

RESEARCH

Open Access



Chromothripsy in lipoblastoma: second reported case with complex *PLAG1* rearrangement

Joel Lanceta^{1*}, Joseph Tripodi², Lynne Karp^{1,3}, Meira Shaham^{1,3}, Nayyara Mahmood^{1,3}, Vesna Najfeld², Morris Edelman^{1,4} and Ninette Cohen^{1,3}

Abstract

Lipoblastomas (LPBs) are rare benign neoplasms derived from embryonal adipose that occur predominantly in childhood. LPBs typically present with numeric or structural rearrangements of chromosome 8, the majority of which involve the pleomorphic adenoma gene 1 (*PLAG1*) proto-oncogene on chromosome 8q12. Here, we report on a LPB case on which showed evidence of chromothripsy. This is the second reported case of chromothripsy in LPB.

Keywords Chromothripsy, Lipoblastoma (LPB), FISH, Microarray, Chromosomes, *PLAG1*

Background

LPBs are rare benign neoplasms derived from embryonal adipose tissue first described more than seven decades ago [1–3]. They are usually diagnosed in children during the first three years of life but can also occur rarely in older children and adolescents. LPBs can occur localized or in a diffuse presentation (lipoblastomatosis) that is extensive and infiltrative [4]. Most LPBs occur in subcutaneous tissue of the trunk and extremities, although they can occur elsewhere in the body. The histomorphology is highly diverse, usually showing a spectrum of lipoblasts, immature and mature adipocytes, primitive mesenchymal cells with a variable myxoid stroma and delicate

vasculature. Treatment is complete surgical removal; however, LPBs have been seen to recur in 13–46% of cases due to incomplete excision [5].

LPBs typically present with numeric or structural rearrangements of chromosome 8. Most chromosomal aberrations seen in LPBs involve the *PLAG1* gene located at chromosome 8q12. *PLAG1* is a proto-oncogene activated in other benign and malignant neoplasms, pleomorphic adenoma of the salivary gland, hepatoblastoma and uterine leiomyosarcoma [6–8]. The expression of *PLAG1* is typically upregulated in LPB, most commonly via gene rearrangements; the resulting promoter swapping brings the *PLAG1* gene under the transcriptional control of a more active promoter gene such as *COL3A1* and *CHCHD7* [9]. These genetic abnormalities in *PLAG1* help distinguish LPBs from other lipomatous neoplasms, although a subset of LPBs express polysomy of chromosome 8 or *HMG2A* gene rearrangements with or without *PLAG1* involvement. New fusion transcripts are being found associated with LPBs, including *MEG3* and *COL1A1* [10].

Here we review the current literature of LPBs and report on a three-month-old male who presented with a slowly enlarging, solitary, soft tissue tumor in the left

*Correspondence:

Joel Lanceta
jlanceta@gmail.com

¹ Department of Pathology and Laboratory Medicine, Northwell Health/
Donald and Barbara Zucker School of Medicine at Hofstra, Manhasset,
New York, USA

² Tumor CytoGenomics, Department of Pathology, Icahn School
of Medicine at Mount Sinai, New York, NY, USA

³ Division of Cytogenetics and Molecular Pathology, North Shore
University Hospital, Manhasset, NY, USA

⁴ Division of Pediatric Pathology, Cohen Children's Medical Center, New
Hyde Park, NY, USA



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

posterior lateral chest wall. The patient did not have any syndromic findings. The pregnancy was reported as uncomplicated, and the baby was full term at birth. There was no family history of genetic or congenital disorders. Ultrasound of the chest found a solitary $2.9 \times 1.2 \times 3$ cm mass in the left posterior lateral chest wall without color flow, touching adjacent ribs and pushing muscles anteriorly. Follow up magnetic resonance imaging (MRI) one month later demonstrated doubling in the size of the mass to $6.0 \times 3.4 \times 5.1$ cm. The mass was surgically removed two months later. The specimen was submitted for pathology examination, and a portion was taken for cytogenetic analysis. The post-operative course was unremarkable with no further follow-up.

Case presentation

Pathology

The resected masses were all submitted fresh to Pathology and fresh unfixed tissue was taken for cytogenetic analysis before fixation of the tumor in 10% neutral buffered formalin. Sections were taken for routine processing. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded tissues using standard techniques.

