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SURGERY

A Supraclavicular ALK-Positive Anaplastic Large-Cell Lymphoma Initially Misdiagnosed and Yet Successfully Treated with Wide Excision and Adjuvant Chemotherapy: a Case Report

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ABSTRACT

Background ALK-positive Anaplastic Large-Cell Lymphomas (ALCL) are chemo-sensitive cancers; combination of histologic and immunophenotypic or genetic studies remains the main strategy to prevent their unnecessary surgical excision as they can mimic soft-tissues sarcomas in histology. In sub-Saharan Africa, however, availability and affordability of immunophenotypic studies, especially extended immunohistochemistry (IHC) tests, constitute major limitations for accurate diagnoses. The case presented herein is an example of a heavy surgical management resulting from an initially inaccurate diagnosis, but eventually treated successfully.

Case presentation A 15-year-old female patient presented with a 5-month history of a painless right supraclavicular mass. The initial biopsies had conflicting histology reports. In view of its rapid growth, it was first managed surgically, as a high-grade sarcoma stage T4N1M0: a wide "en bloc resection" with primary flap covering was done. Post-operative histology with an extended IHC from the widely resected tissue finally revealed an ALK-positive ALCL, which proved to be sensitive to chemo-therapy. An adjuvant chemotherapy of six cycles of CHOP regimen followed with a good response; the patient became clinically stable, and all the investigations that were done, including a PET-CT scan, could not detect any residual active disease. She was still disease-free at 2 years after completion of chemotherapy.

Conclusions Although cost-effective, combined histologic and immunophenotypic studies, especially extended IHC tests, can reduce the incidence of misdiagnosed large-cell lymphoma. As exemplified in this present case, obtaining appropriate and sufficient tissue from the tumor could possibly increase the chance of finding an accurate diagnosis.

Keywords Anaplastic large-cell lymphoma · Case report · Chemotherapy · Fascio-cutaneous flap · IHC · PET-CT scan · Misdiagnosis

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Background

Anaplastic large-cell lymphoma (ALCL) represents a group of T cell lymphoma characterized by a proliferation of large pleomorphic cells with strong expression of the cytokine receptor CD30 [1, 2]. A high proportion of ALCLs are associated with translocations involving the anaplastic lymphoma kinase (ALK) gene: ALK-positive ALCLs [1, 2]. They are non-Hodgkin lymphomas from T cell lineage [3, 4] and have been classified as a distinct clinicopathologic entity by the World Health Organization (WHO) since 2008 [5, 6]. Patients with ALK-positive ALCL present with painless lymphadenopathy [5, 6]. Some patients may present with an isolated lymphadenopathy or an extranodal disease in any anatomical location [3, 7]. The diagnosis of ALK-positive ALCL is made through an excisional biopsy of a lymph node. Histologic, genetic, and immunophenotypic studies are required in a clinical context for interpretation [2, 8]. Tumoral histologic evaluation includes an assessment of both morphology of the individual cells and pattern of lymph node involvement [8]. The immunophenotype of lymphoma cells can be determined by flow cytometry or by immunohistochemistry (IHC). The combination of the above-mentioned studies remains the main strategy to an accurate recognition of ALK-positive ALCL; this avoids unnecessary surgical wide excision of lymphomas. In sub-Saharan Africa, however, the availability and affordability of this combined strategy constitute a major limitation to the pathologists to diagnose accurately. ALK protein expression on tumor cells is an independent predictor of a favorable clinical outcome; thus, ALK-positive ALCLs are generally chemo-sensitive when serum lactate dehydrogenase (LDH) is normal and the International Prognostic Index (IPI) score is below 3 [2, 8–10]. In this article, we intend to highlight the challenge encountered in diagnosing lymphomas, especially ALK-positive ALCLs, and the requirement of extended IHC. ALCLs and soft-tissue sarcomas have a vast morphologic spectrum and present similar microscopic features; so, histology alone might not be sufficient to ensure an accurate diagnosis [4, 11–13]. The following case is an example of a heavy surgical management of an ALK-positive ALCL initially misdiagnosed with conflictual histologic reports and limited IHC tests in a sub-Saharan African setting.

