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CASE REPORT Open Access

SOLAMEN syndrome in a toddler

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Abstract

Background Segmental overgrowth, lipomatosis, arteriovenous malformation, and epidermal nevus (SOLAMEN) syndrome is a segmental overgrowth syndrome that is part of Cowden's Syndrome, a subset of the PTEN hamartoma tumor syndrome cluster. Due to SOLAMEN disease's rarity, clinical suspicion should arise if multiple small nonspecific variably low-attenuated nodular lesions in the back, shoulders, and upper arms are present on CT, which are associated with mucocutaneous lesions. We present a rare case of SOLAMEN syndrome with widespread lipomatous growth, greater than reported in literature, with confirmed PTEN genetic testing.

Case presentation We describe a case of a 2-year-old boy with a slowly growing left neck mass since birth. Physical exam revealed macrocephaly and epidermal nevi on left axilla, arm, and fingers, appearing as pink verrucous and has visible veins on chest wall/abdomen. CT and MRI imaging showed a lipomatous hibernoma extending from the leftward neck to the abdominal cavity, encasing vascular structures form the left carotid and subclavian arteries to the diaphragmatic hiatus, in addition to the spleen and kidney. Biopsy of the left shoulder revealed hibernoma, a fatty neoplasm of benign brown fat. Patient had a resection of his left shoulder hibernoma and is currently asymptomatic, undergoing surveillance.

Conclusion Due to SOMAMEN syndrome's rarity, clinical suspicion should arise if a patient presents with multiple small-nonspecific variably low-attenuated nodular lesions on CT and mucocutaneous lesions. Ongoing monitoring should be done as there is an increased risk of cancer.

Keywords Pediatric radiology, SOLAMEN syndrome, PTEN hamartoma tumor syndrome cluster

Background

Segmental overgrowth, lipomatosis, arteriovenous malformation, and epidermal nevus (SOLAMEN) syndrome is a segmental overgrowth syndrome that is part of Cowden's Syndrome, a subset of the PTEN hamartoma tumor syndrome cluster (PHTS) [1]. SOLAMEN syndrome is a segmental overgrowth syndrome that is part of Cowden's Syndrome, a subset of the PTEN hamartoma tumor syndrome cluster (PHTS). PHTS is a rare genetic disorder caused by a phosphatase and tensin homolog (PTEN) gene mutation; when this tumor suppressor gene is mutated, overgrowth of tissues is observed. PTEN mutations are estimated to affect 1:200,000 people [2]. There have been very few cases described in literature, as such potential for underreporting of this disease as the criteria are extensive.

Due to Cowden disease's rarity, if multiple small nonspecific variably low-attenuated nodular lesions in the back, shoulders, and upper arms are present on CT, as these are associated with mucocutaneous lesions. This multisystemic disease is associated with Lhermitte-Duclose disease and hamartomas of the GI, breast, thyroid, and testicles [2]. In our case report, we present a pediatric patient with macrocephaly and significant widespread enlarged extracerebral hamartomas at a young age, unreported in literature.

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Case presentation

We report a 2-year-old boy presented with a slowly growing neck mass since birth (Fig. 1). Prenatally, a mass on his shoulder and spine were noted on ultrasound, but no external lesion was present on birth. The mother's pregnancy and delivery were uneventful. A cesarean section was performed due to the patient's macrocephaly at 37 weeks, 1 day. He presented with a left neck mass at 1 month of age that has continued to grow. Patient has experienced no symptoms from the mass on his left shoulder. Family history contributory for lipomas in both grandmothers. Physical exam revealed epidermal nevi on left axilla, arm, and fingers, appearing as pink verrucous and has visible veins on chest wall/abdomen. Macrocephaly is noted at the 99th percentile ($z=6.11$), but parents also had large head sizes. He also had minor leg length discrepancy. Patient had been meeting all neurological milestones.