Cytogenetics/cytogenomics

Chromosome analysis was performed as per standard protocol. Metaphase fluorescence in situ hybridization (FISH) was performed using TelVysion 8p Spectrum Green and TelVysion 8q Spectrum Orange (Abbott Molecular), and *MYC* break apart (BA) and CEP 8 probes (Abbott Molecular). In addition, interphase FISH was performed using a custom *PLAG1* BA probe combined with a CEP8, 3' *PLAG1* (centromeric-red), 5' *PLAG1* (telomeric-green). A high-resolution array comparative genomic hybridization (aCGH) platform using Agilent's 2 \times 400 k CGH+SNP GenetiSure Cancer array (Agilent Technologies, Santa Clara, CA) was performed on DNA extracted from formalin-fixed paraffin embedded (FFPE) tissue as previously described (Zimran, E. et al. Haematologica, 2018). Copy number aberrations (CNAs) were filtered to exclude those < 100 kb, nested aberrations, Y chromosome calls in females, and reference DNA CNVs. Regions of CNLOH were called if they contained a minimum of 10 probes and were > 10 Mb in size.

Results

The resected mass was a disc-shaped well circumscribed bosselated fatty mass with a delicate fibromembranous capsule (Fig. 1). Histology showed a prominent lobular pattern with mature adipose tissue, many intervening fibrous septa of variable thickness, and absence of any myxoid component (Fig. 2A, B). Foci of fat necrosis were



Fig. 1 Gross picture of lobulated adipocytic tumor, later confirmed to be a lipoblastoma

present (Fig. 2C) and showed scattered CD163 immunoreactive macrophages (Fig. 2D).

Chromosome analysis revealed an abnormal karyotype with two abnormal derivative chromosomes 8 in addition to a normal copy of chromosome 8 described as 47, XY, +8,der(8) $\times 2$ [10]/46,XY[10] (Fig. 3A). FISH analysis using chromosome 8p and 8q probes revealed abnormal hybridization patterns on both der[8] chromosomes with signals for 8p and 8q probes on both ends of each der(8) (Fig. 3B). FISH results using the *MYC* BA and CEP 8 probes confirmed the abnormal nature of the two der(8) chromosomes (Fig. 3C). FISH analysis on FFPE with a custom *PLAG1* BA probe and CEP8 showed multiple copies of each probe (Fig. 3D). Microarray analysis revealed 50 regions of alternating CNAs occurring on chromosome 8 (39 gains and 19 losses) (Fig. 3E, F). The average size of the CNAs was 1.9 Mb ranging from 17.8 kb to 9.2 Mb. Based on these combined findings, this tumor exhibits chromothripsis of chromosome 8 and is described as arr(8)cth. No other chromosomes were involved in the process of chromothripsis. This is the second known report of chromothripsis described in a benign LPB.

Discussion and conclusions

LPBs were first described in 1926 as a tumor of immature adipose [11], but did not gain acceptance as a separate tumor entity until Vellioz et al. in 1958 described the neoplasm in relation to lipoblastomatosis.³ Microscopically, the excised tumor is composed of sheets of mature adipocytes arranged in a lobular architecture, intermixed