Case Presentation

History A 15-year-old female patient referred to our surgical department, who presented with a right supraclavicular mass about 5 months from its onset. In the history of the presenting complaint, this mass had started as a small firm painless swelling in the right supraclavicular region, noticed in May 2016, and rapidly increased in size. At this stage, the patient was reviewed at a hospital of the eastern region of the Democratic Republic of the Congo, where she lives, and was treated with antibiotics for a period of 3 weeks as having an infectious lesion, but without improvement. She was screened in the meantime for tuberculosis and other chronic disease (including HIV), but the results were negative. As the mass was still increasing in size, an excision biopsy was done in July 2016, and the histology reported a diffuse large-cell lymphoma with differential diagnosis of a poorly differentiated carcinoma. An immunohistochemistry (IHC) was requested to be done in another center, but was not done at this stage. There was a persistent ulceration which developed from the biopsy site. The patient progressively developed a dry cough, and started losing weight during the following weeks. She was referred to a regional hospital of the same region and was put on chemotherapy. The first cycle was given in the beginning of August 2016 with a regimen made of cyclophosphamide, vincristine, and dexamethasone. The chemotherapy was stopped during that first cycle because of non-tolerated side effects of the drugs (epigastric pain and frequent vomiting). Few days later, her relatives decided to abandon modern medical care (chemotherapy) from that regional hospital and considered alternative approaches of treating the patient with traditional medicine (topical herbal medicine). The evolution of the disease was characterized by a rapid regrowth of the right supraclavicular mass and persistent cough while she was still getting that traditional medicine for some weeks; during the 2 months preceding our initial surgical review in October 2016, she lost approximately 8 kg. She denied any history of fever and sweating. She reported frequent post-prandial nonbilious vomiting and loss of appetite for a month. She was referred to our team in the Department of Surgery, Makerere University, Kampala, Uganda.

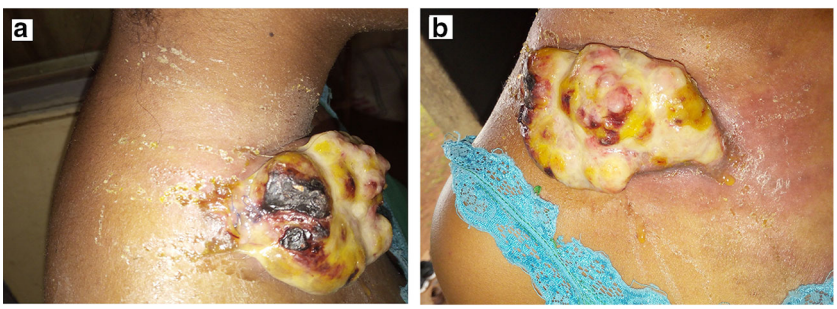

Fig. 1 **a**, **b** Lateral and front views of the initial tumor presentation. (Photo: Lekuya M.H)

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Table 1 Complete blood count trends

	Initial admission	Postop day 14 surgery 1	Postop day 5 surgery 2	Admission for chemo	Day 1 of chemo	Cycle 2 chemo	Cycle 3 chemo	Cycle 4 chemo	Cycle 5 chemo	Cycle 6 chemo	Month 1 review	Month 2 review	Month 6 review	Month 9 review
WBC ($10^3/\mu L$)	7.93	22.78	26.45	15.33	20.23	9.88	3.73	3.29	3.44	4.37	3.82	4.60	4.08	5.21
Neutrophils ($10^3/\mu L$)	4.96 (62.5%)	17.61 (77.3%)	21.03 (79.5%)	11.32 (73.8%)	15.42 (76.2%)	5.73 (58%)	1.48 (39.6-%)	1.19 (36.1-%)	1.35 (39.3-%)	2.79 (63.8-%)	2.24 (58%)	2.54 (55%)	2.41 (59.1%)	2.75 (52.7%)
Lymphocytes($10^3/\mu L$)	1.86 (23.4%)	2.98 (13.1%)	2.64 (10%)	2.66 (17.4%)	2.36 (11.7%)	2.91 (29.5-%)	1.39 (37.3-%)	1.4 (42.6-%)	1.13 (32.8%)	0.88 (20.1-%)	0.89 (23.3%)	1.55 (33%)	1.34 (32.8%)	1.84 (35.3%)
Monocytes ($10^3/\mu L$)	0.55 (6.92%)	1.89 (8.3%)	1.76 (6.7%)	0.9 (5.9%)	1.78 (8.8%)	1.13 (11.4-%)	0.83 (22.3-%)	0.67 (20.4)	0.92 (26.7-%)	0.66 (15.1-%)	0.61 (16%)	0.40 (8.7%)	0.22 (5.4%)	0.54 (10.4%)
Eosinophils ($10^3/\mu L$)	0.52 (6.49%)	0.26 (1.1%)	0.96 (3.6%)	0.42 (2.7%)	0.64 (3.2%)	0.07 (0.7%)	0.02 (0.5%)	0.02 (0.6%)	0.03 (0.9%)	0.02 (0.5%)	0.06 (1.6%)	0.09 (2%)	0.10 (2.5%)	0.06 (1.2%)
Basophils ($10^3/\mu L$)	0.05 (0.67%)	0.04 (0.2%)	0.06 (0.2%)	0.03 (0.2%)	0.03 (0.1%)	0.04 (0.4%)	0.01 (0.3%)	0.01 (0.3%)	0.01 (0.3%)	0.02 (0.5%)	0.02 (0.5%)	0.02 (0.4%)	0.01 (0.2%)	0.02 (0.04)
Hemoglobin (g/dL)	10.2	7.9	8.3	8.8	7.9	11.2	11.9	12.3	11.4	12.4	11.8	12.7	13.1	13.3
Red blood cells ($10^6/\mu L$)	4.14	3.71	3.73	3.95	3.68	5.39	5.42	5.58	5.05	4.84	4.48	4.80	5.04	4.83
Hematocrit (%)	31.7	28.1	27.7	29.8	27.2	42.1	41.9	45.4	39.9	39.1	36.4	39.4	41.1	35.1
MCV (fL)	79.5	75.7	74.3	75.4	73.9	78.1	77.3	81.4	79	80.8	81.3	82.1	81.5	72.7
MCH (pg)	24.6	21.3	22.3	22.3	21.5	20.8	22.0	22.0	22.6	25.6	26.3	26.5	26.0	27.5
MCHC (g/dL)	32.2	28.1	30	29.5	29.0	26.6	28.4	27.1	28.6	31.7	32.4	32.2	39.9	37.9
Platelets ($10^3/\mu L$)	617	1120	762	624	415	140	350	179	439	340	371	368	342	232