Intracranial ultrasound at 7 months showed mild prominence of the extra-axial space benign enlargement of subarachnoid space (BESS). MRI of the left neck and shoulder at 2.5 years showed a lipomatous mass with thin septations and vascular areas that include the left shoulder and extends into the left chest cavity, axilla, and around main vessels of the heart, spleen, and kidney (Figs. 2, 3). At the same time CT of the neck, chest, abdomen, and pelvis revealed a fat attenuating mass extending from leftward neck, mediastinum to the abdominal cavity, encasing the left carotid and subclavian arteries, and encasing the diaphragmatic hiatus (Figs. 5, 6, 7). MRI of the abdomen showed asymmetrical enlargement of the left anterior abdominal extraperitoneal fat with thin septations (Fig. 4).

Given the concern for lipoblastoma, a biopsy was done on the patient. The pathology reported a gross pathology of irregular, ragged piece of pale-yellow, fleshy to fatty soft tissue, and a histological exam showed a mixture of mature fat and multivacuolated brown fat (Fig. 5). There was no myxoid tissue to suggest liposarcoma. Final diagnosis was hibernoma, a fatty neoplasm of benign brown fat. Patient was heterozygous for a pathological variant of PTEN of a codon deletion, patient was also hemizygous for a variant in the OFD1 gene, unrelated to PTEN hamartoma syndrome.

The patient underwent surgery to excise a large neck mass on the left side; patient has recovered well (Fig. 6). The patient will be subject to ongoing follow-up.

Discussion

The clinical diagnosis of Cowden syndrome encompasses three types of criteria. Pathognomonic signs for Cowden syndrome include dysplastic gangliocytoma of the cerebellum and mucocutaneous lesions, such as trichilemmomas, acral keratosis, mucocutaneous neuromas or oral papillomas. Major signs include breast cancer, thyroid cancer, macrocephaly, and endometrial carcinoma. Minor signs include thyroid lesions, neurodivergence, hamartomas, intestinal polyps, and breast