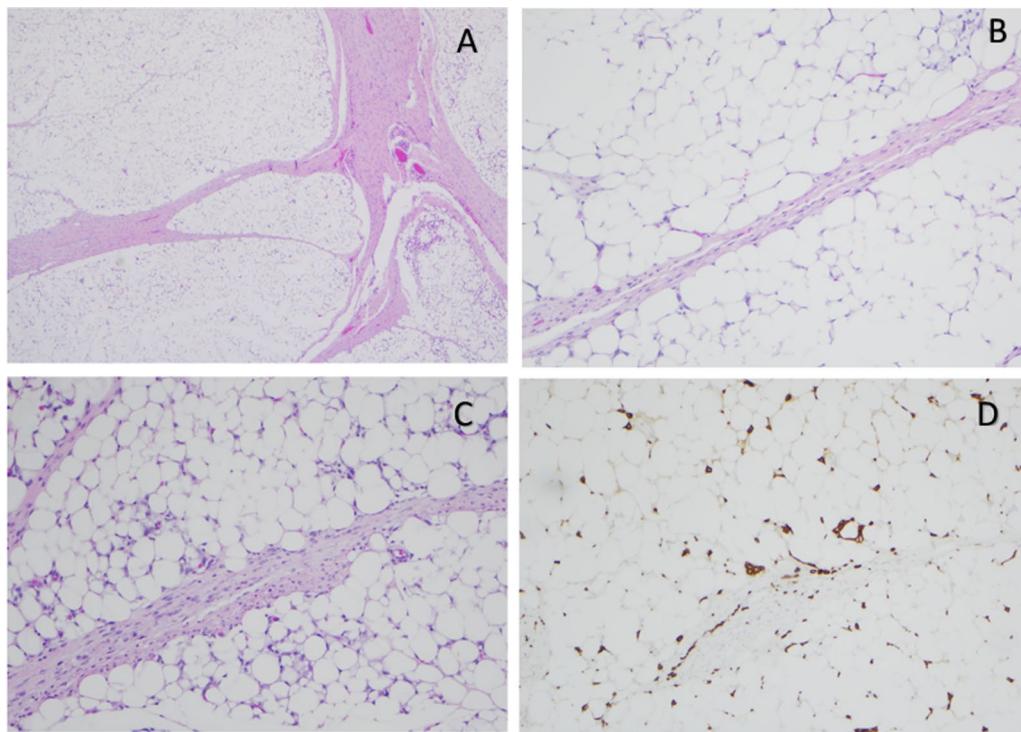


Fig. 2 **A** H&E (20x): Lobular architecture with fibrous septa and lobules of mature adipose tissue. **B** H&E (20x): Fibrous septum and mature adipose tissue. No myxoid component and no spindle cell proliferation present. **C** H&E (20x): Fibrous septum and mature adipose tissue. Scattered macrophages present. **D** H&E (100x): CD163 immunoreactive macrophages present

with other adipocyte cells in varying stages of maturation. Literature review showed that LPBs are further subdivided into three histologic categories: a classic subtype composed primarily of embryonal white fat [12], a mature adipocytic subtype [12], and a myxoid subtype showing a plexiform vascular network with thin fibrous septa and pools of myxoid matrix [4, 5, 12].

Adipocytic tumors overall are exceptionally rare in children under the age of 10 years old. Over 80% of LPBs are diagnosed in children before three years of age with some present at birth and may show a male predilection [13–16]. The most affected regions are subcutaneous tissue of the extremities, but other locations include the head and neck [8], pelvis [17, 18], mediastinum [8, 19], mesentery [20], axilla [21], and abdomen [6, 19, 22]. A subset of patients diagnosed with LPB have developmental delays, seizures, familial lipoma syndromes, and

congenital malformations such as cleft lip, cleft palate, cephalic malformations, seizures [1, 12, 23]. The prognosis after surgical removal is excellent, with no reported cases of malignant transformation. Follow-up is recommended for 5–10 years post-resection, as the recurrence rate for LPB is estimated to be 13–46% due to positive surgical margins, incomplete tumor resection, or lipoblastomatosis in the patient [5, 18].

The molecular hallmark of LPB is chromosomal alterations involving the *PLAG1* gene, although the exact pathogenesis remains unknown. [9] The current literature estimates that 60–70% of LPBs have a simple, aneuploid or hyperdiploid karyotype with a structural alteration in the 8q11–13 region, leading to the *PLAG1* rearrangement [1, 4, 5, 24, 25]. *PLAG1* encodes a zinc finger proto-oncogene with two putative nuclear localization signals. The majority of LPBs have identified *PLAG1*

(See figure on next page.)