Table 2 Blood chemistry trends

	Admission	Post op D5 revision surgery	Day 1 of cycle 1	Day 1 of cycle 2	Month 1 review	Month 3 review	Month 6	Month 9
LDH (U/L)	180	–	330.8	–	369.9	164.6	233.8	159.4
Creatinine (μmol/-L)	54.1	196.4	37.2	39	48.9	–	45.2	–
Urea (mmol/-L)	2.78	7.51	1.22	–	3.16	–	2.26	–
T-Bill (μmol/-L)	2.52	–	3.57	–	6.93	–	6.83	7.4
AST (U/L)	14.2	13.6	–	29.7	26	–	20.2	–
ALP (U/L)	109.2	166.7	253.4	105	63.4	–	103.1	77.2
ALT (U/L)	17.3	7.8	38	14.5	7.6	–	8.8	15.3
GGT (U/L)	71.0	123.2	248.6	–	22.5	–	18.8	20.2
TP (g/L)	68.8	63.3	71.1	–	67.6	–	73.5	61.4
Na (mmol/-L)	153.1	–	–	144	142.1	–	144.1	141.8
K (mmol/-L)	4.71	–	–	4.63	5.16	–	4.34	4.47
Cl (mmol/-L)	109.2	–	–	106.1	107.9	–	107.3	107.4

Physical Examination On our initial examination, she was in performance status 1 of the Eastern Cooperative Oncology Group (ECOG), the vitals were as follows: temperature 36.6° C, BP 120/75 mmHg, pulse rate 95 bpm, RR 18 cpm, SpO_2 99% on room air. She was not pale, not dehydrated, no jaundice, no enlarged lymph node in the superficial palpation of the neck and chest region, or elsewhere in the body. Locally in the supraclavicular region, there was a fungating mass, 15 × 10 cm, yellowish, mobile, discharging serous secretion (Fig. 1a, b). The other systems were unremarkable.

Medical Investigations Laboratory results are summarized in Tables 1 and 2. Chest X-ray showed an isolated radiopaque lesion at the right supraclavicular region (Additional File 1). Abdominal ultrasound scan, electrocardiography, and echocardiography were normal. Cervical and chest computerized tomography (CT) scan reported a hypodense lesion in the right supraclavicular region with few enlarged axillary lymph nodes; the mass was free from the major neuro-vascular structures and from the pleura (Fig. 2a, b). A wedged biopsy was taken from the mass and sent to pathology. Histology and IHC showed that vimentin was strongly positive, and

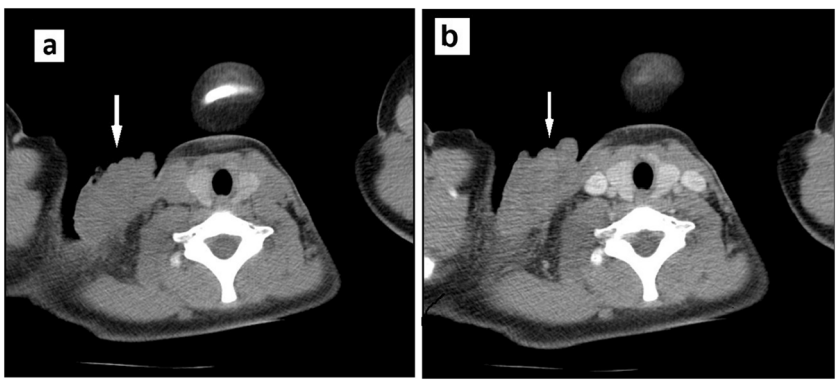

Fig. 2 Thoracic CT scan at the level of T1 vertebra; the white arrow shows the tumor in relationship with underlying structures. **a** Non-contrasted CT scan. **b** Contrasted CT scan