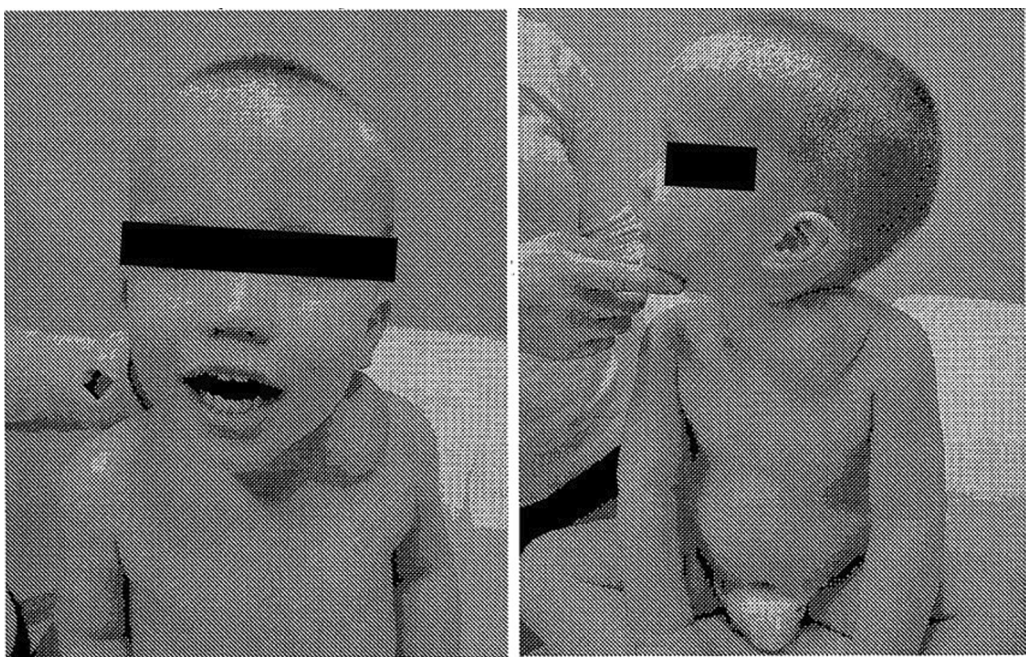

Fig. 1 Picture of the child prior to hibernoma resection

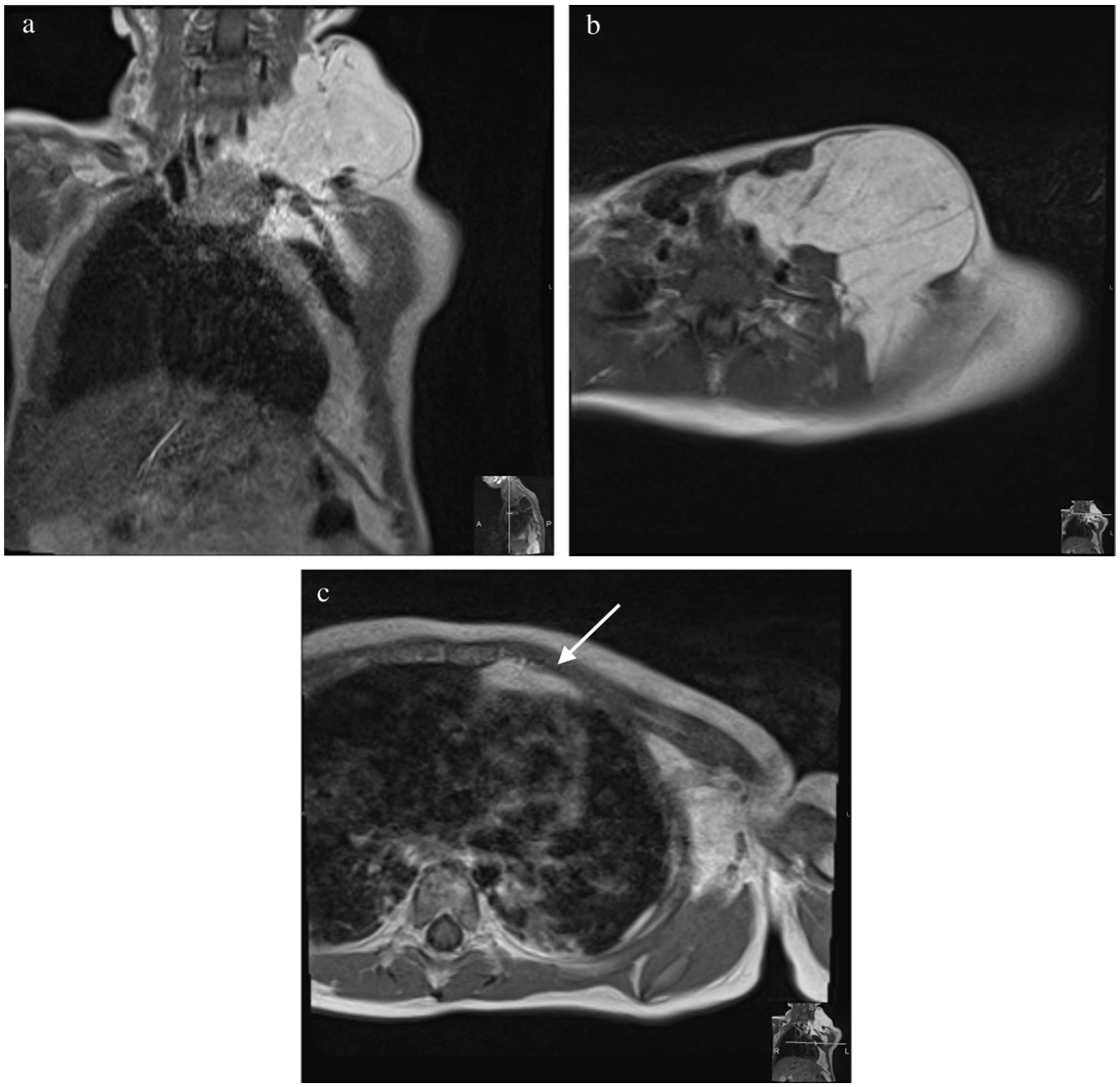

Fig. 2 **a** Coronal T1 MRI Neck with contrast shows a large lobulated fat containing mass in the leftward neck extending into the mediastinum, subscapular region, and axilla. **b** Axial T1 MRI Neck with contrast shows a large lobulated fat containing mass in the leftward neck extending into the mediastinum, subscapular region, and axilla. **c** Axial T1 MRI Neck with contrast shows a large lobulated fat containing mass in the leftward neck extending into the mediastinum (white arrow), subscapular region, and axilla

fibrocystic disease. When a patient meets one of the pathognomonic criteria, two or more major criteria, one major and three minor criteria, or four or more minor criteria, a clinical diagnosis is made [2].