Fig. 3 **A** Karyotype showing a 47,XY,+8,der(8)×2. **B** Metaphase FISH analysis with TelVysion 8p (green) and TelVysion 8q (orange) showing signals of 8p and 8q on the terminal ends of the short and the long arms on both abnormal der(8) chromosomes. **C** Metaphase FISH analysis with CEP8 (aqua) and MYC BA (green-red) probe showing all three signals present on both ends of the abnormal der(8) chromosomes. **D** FISH analysis on FFPE showing multiple copies of 3' *PLAG1* (centromeric-red), 5' *PLAG1* (telomeric-green) and CEP8 (aqua). **E** Vertical CGH plot showing alternating 39 gains and 19 losses on chromosome 8. **F** Vertical plot of CGH with similar gains and losses. Blue denotes gain; Red denotes loss

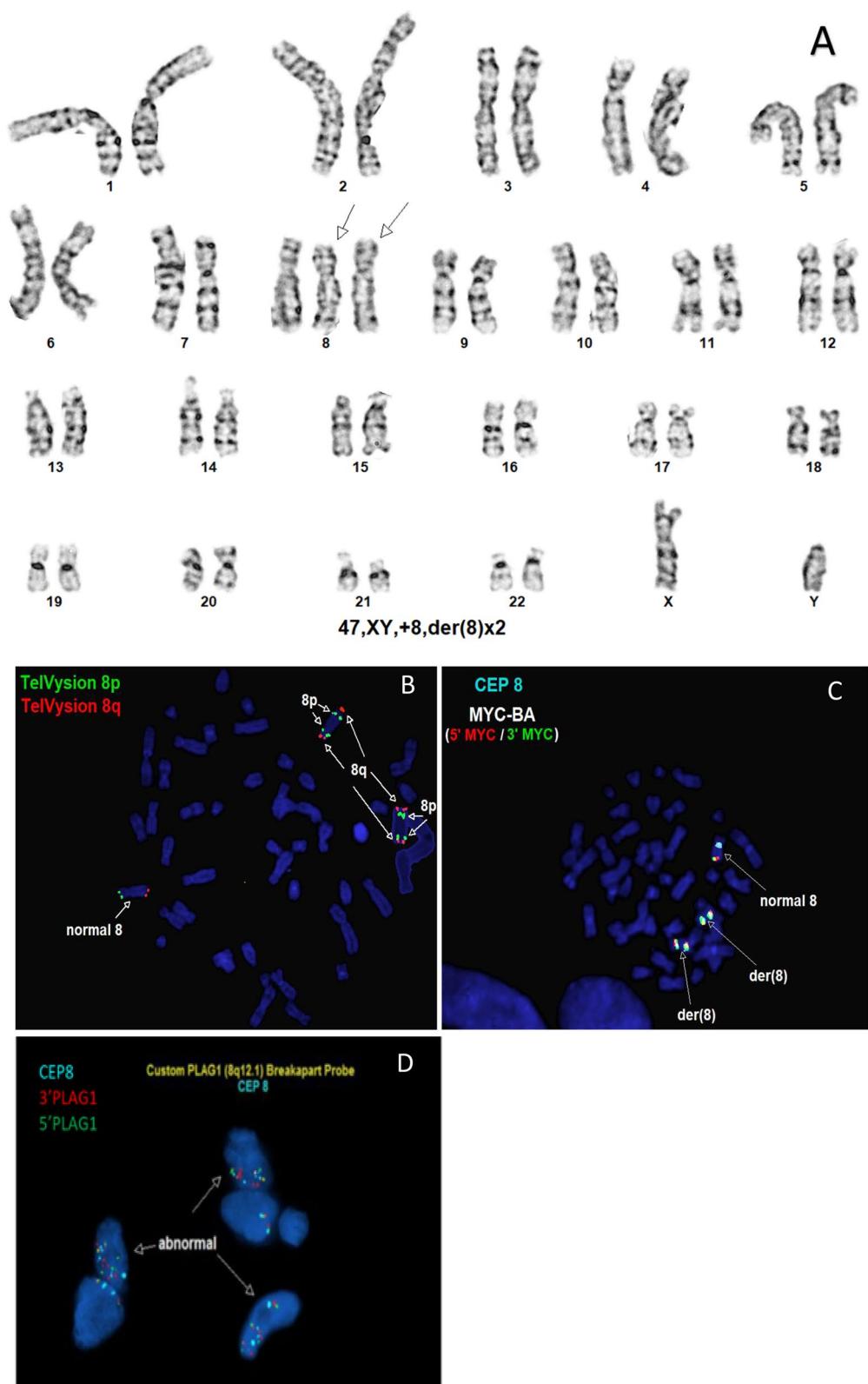


Fig. 3 (See legend on previous page.)