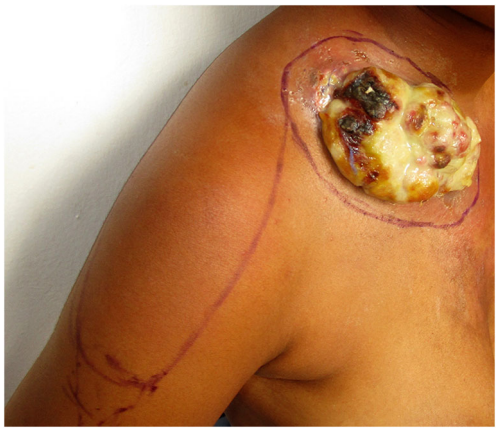

Fig. 3 Planning of the flap. (Photos: Lekuya M.H)

pancytokeratin, CD 45, and S 100 were negative (Additional File 2); at this stage of investigation, it was concluded to be a poorly differentiated high-grade soft tissue sarcoma. Both surgical and medical oncology teams agreed at this stage with the diagnosis of a high-grade soft tissue sarcoma, T4N1M0. Considering that no radiotherapy treatment modality was available in Uganda at that time, it was decided to start by plastic surgery with wide "en-bloc resection" (EBR) for cytoreduction and defect covering, then to send that mass to pathologists in parallel for final diagnosis before starting the adjuvant chemotherapy at Uganda Cancer Institute (UCI), an independent unit of the Hospital for Cancer Treatment.

Surgical Management The patient was prepared for surgery the following week. After skin marking (Fig. 3), the patient was positioned in dorsal decubitus, intubated under general anesthesia. An EBR with 2-cm margin of the tumor was done (Fig. 4a), and one regional lymph node was harvested. The frozen section biopsy could not be applied at the hospital during the surgical procedure. The clavicular head of the right sternocleidomastoid muscle was resected from its attachment. Intra-operatively, it was found that the tumor was already invading the right suprapleural membrane (Sibson's fascia) and adhering to the superior-anterior wall of the right subclavian vein. An intra-operative hemorrhage after accidental vascular injury was controlled by direct pressure and primary repair of the slit on the vessel with application a small piece of Surgicel® Fibrillar™ absorbable hemostat over the sutured slit. The invaded fascia was not further dissected since there was no clear demarcated plane between the tumor and that membrane, and the thoracic surgery team was not around. The defect was closed with a random fascio-cutaneous rotational deltoid flap (Fig. 4b); the flap donor site was closed primarily in combination with a full-thickness skin graft (FTSG) from the left loin. A Jackson-Pratt drain was left to collect hematoma and was removed 2 days later after collecting 15 mL of blood. The resected mass was taken to three different pathology laboratories to insure the accuracy of the diagnosis. Blood transfusion of two units of packed blood cells was given post-operatively. Post-operative care was uneventful and she was discharged home the following day. The shoulder joint was contained in an arm sling for 2 days. She benefited from analgesia and antibiotics cover with ceftriaxone 2 g daily for 5 days.

After 5 days, during the change of dressing, we found that the flap margin became necrotic (Fig. 5a); progressively the flap started to retract, and the sutures were released. The patient progressively developed a surgical site infection. A culture and sensitivity of the wound swab found *Staphylococcus aureus* sensitive only to vancomycin and oxacillin. Serial wound dressing and debridement (both surgical and enzymatic) was done for 2 weeks, leaving a new defect from the previous tumor bed (Fig. 5b). Three weeks after the first surgery, a flap revision was done, with the patient being intubated under general anesthesia. A debridement and refreshment of margins was performed. No obvious abnormal mass was found on the tumor bed. A direct closure of the salvaged flap was achieved without tension and a 3 × 3 cm remaining defect was covered by a split-thickness skin graft (STSG) harvested from the same arm. The post-operative care was uneventful. After 7 days, during the change of wound dressing, we found that the flap was still attached, the STSG was partially taken, but the wound delayed to granulate at the area of the previous tumor (Additional File 3a, b). Wound dressing was done alternately daily for 2 weeks, and antibiotics and analgesia were given during the ten following days. The cough stopped, the appetite regained progressively, and the

