually resolved after resection (not shown)
tumor was decided. With regard to the surgical approach, median laparotomy versus a right upper abdominal laparotomy was discussed. In order to get a good overview as well safe access to the tumor, the vena cava inferior and the right kidney, it was decided to choose a right upper abdominal laparotomy. After laparotomy, a well-circumscribed mass was encountered in the retroperitoneum that could be completely resected without injury to adjacent structures. Grossly, we found a 13 × 10.5 × 8.7 cm large tumor (weighing 585 g), with a thin, fibrous capsule and a pale yellow, lobulated fatty parenchyma with small cysts (Fig. 2a and b). Histological examination revealed a lipomatous tumor with a vaguely lobular appearance with occasionally fibrous septae (Fig. 3a). The degree of cellular maturation was variable within the tumor, with a focally myxoid appearance and lipoblasts (3c and d), but also areas with much more mature adipocytes (3b), altogether leading to the final diagnosis of a maturing lipoblastoma.

Fig. 2 Gross appearance of the resected retroperitoneal mass: The tumor is covered by a thin fibrous capsule (a) and shows a pale yellow, slightly lobulated cut surface with small cysts (b)

Fig. 3 Microscopic examination of the resection specimen revealed a fatty tumor with focal fibrous septae (a) and morphologically different areas with focal myxoid appearance and lipoblasts (c, d), but also areas with much more mature adipocytes (b). The arrows in d indicate lipoblasts. The length of the scale bar is 500 μm in a, 100 μm in b and c, and 50 μm in d
The postoperative course was uneventful and the patient recovered promptly from surgery. Follow-up (6 months) revealed no evidence of recurrence so far.

In addition, we performed a literature review by searching the PubMed database using the key words “retroperitoneal lipoblastoma” and “lipoblastoma” and “retroperitoneum” etc. and additional papers were identified by searching the references of relevant articles. We identified 23 cases of circumscribed retroperitoneal lipoblastomas including the here presented case. A tabular overview is given in Table 1, which, however, makes no claim of absolute completeness, since we may have missed single additional reports in journals not published in English or very old reports.

**Discussion and conclusion**

Lipoblastomas are rare benign mesenchymal tumors of infancy and early childhood with often rapid growth that show an excellent prognosis after complete resection. However, the clinical differential diagnosis is broad, particularly in more rarely encountered localizations, and includes various benign and malignant tumors.

Retroperitoneal lipoblastoma is especially rare (< 30 well-documented cases, for overview see Table 1), often large and difficult to diagnose preoperatively, and the differential diagnosis in this location comprises primarily malignant tumors including sarcomas, nephroblastomas, neuroblastomas and teratomas.

Histologically, the diagnosis of lipoblastoma can also be challenging, particularly in small biopsies, since lipoblastomas can show morphological variable areas, with a prominent myxoid change, but also regions with an extensive maturation towards mature adipose tissue [2]. The histological differential diagnoses include lipoma, myxoid liposarcoma, well-differentiated liposarcoma/atypical lipomatous tumor and may, particularly in small biopsies of maturing areas, also comprise orthotopic adipose tissue. In the genital area, lipoblastoma-like tumor of the vulva is also among the differential diagnosis [24]. Myxoid liposarcoma and well-differentiated liposarcoma/atypical lipomatous tumor are very rare in the typical age group of patients with lipoblastoma, and show characteristic molecular alterations, namely the translocation t(12;16) (q13;p11) leading to a fusion of the