Macrocephaly and one of the following secondary criteria are required for the diagnosis of PHTS syndrome in children: neurodivergence; dermatological features like lipomas, oral papillomas, trichilemmomas, and penile freckling; endothelial lesions like vascular malformations or hemangiomas; gastrointestinal polyps; or pediatric-onset thyroid cancer or germ cell tumors [3].

One major criterion (macrocephaly) and one minor criterion (lipomas) of Cowden Disease was found in our patient. The criteria for pediatric PHTS diagnosis were met by our patient, as evidenced by the presence of macrocephaly and the occurrence of lipomatous growth. In addition, our patient has a molecular genetic diagnosis of PTEN due to his heterozygous germline pathogenic variant. What makes this an atypical Cowden syndrome case is that the patient has a limb-length discrepancy and linear epidermal nevus. In addition, patients do not usually present with such large lipomatous overgrowth,

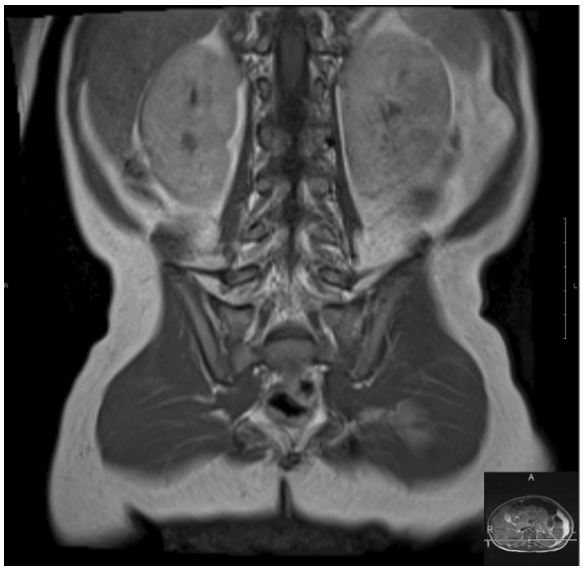

Fig. 3 This T1 Coronal MRI displays crescentic lobulated asymmetrical enlargement of the left extraperitoneal intra-abdominal fat with thin septations when compared to the right abdominal wall directly deep to the lateral abdominal musculature

even in the setting of Cowden syndrome. Our patient's lipomatous overgrowth/hibernoma is more significant than is commonly reported in PTEN related conditions with one germline mutation. However, this patient has multiple lipomatous masses present throughout the rest of the body, which along with genetic testing, suggests the diagnosis of SOLAMEN syndrome. The differential includes lipoblastoma, sarcoma, or lymphoma, atypical lipoma, lymphangioma, and other PTEN hamartomas syndromes, namely CLOVES syndrome, Proteus syndrome.

Cowden syndrome, a genetic disorder characterized by the development of hamartomas (benign growths) and an increased risk of cancer, can be inherited in an autosomal dominant manner or caused by a de novo (new) germline mutation in the PTEN gene. About 45% of Cowden syndrome cases are due to de novo mutations. The PTEN gene, located on chromosome 10, is a tumor suppressor gene that plays a crucial role in controlling cell division and growth. It also inhibits the PI3K/AKT/mTOR signaling pathway, which is involved in cell growth, glucose metabolism, and protein synthesis. PTEN protein is found in many tissues, including the nervous system, endocrine system, reproductive system, cardiovascular system, immune system, and epithelial tissues. The "two-hit hypothesis" proposes that the loss of both copies of the PTEN gene is necessary for tumor formation. The first hit may occur in the germline (reproductive cells), leading to Cowden syndrome. The second hit may occur in a somatic cell (any cell other than a reproductive cell), leading to cancer. PTEN mutations are associated with an increased risk of several types of cancer, including endometrial cancer, thyroid cancer, breast cancer, and colorectal cancer [3].