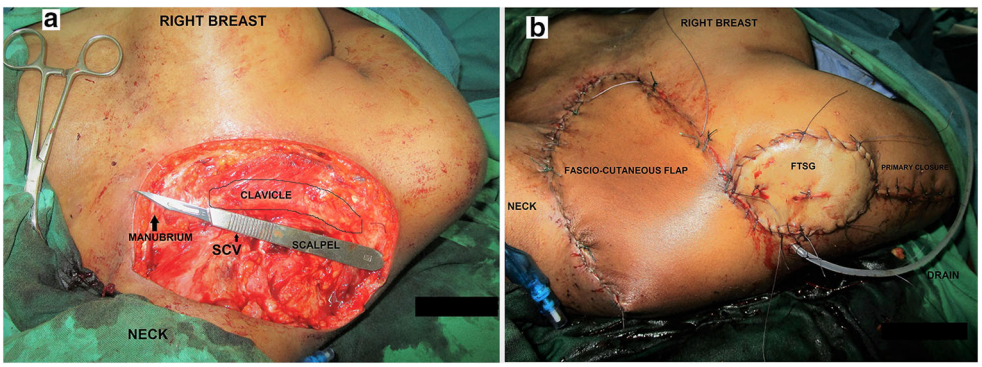

Fig. 4 **a** Big defect after wide excision of the tumor; SCV = subclavian vein, seen under the scalpel. **b** Covering of the defect with a deltoid fascio-cutaneous flap, and covering of the donor site with a FTSG from the left groin combined with primary closure. (Photo: Kalanzi W.E)

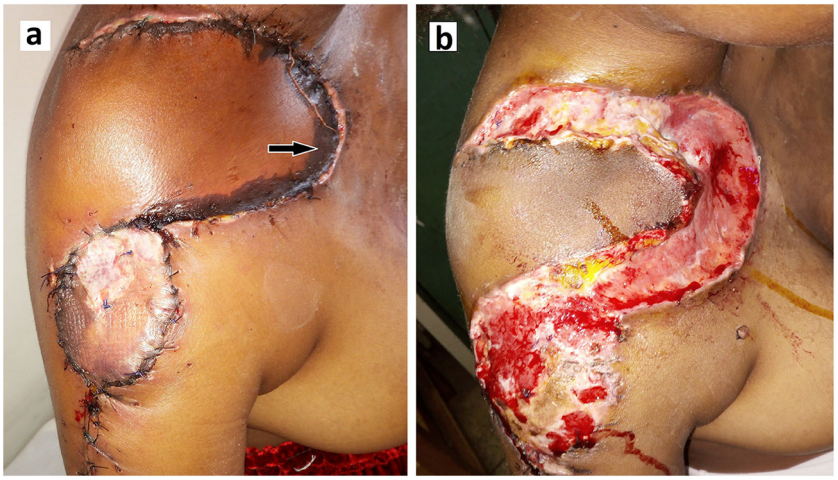

Fig. 5 **a**, **b** Flap margins necrosis. (Photos: Lekuya M.H)

patient was in fair general condition, and then transferred to UCI for chemotherapy.

Post-Operatory Diagnosis from Pathology After the tumor resection (first surgery), the samples had been sent to three different pathology laboratories (excluding the previous laboratory). All the results were available within 2 weeks of the first surgery. Two of those newly requested laboratories reported findings of large-cell lymphoma and the other one reported a poorly differentiated high-grade sarcoma.

For the reported diagnosis of ALCL, the first pathology reported an extensive ulcerated skin with a massive, diffuse partially nodular infiltration by large, anaplastic tumor cells with kidney-shaped nuclei (hallmark cells) with prominent nucleoli. The mitotic figures were frequent. The IHC panel test showed a strong expression of CD30 in the tumor cells; co-expression of CD5 was evident, as well as a nuclear and cytoplasmic strong staining of ALK1; the proliferation index (Ki67) reached 60–70%. There was no EBV association (EBER in situ hybridization); CD20 remained negative. They concluded the presence of an infiltration of the skin by a CD30-positive ALK1-positive ALCL (T cell origin). The second laboratory reported again large-cell lymphoma in histology; they described that both samples (tumor and lymph node) revealed sheets of large neoplastic lymphocytes with prominent nucleoli and brisk mitotic activity (Fig. 6a, b), consistent with a large-cell lymphoma, but they did not perform immunoperoxidase stains using CD3 and CD20. For the diagnosis of high-grade sarcoma, the other pathology laboratory described atypical large cells and the lymph node was effaced by high-grade tumor. In their IHC, they found that CD20 and CD45 were positive. Because of the complexity of the available conflicting pathology reports in consideration of the previous two conflicting ones prior to the first surgery, the case was appointed for discussion in a specialists' tumor board, composed of pathologists, oncologists, surgeons, radio-oncologists, and hematologists from Makerere University, UCI, and Fred Hutchinson Cancer Research Center/UCI. In view of the panel of the relevant IHC tests done, based on the clinical and epidemiological parameters to differentiate the two diseases (lymphoma versus sarcoma), the tumor board agreed on the diagnosis of "CD30-Positive, and ALK1-Positive ALCL (of T cell origin)", stage II B (bulky disease), performance score ECOG 1. It was then requested to do a bone marrow analysis for advanced disease staging.