---

**Table 1** Reported cases of circumscribed retroperitoneal lipoblastomas (n = 23)

| Author                     | Year | Sex | Age         | Max. diameter |
|----------------------------|------|-----|-------------|---------------|
| Tanyel [11]                | 1986 | F   | 3 years     | 8 cm          |
| Jimenez [12]               | 1986 | M   | 12 years    | 19.5 cm       |
|                            |      | M   | 7 months    | 15 cm         |
| St Omer [13]               | 1992 | M   | 5 years     | n.r.          |
| Collins [14]               | 1997 | M   | 2 years 10 months | 21 cm   |
| Pollono [15]               | 1999 | M   | 5 months    | 14 cm         |
|                            |      | F   | 1 year 7 months | 18 cm   |
| Chun [16]                  | 2001 | M   | 2 years 5 months | 19.5 cm |
| Dokucu [17]                | 2003 | M   | 1 year      | 12 cm         |
| McVay [18]                 | 2006 | M   | 1 year 5 months | 17 cm   |
| De Saint Aubain Somerhausen [3] | 2008 | F   | 24 years    | > 10 cm       |
| Kok [7]                    | 2010 | F   | 4 years     | 25 cm         |
| Api [19]                   | 2010 | F   | 22 days     | 6.2 cm        |
| Burchhardt [20]            | 2012 | F   | 2 years     | 15 cm         |
| Susam-Sen [4]              | 2017 | M   | 1 year      | 9 cm          |
|                            |      | M   | 2 years 5 months | 13 cm   |
| Sakamoto [21]              | 2018 | F   | 3 years     | 12 cm         |
| Miyagi [22]                | 2018 | F   | 3 years     | 17.5 cm       |
| Abdul-Gafar [5]            | 2018 | F   | Not exactly specified, 2–5 years | 13 cm |
|                            |      | M   | Not exactly specified, 2–5 years | 28 cm |
| Wang [23]                  | 2019 | M   | 1 year 5 months | 15 cm   |
| Lopez-Nunez [10]           | 2020 | M   | 1 year      | 5.5 cm        |
| Our case                   | 2021 | F   | 2 years     | 13 cm         |

*n.r.* Not reported
FLI1 and DDIT3 gene in the former and amplification of the 12q14–15 region affecting MDM2 and CDK4 in the latter [1].

Lipoblastoma is characterized on the molecular level by 8q11–13 chromosomal alterations targeting PLAG1 (pleomorphic adenoma gene 1) located on 8q12 [9]. These alterations lead to PLAG1 overexpression, most commonly caused by chromosomal rearrangements resulting in a replacement of the PLAG1 promoter by a more active promoter of the fusion partner. The most commonly described PLAG1 fusion partners are HAS2 (8q24.1) and COL1A2 (7q22) [9], but more recently also several other genes (e.g. COL3A1, RAB2A, RAD51L) identified to be fused to PLAG1 in lipoblastoma [10, 25, 26]. Thus, the detection of a PLAG1 rearrangement, like the classical HAS2-PLAG1 fusion identified in the presented case, as well as exclusion of the previously mentioned DDIT3 rearrangement and 12q amplification, nowadays most commonly via FISH and/or targeted RNA sequencing approaches, can be a helpful diagnostic adjunct in challenging cases.

Taken together, Lipoblastomas can occur in a wide variety of localizations with a broad spectrum of clinical differential diagnoses. After complete resection, even patients with very large lipoblastomas have an excellent prognosis. Retroperitoneal lipoblastomas, such as the presented case, are particularly rare but often large tumors, and the clinical differential diagnoses in this setting include highly malignant tumors, like nephroblastoma and clear cell sarcoma of the kidney, that would lead to aggressive therapy. In conclusion, although rare, lipoblastoma should be included in the differential diagnoses of retroperitoneal tumors in infants and children and although the histopathological picture is the mainstay for the correct diagnosis, molecular diagnostic approaches may be a helpful diagnostic adjunct in challenging cases.

Abbreviations
PLAG1: Pleomorphic adenoma gene 1; NSE: Neuron specific enolase; beta-HCG: Human chorionic gonadotropin; MRI: Magnetic resonance imaging; CT: Computer tomography; FISH: Fluorescence in situ hybridization

Acknowledgements
We thank Sabine Roth and Erwin Schmitt for expert technical assistance.

Authors’ contributions
All authors contributed to the conception and design of the case report. Collection of specimens, data and material preparation were performed by EGH, VW, CB, TM and KM. The project was supervised by AR and KE. The first draft of the manuscript was written by EGH and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
The authors have no fundings to disclose. Open Access funding enabled and organized by Projekt DEAL.