Fat content within these lesions may be confirmed on MRI by visualizing signal-intensity loss after fat-saturation techniques [4]. Cowden Syndrome can be detected in the GI system through conventional radiography, revealing a radiolucent mass without mineralization. Ultrasound imaging demonstrates a well-defined hyperechoic mass with clear boundaries, while Doppler imaging may reveal increased vascularity. CT and MR imaging reveal well-defined heterogeneous vascular lesions in various locations: intermuscular, intramuscular, subcutaneous, or retroperitoneal [5]. A distinguishing characteristic of Cowden Syndrome on CT scans is the presence of prominent branching and serpentine high-flow and low-flow vascular structures exhibiting contrast enhancement and low signal intensity across all MR pulse sequences. Although these features may suggest a well-differentiated liposarcoma, such distinct vascularity is not observed in liposarcoma cases. These lesions are hamartomas, lipomas, or fibromas. Cowden Syndrome's tissue appears similar to fat yet displays branching vascular structures or high-water contrast [2].

Neurologically, individuals with Cowden Disease present specific features, notably Lhermitte–Duclos Disease, characterized by the presence of a benign gangliocytoma located in the cerebellum. This condition is distinguishable through MRI scans, showcasing a high T2 signal and a low T1 lesion that does not enhance with contrast. Furthermore, a distinctive tiger-stripe pattern consisting of hypoattenuating and hyperattenuating bands can be observed. Additionally, enlarged perivascular spaces, also referred to as Virchow–Robin spaces, which extend from the pia mater into the arteries, along with heightened white matter hypointensities, contribute to the neurological profile of Cowden Disease [2].

Characterization of PTEN syndromes determine management. Given the rareness of the disease and the wide spectrum of possible PTEN findings. Further genetic sequencing is recommended and continued surveillance of various conditions is recommended. The prevalent neck masses recommended treatment involves complete surgical resection, and the prognosis is generally favorable due to the benign nature of the tumor. Resection is used to treat hamartomas. mTor inhibitors such as sirolimus and everolimus have been shown in clinical trials to be useful to treat symptoms [6].