The bone marrow aspirate done on the following day reported that the particles were present; the cellularity was normal for age and the erythropoiesis was markedly reduced, but normoblastic; the megacaryocytes were present and normal, the myelopoiesis was present orderly and maturing well. The myeloblast count was less than 5%. The lymphocytes were present and normal with no atypical lymphoid cells seen. The plasma cells were normal and no extrinsic cells seen. The bone marrow biopsy in microscopic appearance under hematoxylin and eosin showed normocellular marrow for age with normal

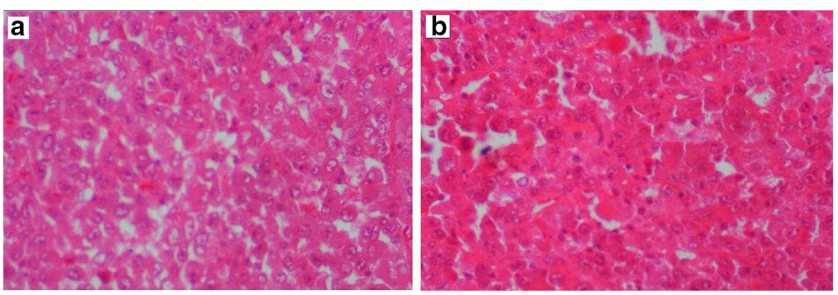

Fig. 6 Microscopy of large-cell lymphoma. Section of both samples revealed sheets of large neoplastic lymphocytes with prominent nucleoli and brisk mitotic activity, consistent with large-cell lymphoma. **a** Resected mass from surgery. **b** Harvested lymph node

trilineage hematopoiesis. There were no foci or sheets of atypical lymphoid cells and no extrinsic cells to be seen. It was concluded that there was no evidence of a non-Hodgkin's lymphoma in the bone marrow. The LDH was high at 330.8 U/L and the IPI was 1 (low grade). The tumor board decided to treat the patient with a CHOP regimen of six cycles.

Oncology Review and Chemotherapy This review was done first at UCI Outpatient Clinics. The patient started chemotherapy on CHOP regimen 3 weeks after the flap revision. She received a total of six cycles of CHOP (every 3 weeks during 4 months). She received intravenous cyclophosphamide 1088 mg, doxorubicin 72.5 mg, and vincristine 2 mg on day 1 of the cycle and tablets of prednisolone 50 mg twice a day from day 1 to day 4. A pre-medication of intravenous dexamethasone 8 mg and intramuscular ondansetron 8 mg was given at day 1 of each cycle before chemotherapy. She received syrup of iron, tablets of omeprazole, buccal spray of antiseptic, and analgesics during the first week of each cycle to balance the side effects. The granulation of the wound from the defect of the previous tumor site was accelerated after the second cycle, and the wound was left to be healed by secondary intention. There were no major side effects of chemotherapy, except for the low count of neutrophils during the first and the third cycle. She developed photophobia, dry oral mucosa, dry skin, onycholysis, and alopecia during the six cycles. The laboratory results during and after chemotherapy are summarized in Table 1.

Follow-Up Post Chemotherapy From the tenth week after the initiation of chemotherapy, the patient became clinically stable and the wound had healed by secondary intention. The right shoulder had regained almost its previous range of motion after frequent self-exercising of that joint. The scar became hypertrophic (Additional File 4a, b). She regained about 10 kg as compared with her weight after the first cycle of chemotherapy. Complete blood count and chemistry remained within the normal range during the rest of the follow-up (Tables 1 and 2). The repeated chest X-rays and abdominal ultrasound scans at 3, 6, and 9 months post chemotherapy did not show any abnormal findings. The further repeated cervico-thoraco-abdominal contrasted CT scans were normal (Additional File 5a, b). A positron-emission tomography (PET) scan coupled with a CT scan was done at 6 months after completion of the six cycles of chemotherapy. During this PET-CT scan, a dose of 12.3 mCi of fluorodeoxyglucose (FDG) was given intravenously; the fasting blood sugar level prior to administration was 5.1 mmol/L. The scan uptake time of the whole body was 100 min. There was no active neoplastic disease detected, and FDG-PET/CT scan test was scaled Deauville 1 (Fig. 7). The patient was rescheduled and been reviewed every 6 months in