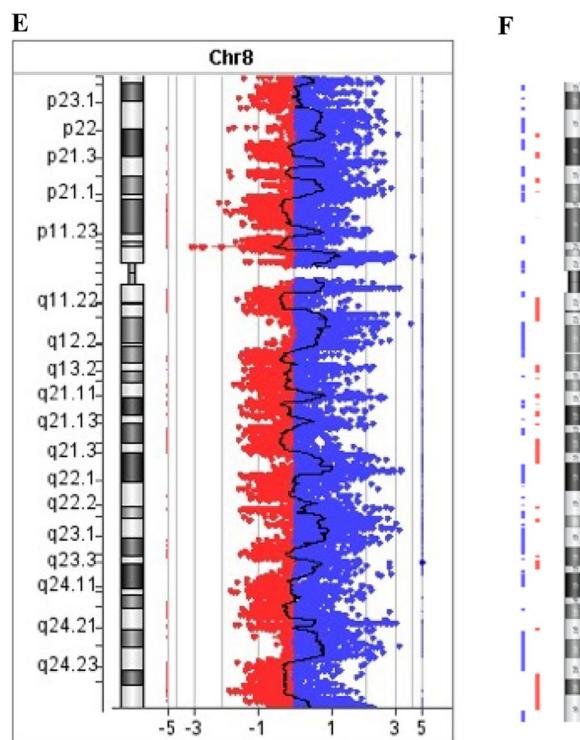


Fig. 3 continued

upregulation through promotor swapping with a more active promotor of the fusion genes, the most common being *HAS2* and *COL1A2* [13]. The number of possible fusion transcripts described in lipoblastomas have increased considerably over the past decade, as *SRSF3*, *HNRNPC*, *PCMTD1*, *YWHAZ*, *CTDSP2*, *PPP2R-2A*, *COL3A1*, *MEG3*, *RAD51B*, *BOC*, and two genes neighboring *PLAG1*, *RAB2A* and *CHCHD7*, have been identified as potential fusion partners [5, 8–10, 24, 24–29]. LPBs are immunohistochemically negative for *MDM2* and *CDK4* expression, as compared to well differentiated liposarcomas which are *MDM2* and *CDK4* positive with no associated clonal rearrangements of *PLAG1* [4].

Our patient showed chromosome 8 abnormalities with typical histologic findings. Some larger, multi-institutional studies have focused on the morphologic and immunophenotypic features of lipoblastomas [1, 30], while other series have looked at the molecular characteristics [9, 12]. The case presented in this report is unique in that microarray analysis clearly revealed evidence of chromothripsis. The overexpression of *PLAG1* suspected by FISH analysis was confirmed by the pronounced clustering of breakpoints and the oscillating copy-number profiles derived from the microarray supporting chromothripsis at 8q11-13 being responsible for the oncogenic process seen in this tumor.

Recently identified as an independent genetic phenomenon through genomic sequencing, chromothripsis results in massive chromosomal rearrangements and multiple downstream genomic aberrations [31–38]. While the underlying mechanisms resulting in chromothripsis are mostly unknown, chromothripsis has been associated with *TP53* mutations in subsets of medulloblastoma and acute myeloid leukemia [39–41]. The status of *TP53* was not tested for our patient and is unknown.

Although initial estimates of chromothripsis in tumors were low, there is growing evidence that it is associated with the genetic oncogenesis across a wider spectrum of cancers than initially believed, as more tumors are genetically sequenced [40, 42]. Chromothripsis has been detected in a diverse range of solid tumors, and hematological malignancies, resulting in aggressive tumor behavior and poor diagnostic outcomes [42–46]. Typically, *PLAG1* is activated in lipoblastoma and coincides with low-level amplification, (47) while in our case chromothripsis results in high level amplification in chromosome 8, while no other chromosomes were involved.