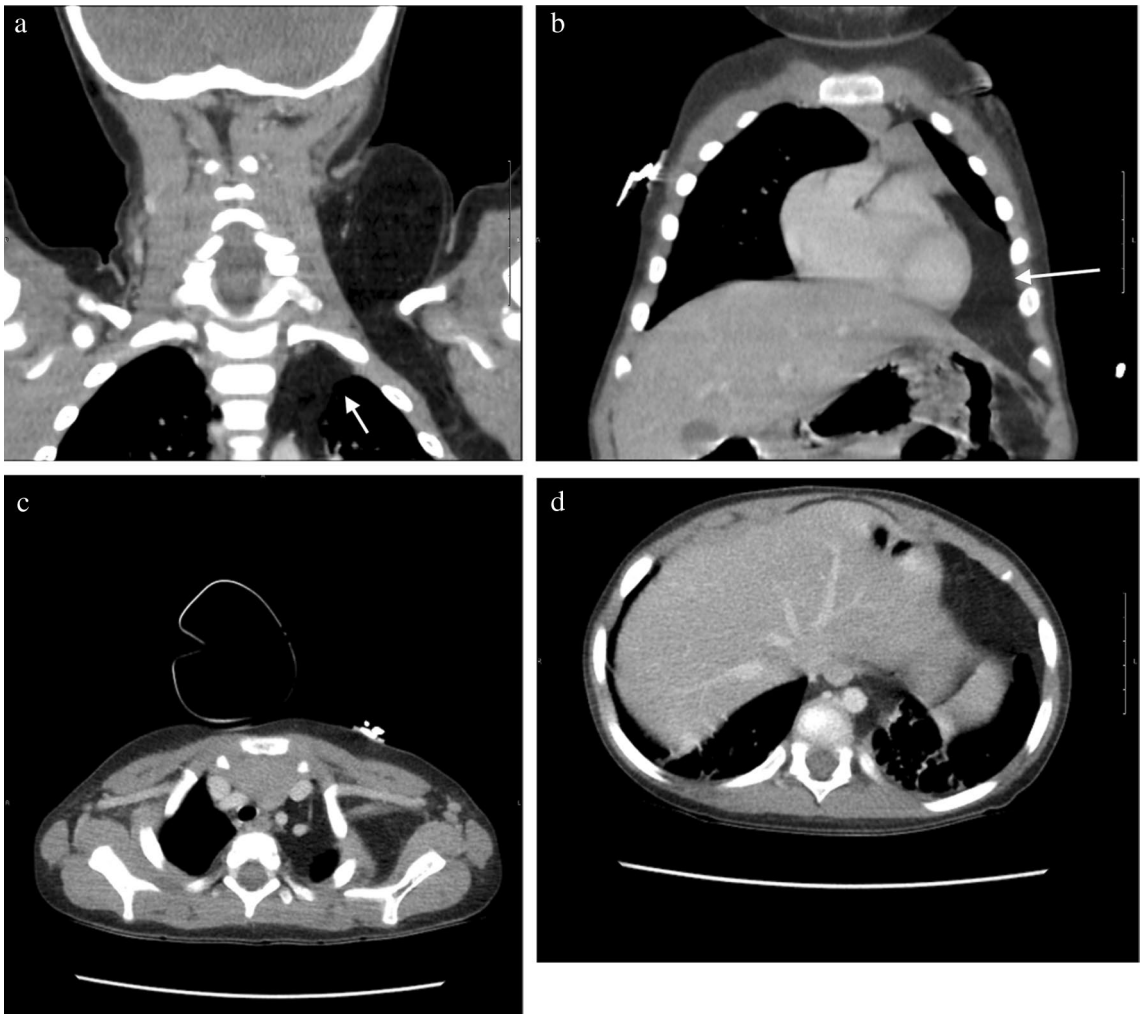

Fig. 4 **a** Coronal CT Neck presents with large lobulated fat attenuating mass in the left neck extending into the left axilla, left superior mediastinum and left heart border (white arrow). **b** CT Coronal of the Chest/Abdomen presents with a fat attenuating mass extending from the left heart border to the abdominal cavity (white arrow). **c** CT Axial of the Neck presents with a fat attenuating mass characterized above extending from leftward neck mediastinum encasing the left carotid and subclavian arteries. **d** CT Axial of the Chest presents with a fat attenuating mass with encasement of the aorta by the mass at the diaphragmatic hiatus

SOLAMEN syndrome is the germline mutation of PTEN, as such cancer surveillance is recommended due to the high risk of breast, thyroid, kidney, and endometrial cancer. Cancer surveillance guidelines for individuals with PTEN hamartoma syndrome should be screened annually for a skin and thyroid. Thyroid ultrasound should start at 18 and be offered annually Renal ultrasound should be offered at 40 and every 2 years. Colonoscopy should be started at 35–40 and surveillance adjusted from then. In addition, women should receive an annual MRI breast cancer screening starting at 30. Genetic testing and screening of their family members should be recommended [7].

Conclusions

In conclusion, we report a rare case of SOLAMEN showing rapid growth despite a young age. A diagnosis of exclusion, this multisystemic disease is associated with Lhermitte-Duclos disease and hamartomas of the GI, breast, thyroid, and testicles. Due to SOMAMEN syndrome's rarity, clinical suspicion should arise if multiple small nonspecific variably low-attenuated nodular lesions in the back, shoulders, and upper arms are present on CT, which are associated with mucocutaneous lesions. Ongoing monitoring should be done as there is an increased risk of cancer.

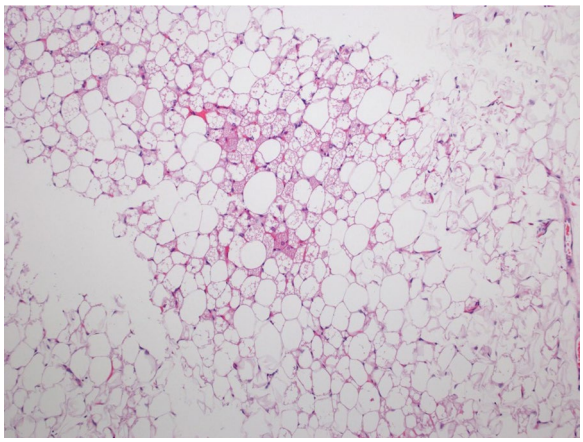

Fig. 5 Benign fatty tissue including brown and white fat with focal lymphoid aggregates and biopsy site changes, clinically PTEN-related hamartoma tumor syndrome at 20X magnification. The tissue removed consists of mature-appearing fatty tissue with patches of brown fat and focal benign- appearing lymphoid aggregates. This is in company with areas of fibrosis, fat necrosis and histiocytes accumulation