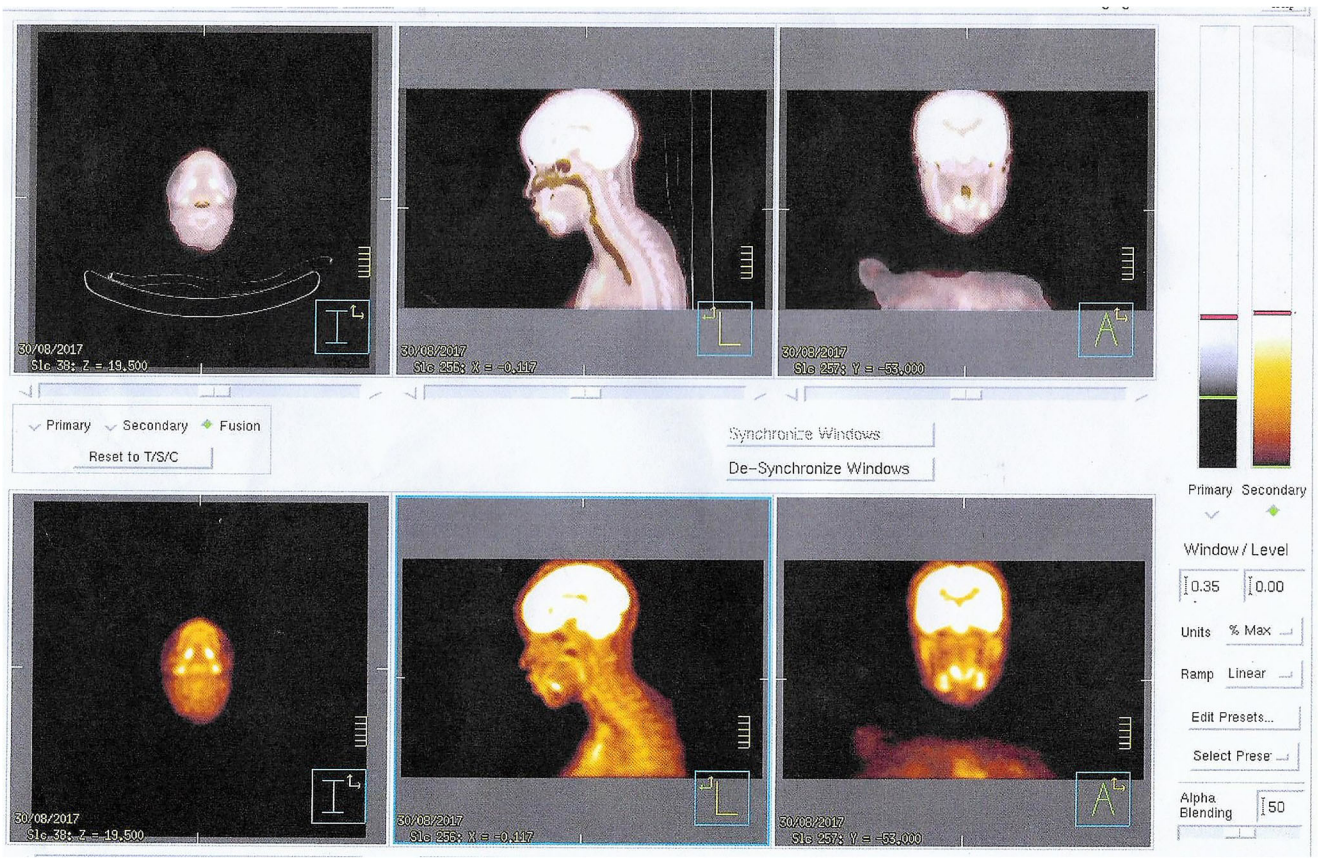

Fig. 7 FDG PET-CT scan at 6 months post chemotherapy

the outpatient clinics for 2 years and was found clinically stable without complaint. She is still performing very well at school, psychologically stable, and doing sport.

Plastic Surgery Scar Revision A plastic surgery for scars' cosmesis on the right supraclavicular region was done successfully under local anesthesia after 16 months post chemotherapy. The surgery was uneventful, and the scars became more acceptable in term of cosmesis (Additional File 6a-b). No further complaint was reported after 2 years post chemotherapy.

Discussion

We successfully managed this case of ALK-positive ALCL in a multi-disciplinary approach, and we faced different challenges, mainly related to the controversial pathology reports in the context of sub-Saharan Africa. This delay of getting documented pathologic diagnosis of malignant processes is very frequent in our clinical practice as it is commonly difficult to diagnose malignancy at an earlier stage of the disease in most of sub-Saharan African settings due to several reasons [14]. The first challenge was brought by that very first laboratory, which analyzed the histology from the excision biopsy; this pathology unit was unable to do further IHC tests at this stage to differentiate diffuse large-cell lymphoma versus poorly differentiated carcinoma. It can be explained by the frequent out of stock of IHC reagents as it happens in most of the sub-Saharan hospitals. Probably, it could have been an important point to control the disease progression at the early stage and avoid uncertainty. This is a real problem in getting accurate pathological diagnosis in sub-Saharan Africa. In addition to that problem, the visit to traditional medicine caused another waste of time in the management of this patient, even after having a histologic diagnosis. It was reported by the WHO that up to 80% of Africans are still attending primarily traditional medicine for health-related problems [15]. It is often when there is a complication that patients will be referred to modern health care. Further steps in management were characterized by several conflictual pathology reports. It is well known that ALK-positive ALCL shows a broad morphologic spectrum [4]; this might require additional IHC to confirm the diagnosis. The major problems were directly linked with the weak pathology reports with a narrow panel of IHC tests and some time without available IHC tests. This weakness has been in the middle of all the challenges encountered in different clinical decisions during the management of this patient. This was unfortunately the primary misleading diagnosis, which oriented the clinicians to the decision of a wide excision of tumor for cytoreduction and availing appropriate tissues for further analysis before adjuvant chemotherapy. Although controversial, and found to be essential in breast implant-associated ALCL with the benefit of implant removal [16, 17], surgical excision of ALCL might have a role in certain types of superficial single malignant tumors in terms of cytoreduction of malignant cells. Nevertheless, it was difficult to tell in this present case how far one could have possibly achieved the macroscopic tumor-free margins. The surgical cytoreduction was achieved with the costs of several complications and corrective surgeries. The initial flap failure could be explained by many reasons, such as the large size of defect following the resection, the anatomic location of the rotational flap, the tension on the anchoring sutures, and the mobility of the underlying shoulder joints. Although the choice of this flap was not classical, it had the benefit of sparing the skin near the right breast, which could have been an alternative option. Although the surgical management was heavy, it helped to achieve significant tumor cytoreduction and provided sufficient tissues and lymph node for further histology, despite the unavailable frozen section for the tumor bed and margin clearance at our hospital.