Chromothripsis has only once been previously reported in a lipoblastoma in the thigh of a 5-year-old male. Array CGH + SNP analysis of that LPB found multiple rearrangements localized on the long arm of chromosome 8 and pronounced clustering of breakpoints

detected on chromosomal analysis [37]. Our patient and this previously reported case both show chromothripsis without *PLAG1* rearrangement, which suggests that chromothripsis is an alternative oncogenic mechanism in LPBs when no *PLAG1* fusions can be detected.

To the best of our knowledge this is only the second known report of chromothripsis described in a benign LPB and these findings broaden our understanding of the varied cytogenetic events in LPBs. Additional molecular studies of LPB are needed to understand the pathogenesis of this unusual tumor.

Abbreviations

LPB	Lipoblastoma
FISH	Fluorescence in situ hybridization
<i>PLAG1</i>	Pleomorphic adenoma gene 1
BA	Break apart
aCGH	Array comparative genomic hybridization
CAN	Copy number aberration

Acknowledgements

We would like to thank the Cytogenetics team at North Shore University Hospital and the Tumor CytoGenomics team at Icahn School of Medicine at Mount Sinai for their work on these cases. In addition, we would like to thank Dr. Naima Loayza for her assistance in editing the manuscript.

Author contributions

All authors approved the submitted version and agreed to be personally accountable for the author's own contributions.

Funding

None.

Declarations

Ethics approval and consent to participate

Our case report represents findings from a patient who had consented to be included in any publication. All presented data are anonymous and do not allow identification of the individual patients and were obtained during routine diagnostic procedures.

Consent for publication

Available upon request.

Competing interests

The authors declare that they have no competing interests.