Availability of data and materials
The data and material of this case report are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval was granted by the ethical comitee of the Medical Faculty of the University of Wuerzburg. The parents of the patient as legally authorized representatives gave their written informed consent.

Consent for publication
Written informed consent for publishing patient information and images was provided by the parents of the patient as legally authorized representatives and is available for review by the Editor.

Competing interests
The Authors declare no conflict of interest.

Author details
1Department of Pathology, University of Würzburg, Josef-Schneider-Str. 2, 97080 Würzburg, Germany. 2Comprehensive Cancer Center Mainfranken, Würzburg, Germany. 3University Children’s Hospital Würzburg, Würzburg, Germany. 4Division of Pediatric Radiology, University Department of Radiology, Würzburg, Germany. 5Division of Pediatric Surgery, University Medical Center ZOM, Würzburg, Germany.

Received: 10 December 2020 Accepted: 24 March 2021

Published online: 04 April 2021

References
1. WHO Classification of Tumours. Soft Tissue and Bone Tumours. 5th ed. Lyon, France: International Agency for research on Cancer (IARC); 2020.
2. Coffin CM, Lowichik A, Putnam A. Lipoblastoma (LPB): a clinicopathologic and immunohistochemical analysis of 59 cases. Am J Surg Pathol. 2009; 33(11):1705–12. https://doi.org/10.1097/PAS.0b013e3181b76462.
3. de Saint Aubain Somerenhausen N, Coindre JM, Debiec-Rychter M, Delplace J, Sciorti R. Lipoblastoma in adolescents and young adults: report of 23 cases with FISH analysis. Histopathology. 2008;53(3):294–8. https://doi.org/10.1111/j.1365-2559.2007.02954.x.
4. Susam-Sen H, Yalcin B, Kutlut K, Cahit Tanyel F, Halliloglu M, Orhan D, et al. Lipoblastoma in children: review of 12 cases. Pediatr Int. 2017;59(5):545–50. https://doi.org/10.1111/ped.13239.
5. Abdul-Ghafar J, Ahmad Z, Tariq MU, Kayani N, Uddin N. Lipoblastoma: a clinicopathologic review of 23 cases from a major tertiary care center plus detailed review of literature. BMC Res Notes. 2018;11(1):42. https://doi.org/10.1186/s13104-018-3153-8.
6. Han JW, Kim H, Youn JK, Oh C, Jung SE, Park KW, et al. Analysis of clinical features of lipoblastoma in children. Pediatr Hematol Oncol. 2017;34(4):212–20. https://doi.org/10.1080/08880018.2017.1354949.
7. Kok KY, Telkinghe PU. Lipoblastoma: clinical features, treatment, and outcome. World J Surg. 2010;34(7):1517–22. https://doi.org/10.1007/s00268-010-0466-8.
8. Coffin CM, Alaggio R. Adipose and myxoid tumors of childhood and adolescence. Pediatr Dev Pathol. 2012;15(1 Suppl):239–54. https://doi.org/10.1080/10920197.2011.573119.
9. Hibbard MK, Kozakewich HP, Dal Cin P, Sciorti R, Tan X, Xiao S, et al. PLAG1 fusion oncogenes in lipoblastoma. Cancer Res. 2000;60(17):4660–72.
10. Lopez-Nunez O, Alaggio R, Ranganathan S, Schmitt L, John L, Buchj CH, et al. New molecular insights into the pathogenesis of lipoblastomas: clinicopathologic, immunohistochemical, and molecular analysis in pediatric cases. Hum Pathol. 2020;104:50–41. https://doi.org/10.1016/j.humpath.2020.07.016.
11. Tanyel FC, Erdener A, Gunhan O, Alpaslan F. Retropertioneal lipoblastoma in a three-year-old child. Turk J Pediatr. 1986;28(4):259–61.
12. Jimenez JF. Lipoblastoma in infancy and childhood. J Surg Oncol. 1986;32(4):238–44. https://doi.org/10.1002/jso.2890320413.
13. St Omer L, Moule N, Duncan N, Escoffery C. Retroperitoneal lipoblastoma. Report of a case and review of the literature. West Indian Med J. 1992;41(4):164–5.
14. Collins MH, Chatten J. Lipoblastoma/lipoblastomatosis: a clinicopathologic study of 25 tumors. Am J Surg Pathol. 1997;21(10):1131–7. https://doi.org/10.1097/00000478-199710000-00002.
15. Pollono DG, Tomarchio S, Druol R, Zairitsky M, Otero L, Vasquez AJ, et al. Retroperitoneal and deep-seated lipoblastoma: diagnosis by CT scan and...
fine-needle aspiration biopsy. Diagn Cytopathol. 1999;20(5):295–7. https://doi.org/10.1002/(SICI)1097-0339(199905)20:5<295::AID-DC9>3.0.CO;2-K.