The resected tumor was sent to three different laboratories for accurate comparative diagnosis. This significantly increased the cost of the treatment, but was necessary in view of previous conflicting reports. It is frequently reported that when ALCL appear primarily in the soft tissue without peripheral lymphadenopathy, they create considerable diagnostic difficulties for the pathologist, as they may be mistaken for sarcomas [11, 13]. Most of the laboratories in sub-Saharan Africa proceed with only histology and a limited number of IHC tests. In addition, there are only few qualified general pathologists in East Africa, and they are dealing with all types of pathologies at the same time. Very few of them remarkably have specific expertise from specialized pathology trainings [14, 18]. These major problems show that there is an urgent need of training more specialized pathologists and equipping pathology laboratories with updated technologies in sub-Saharan Africa to improve cancer care. The patient responded efficiently to chemotherapy despite some tolerable side effects, mainly during the first three cycles. Indeed, excellent results with a low IPI score have been reported with a variety of anthracycline-based chemotherapy regimens including CHOP [9, 10]. The wound-healing process was not affected by chemotherapy. During the entire management, the patient was exposed to radiation on several occasions (three times for chest X-rays, three times for cervico-thoraco-abdominal CT scans, and once, during PET scan). Most of the radiological investigations turned out negative; this assumes the need to balance risks and benefits of frequent X-rays investigations of ALK-positive ALCL patients with a low IPI score. In our view, this case report is very consistent since we investigated in-depth and managed eventual challenges with a multidisciplinary approach despite being in a resource-limited country.

Conclusions

In the present case, potential risks of surgery and its heavy costs could have been avoided if a proper diagnosis had been obtained

at early management. Definitively, an extended panel of IHC tests could have reduced the unnecessary cost of extra procedures, but also would have been cheaper for the patient in a risk/benefit approach. Availability of these valuable diagnostic methods can reduce the incidence of misdiagnosed anaplastic large-cell lymphoma versus soft-tissue sarcoma. Requesting a second opinion from another pathologist can also reduce the risk of misdiagnosis, although it may likewise give conflicting answers and tends to increase the costs. On the other hand, surgery may have possibly played a significant role of cytoreduction and availing tissue. Therefore, obtaining appropriate and sufficient tissue from the tumor with pertinent techniques could possibly increase the chance of an accurate diagnosis. We finally recommend further collaboration between academic institutions to encourage training of specialized pathologists and equip the pathology laboratories with modern technology in sub-Saharan Africa.

Patient's perspectives She was scheduled to be reviewed every year for the next 3 years.

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Authors' Contributions HML: Medical and surgical management, manuscript writing, images' archives; EWK: Surgical management and manuscript review; RM: Medical management and manuscript review; AO: Oncological management and manuscript review; AR: Pathology analysis and manuscript review; GL: Surgical scar revision and manuscript review; GB: Medical suggestions and critical manuscript review.

Availability of Data and Material Datasets used in the current article are available from the corresponding author on reasonable request.

Compliance with Ethical Standards

Ethics Approval and Consent to Participate A clearance from the School of Medicine Research and Ethics Committee (SOMREC) of Makerere University College of Health Sciences, registered as #REC REF 2018–044 was obtained after verification of all ethical concerns before submission for publication. A written informed consent was obtained from the patient and her parents for publication of this case report and accompanying images.

Competing Interests The authors declare that they have no competing interests for this case.

Abbreviations ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; CHOP, cyclophosphamide-doxorubicin-vincristine-prednisone; CT scan, computerized tomography scan; EBR, en-bloc resection; ECOG, Eastern Cooperative Oncology Group; GGT, gamma-glutamyl transferase; IHC, immunohistochemistry; IPI, International Prognostic Index; LDH, lactate dehydrogenase; PET scan, positron-emission tomography scan; RFT, renal function tests; STSG, split-thickness skin graft; UCI, Uganda Cancer Institute; WHO, World Health Organization

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