Received: 17 October 2023 Accepted: 14 November 2023

Published online: 27 November 2023

References

1. 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.
2. Kauffman SL, Stout AP. Lipoblastic tumors of children. Cancer. 1959;12(5):912–25.
3. Vellios F, Baez J, Shumacker HB. Lipoblastomatosis: a tumor of fetal fat different from hibernoma. Am J Pathol. 1958;34(6):1149.
4. Ameloot E, Cordier F, Van Dorpe J, Creytens D. Update of pediatric lipomatous lesions: a clinicopathological, immunohistochemical and molecular overview. J Clin Med. 2022;11(7):1938.
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):1–6.
6. Choi J, Bouron Dal Soglio D, Fortier A, Fetni R, Mathonnet G, Cournoyer S, Lallier M, Isler M, Beaulieu Bergeron M, Patey N. Diagnostic utility of molecular and cytogenetic analysis in lipoblastoma: a study of two cases and review of the literature. Histopathology. 2014;64(5):731–40.
7. Fletcher JA, Kozakewich HP, Schoenberg ML, Morton CC. Cytogenetic findings in pediatric adipose tumors: consistent rearrangement of chromosome 8 in lipoblastoma. Genes Chromosom Cancer. 1993;6(1):24–9.
8. Fritchie K, Wang L, Yin Z, Nakitandwe J, Hedges D, Horvai A, Mora JT, Folpe AL, Bahrami A. Lipoblastomas presenting in older children and adults: analysis of 22 cases with identification of novel *PLAG1* fusion partners. Mod Pathol. 2021;34(3):584–91.
9. Logan SJ, Schieffer KM, Conces MR, Stonerock E, Miller AR, Fitch J, LaHaye S, Voytovich K, McGrath S, Magrini V, White P. Novel morphologic findings in *PLAG1*-rearranged soft tissue tumors. Genes Chromosom Cancer. 2021;60(8):577–85.
10. Theis B, Alhusami I, Kämmerer E, Kentouche K, Vokuhl C, Gassler N, Katenkamp K. New *PLAG1*-fusion transcripts in the spectrum of pediatric fibrotic, lipofibrotic, and mature lipomatous tumors. Int J Clin Exp Pathol. 2022;15(10):425.
11. Jaffe R. Recurrent lipomatous tumors of the groin: liposarcoma and lipoma pseudomyxomatodes. Arch Pathol. 1926;1:381–7.
12. Gisselsson D, Hibbard MK, Dal Cin P, Sciot R, Hsi BL, Kozakewich HP, Fletcher JA. *PLAG1* alterations in lipoblastoma: involvement in varied mesenchymal cell types and evidence for alternative oncogenic mechanisms. Am J Pathol. 2001;159(3):955–62.
13. Gerhard-Hartmann E, Wiegering V, Benoit C, Meyer T, Rosenwald A, Maurus K, Ernestus K. A large retroperitoneal lipoblastoma as an incidental finding: a case report. BMC Pediatr. 2021;21:1–6.
14. Goldblum JR, Folpe AL. Benign lipomatous tumors. Enzinger & Weiss's Soft Tissue Tumors.
15. Johnson CN, Ha AS, Chen E, Davidson D. Lipomatous soft-tissue tumors. JAAOS-J Am Acad Orthopaed Surg. 2018;26(22):779–88.
16. Miller GG, Yanchar NL, Magee JF, Blair GK. Tumor karyotype differentiates lipoblastoma from liposarcoma. J Pediatr Surg. 1997;32(12):1711–2.
17. Somers GR, Teshima I, Nasr A, Cook A, Khouri AE, Taylor GP. Intrascrotal lipoblastoma with a complex karyotype: a case report and review of the literature. Arch Pathol Lab Med. 2004;128(7):797–800.
18. Spătaru RI, Cîrstoveanu C, Iozsa DA, Enculescu A, Tomescu LF, Șerban D. Lipoblastoma: diagnosis and surgical considerations. Exp Ther Med. 2021;22(2):1–7.
19. Benato C, Falezza G, Lonardoni A, Magnanelli G, Ricci M, Giloli E, Calabro F. Acute respiratory distress caused by a giant mediastinal lipoblastoma in a 16-month-old boy. Ann Thorac Surg. 2011;92(6):e119–20.
20. Miscia ME, Lisi G, Lauriti G, Riccio A, Di Renzo D, Cascini V, Lelli CP. A rare case of giant mesenteric lipoblastoma in a 6-year-old child and review of the literature. Case Rep Surg. 2020;24:2020.
21. Abel RM, Bryan RT, Rafaat F, Haigh F, Sethia B, Parikh D. Axillary lipoblastoma—tumor recurrence in the right atrium. J Pediatr Surg. 2003;38(8):1246–7.
22. Jalles F, Pinto PL, Martins AP, Gonçalves M. Lipoblastoma of the abdominal wall. J Pediatr Surg Case Rep. 2019;1(50):101203.
23. Alperovich M, Ayo D, Staffenberg DA, Sharma S. Lipoblastoma of the hand and cleft palate: Is there a genetic association? J Craniofac Surg. 2014;25(2):e189–91.
24. Bartuma H, Domanski HA, Von Steyern FV, Kullendorff CM, Mandahl N, Mertens F. Cytogenetic and molecular cytogenetic findings in lipoblastoma. Cancer Genet Cytogenet. 2008;183(1):60–3.
25. Dadone B, Refaei S, Lemarié-Delaunay C, Bianchini L, Pedeutour F. Molecular cytogenetics of pediatric adipocytic tumors. Cancer Genet. 2015;208(10):469–81.
26. Hibbard MK, Kozakewich HP, Cin PD, Sciot R, Tan X, Xiao S, Fletcher JA. *PLAG1* fusion oncogenes in lipoblastoma. Can Res. 2000;60(17):4869–72.
27. Moreira C, Rapella A, Rosanda C, Tassano E, Gambini C, Romagnoli G, Panarello C. *PLAG1-HAS2* fusion in lipoblastoma with masked 8q intrachromosomal rearrangement. Cancer Genet Cytogenet. 2005;156(2):183–4.
28. Nitta Y, Miyachi M, Tomida A, Sugimoto Y, Nakagawa N, Yoshida H, Ouchi K, Tsuchiya K, Ichera T, Konishi E, Umeda K. Identification of a novel