16. Chun YS, Kim WK, Park KW, Lee SC, Jung SE. Lipoblastoma. J Pediatr Surg. 2001;36(5):905–7. https://doi.org/10.1053/jpsu.2001.23969.

17. Dokucu AI, Ozturk H, Yildiz FR, Kaya M, Aras N, Bukte Y, et al. Retroperitoneal lipoblastoma involving the right common iliac artery and vein. Eur J Pediatr Surg. 2003;13(4):268–71. https://doi.org/10.1055/s-2003-4231.

18. McVay MR, Keller JE, Wagner CW, Jackson RJ, Smith SD. Surgical management of lipoblastoma. J Pediatr Surg. 2006;41(6):1067–71. https://doi.org/10.1016/j.jpedsurg.2006.02.025.

19. Api O, Akil A, Uzun MG, Aciloglu HC, Yalcin O, Api M, et al. Fetal retroperitoneal lipoblastoma: ultrasonographic appearance of a rare embryonal soft tissue tumor. J Matern Fetal Neonatal Med. 2010;23(9):1069–71. https://doi.org/10.3109/14767050903301025.

20. Burchhardt D, Fallon SC, Lopez ME, Kim ES, Hicks J, Brandt ML. Retroperitoneal lipoblastoma: a discussion of current management. J Pediatr Surg. 2012;47(10):e51–4. https://doi.org/10.1016/j.jpedsurg.2012.07.052.

21. Sakamoto S, Hashizume N, Fukushima S, Ishii S, Saikusa N, Yoshida M, et al. A large retroperitoneal lipoblastoma: a case report and literature review. Medicine (Baltimore). 2018;97(40):e12711. https://doi.org/10.1097/MD.0000000000012711.

22. Miyagi H, Honda S, Minato M, Iguchi A, Takakuwa E, Taketomi A. Differential diagnosis of a large size tumor in the retroperitoneum: a case report of retroperitoneal lipoblastoma. Afr J Paediatr Surg. 2018;15(3):151–3. https://doi.org/10.4103/ajps.AJPS_30_17.

23. Wang G, Guzman MA, Batanian JR. Three novel aberrations involving PLAG1 leading to Lipoblastoma in three different patients: high amplification, partial deletion, and a unique complex rearrangement. Cytogenet Genome Res. 2019;159(2):81–7. https://doi.org/10.1159/000503158.

24. Schoolmeester JK, Michal M, Steiner P, Folpe AL, Sukov WR. Lipoblastoma-like tumor of the vulva: a clinicopathologic, immunohistochemical, fluorescence in situ hybridization and genomic copy number profiling study of seven cases. Mod Pathol. 2018;31(12):1862–8. https://doi.org/10.1038/s41379-018-0102-y.

25. Yoshida H, Miyachi M, Ouchi K, Kuxwahara Y, Tsuchiya K, Iehara T, et al. Identification of COL3A1 and RAB2A as novel translocation partner genes of PLAG1 in Lipoblastoma. Genes Chromosomes Cancer. 2014;53(7):686–11. https://doi.org/10.1002/gcc.22170.

26. Deen M, Ebrahim S, Schloff D, Mohamed AN. A novel PLAG1-RAD51L1 gene fusion resulting from a t(8;14)(q12;q24) in a case of lipoblastoma. Cancer Genet. 2013;206(6):233–7. https://doi.org/10.1016/j.cancergen.2013.05.019.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.