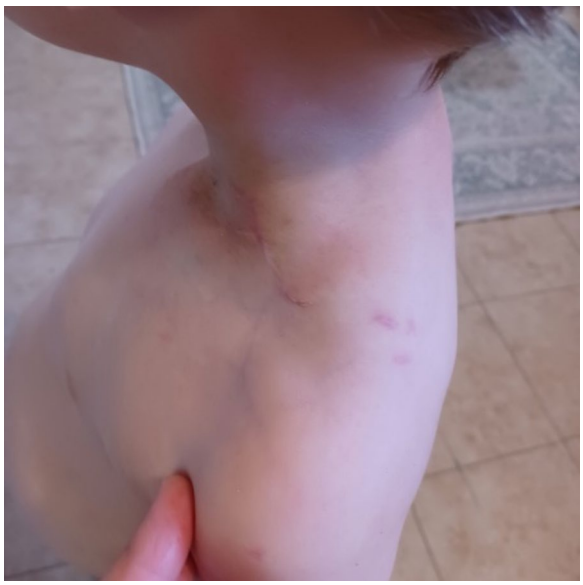

Fig. 6 Picture of the child post hibernoma resection

Abbreviations

SOLAMEN	Segmental overgrowth, lipomatosis, arteriovenous malformation, and epidermal nevus
PTEN	Phosphatase and tensin homolog
CT	Computed tomography
MRI	Magnetic resonance imaging
PHTS	PTEN hamartoma tumor syndrome
GI	Gastrointestinal
PI3K/AKT/mTOR	Phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin
CLOVES	Congenital lipomatous overgrowth, vascular malformations, epidermal nevis, spinal/skeletal anomalies/scoliosis

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Author contributions
The authors confirm contribution to the paper as follows: case report conception and design: AW, EG, BC; draft manuscript preparation: AW, EG, BC. All authors reviewed the results and approved the final version of the manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests
The authors declare that they have no competing interests.

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References

1. Caux F, Plauchu H, Chibon F, Faivre L, Fain O, Vabres P, Bonnet F, Selma ZB, Laroche L, Gerard M, Longy M (2007) Segmental overgrowth, lipomatosis, arteriovenous malformation and epidermal nevus (SOLAMEN) syndrome is related to mosaic PTEN nullizygosity. Eur J Hum Genet 15:767–773. https://doi.org/10.1038/sj.ejhg.5201823
2. Dragoo DD, Taher A, Wong VK, Elsaiey A, Consul N, Mahmoud HS, Mujtaba B, Stanietzky N, Elsayes KM (2021) PTEN hamartoma tumor syndrome/cowden syndrome: genomics, oncogenesis, and imaging review for associated lesions and malignancy. Cancers 13:3120. https://doi.org/10.3390/cancers13133120
3. Yehia L, Keel E, Eng C (2020) The clinical spectrum of PTEN mutations. Annu Rev Med 71:103–116. https://doi.org/10.1146/annurev-med-052218-125823
4. Murphey MD, Carroll JF, Flemming DJ, Pope TL, Gannon FH, Kransdorf MJ (2004) From the archives of the AFIP: benign musculoskeletal lipomatous lesions. Radiographics 24:1433–1466. https://doi.org/10.1148/rg.245045120
5. Rasalkar DD, Paunipagar BK (2010) Testicular hamartomas and epididymal tumor in a cowden disease: a case report. Case Rep Med 2010:135029. https://doi.org/10.1155/2010/135029
6. Mussa A, Carli D, Cardaropoli S, Ferrero GB, Resta N (2021) Lateralized and segmental overgrowth in children. Cancers 13:6166. https://doi.org/10.3390/cancers13246166
7. Tischkowitz M, Colas C, Pouwels S, Hoogerbrugge N, Group PGD, European Reference Network G (2020) Cancer Surveillance Guideline for individuals with PTEN hamartoma tumour syndrome. Eur J Hum Genet 28:1387–1393. https://doi.org/10.1038/s41431-020-0651-7

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