- BOC-PLAG1 fusion gene in a case of lipoblastoma. *Biochem Biophys Res Commun.* 2019;512(1):49–52.
29. Yoshida H, Miyachi M, Ouchi K, Kuwahara Y, Tsuchiya K, Iehara T, Konishi E, Yanagisawa A, Hosoi H. Identification of COL3A1 and RAB2A as novel translocation partner genes of PLAG1 in lipoblastoma. *Genes Chromosom Cancer.* 2014;53(7):606–11.
 30. Mentzel T, Calonje E, Fletcher CD. Lipoblastoma and lipoblastomatosis: a clinicopathological study of 14 cases. *Histopathology.* 1993;23(6):527–33.
 31. Korbel JO, Campbell PJ. Criteria for inference of chromothripsis in cancer genomes. *Cell.* 2013;152(6):1226–36.
 32. Luijten MN, Lee JX, Crasta KC. Mutational game changer: chromothripsis and its emerging relevance to cancer. *Mutat Res/Rev Mutat Res.* 2018;1(777):29–51.
 33. Zhang CZ, Spektor A, Cornils H, Francis JM, Jackson EK, Liu S, Meyerson M, Pellman D. Chromothripsis from DNA damage in micronuclei. *Nature.* 2015;522(7555):179–84.
 34. Simovic M, Ernst A. Chromothripsis, DNA repair and checkpoints defects. In: Seminars in Cell & developmental biology, vol. 123. New York: Academic Press; 2022. p. 110–4.
 35. Rode A, Maass KK, Willmund KV, Lichter P, Ernst A. Chromothripsis in cancer cells: An update. *Int J Cancer.* 2016;138(10):2322–33.
 36. Stephens PJ, Greenman CD, Fu B, Yang F, Bignell GR, Mudie LJ, Pleasance ED, Lau KW, Beare D, Stebbings LA, McLaren S. Massive genomic rearrangement acquired in a single catastrophic event during cancer development. *Cell.* 2011;144(1):27–40.
 37. Pederiva F, Candalera V, Cleva L, Pecile V. Chromothripsis in Lipoblastoma. *J Cell Sci Ther.* 2016;7(249):2.
 38. Schoolmeester JK, Michal M, Steiner P, Michal M, 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.
 39. Rausch T, Jones DT, Zapatka M, Stütz AM, Zichner T, Weischenfeldt J, Jäger N, Remke M, Shih D, Northcott PA, Pfaff E. Genome sequencing of pediatric medulloblastoma links catastrophic DNA rearrangements with TP53 mutations. *Cell.* 2012;148(1):59–71.
 40. Ernst A, Jones DT, Maass KK, Rode A, Deeg KI, Jebaraj BM, Korshunov A, Hovestadt V, Tainsky MA, Pajtler KW, Bender S. Telomere dysfunction and chromothripsis. *Int J Cancer.* 2016;138(12):2905–14.
 41. Shoshani O, Brunner SF, Yaeger R, Ly P, Nechemia-Arbely Y, Kim DH, Fang R, Castillon GA, Yu M, Li JS, Sun Y. Chromothripsis drives the evolution of gene amplification in cancer. *Nature.* 2021;591(7848):137–41.
 42. Chudasama P, Mughal SS, Sanders MA, Hübschmann D, Chung I, Deeg KI, Wong SH, Rabe S, Hlevnjak M, Zapatka M, Ernst A. Integrative genomic and transcriptomic analysis of leiomyosarcoma. *Nat Commun.* 2018;9(1):144.
 43. Leibowitz ML, Papathanasiou S, Doerfler PA, Blaine LJ, Sun L, Yao Y, et al. Chromothripsis as an on-target consequence of CRISPR–Cas9 genome editing. *Nat Genet.* 2021;53(6):895–905.
 44. Fontana MC, Marconi G, Feenstra JD, Fonzi E, Papayannidis C, Luserna G, di Rorá A, Padella A, Solli V, Franchini E, Ottaviani E, Ferrari A. Chromothripsis in acute myeloid leukemia: biological features and impact on survival. *Leukemia.* 2018;32(7):1609–20.
 45. Kim YS, Shin S, Jung SH, Chung YJ. Pathogenic NF1 truncating mutation and copy number alterations in a dedifferentiated liposarcoma with multiple lung metastasis: a case report. *BMC Med Genet.* 2020;21:1–5.
 46. Röpke A, Kalinski T, Kluba U, Von Falkenhausen U, Wieacker PF, Röpke M. PLAG1 activation in lipoblastoma coinciding with low-level amplification of a derivative chromosome 8 with a deletion del (8)(q13q21.2). *Cytogenet Genome Res.* 2007;119(1–2):33–8.

Publisher's Note

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

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

