International Clinical and Medical Case Reports Journal
Research Article (ISSN: 2832-5788)

Cervicofacial Cystic Hygroma: Experience with Intralesional Tetracycline Sclerotherapy

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Citation: *Adekunle Y Abdulkadir, Stephen A. Kache, Bilkisu I. Garba, Peter O. Enesi, Alfred A. Tume. Cervicofacial Cystic Hygroma: Experience with Intralesional Tetracycline Sclerotherapy. Int Clinc Med Case Rep Jour. 2022;1(8):1-9.* DOI: https://doi.org/10.5281/zenodo.7322917

Received Date: 08 November, 2022; **Accepted Date:** 13 November, 2022; **Published Date:** 15 November, 2022

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ABSTRACT

Background: Cystic Hygroma (CH) is a benign, painless loculated lymphatic malformation that is commoner at the cervicofacial region. About 90% of cases present before age 2 years. The ideal treatment of cervicofacial cystic hygroma (CCH) is complete surgical excision. This is often difficult to achieve without sacrificing important neurovascular structures. Intralesional Tetracycline (ILTCN) sclerotherapy explored in this study is a cheaper and safer option devoid of cosmetic challenges, morbidity and mortality of surgery.

Aims and Objectives: To document our experience and response of CCH to ILTCN as a primary modality of treatment.

Materials and Methods: Eleven patients with CCH treated by drainages and instillation of 100mg/ml of ILTCN between 2014 and 2019 are presented. A repeated injection was performed at an interval of 3-4 weeks where necessary.

Results: Eleven patients, 7 males and 4 females aged between 1- 14 years were treated. Complete resolution was achieved with a single injection in about 80% and nearly 100% with 3 injections. One patient had a residual echogenic solid nodule (15.9mm × 14.7mm). There was no recorded case of adverse reactions other than pain at the site of injection which rarely persisted beyond 30mins.

Conclusion: Sclerotherapy with IL-TCN is a readily available, cheap, simple, safe, and effective option that can be considered as first line treatment for CCH. Surgery should be restricted to cases without satisfactory response to sclerotherapy. With 1-2 injections of ILTCN, complete resolution in about 90% of patients is possible if as many locules of a multiloculated hygromas are drained and injected.

Keywords: Cystic hygroma; Cervicofacial hygroma; Tetracycline; Sclerotherapy; Intra-lesional

BACKGROUND

Cystic Hygroma (CH) is a benign, painless loculated lymphatic malformation, which may result from combination of sequestration from developing lymphatic system, abnormal budding of the lymphatic system or lack of development of the normal connections between venous and lymphatic drainage.[1-3] Typically, it occurs at the original sites of the primordial lymph sacs at any anatomic location. Cervicofacial region is the most common location.[1-9] Occurrences in several other body locations such as mediastinum, axilla, arm, chest wall, breast, abdomen, inguinal region, leg, scrotum and tongue have been documented.[2,3-9]

Nearly 50% of the cases are diagnosed at birth and 80- 90% before the age of 2years.[1-4] Few cases have been diagnosed in-utero and in adulthood.[1-9]

Cervicofacial Cystic Hygromas (CCH) is easy to diagnose. Ultrasound equipped with Doppler facility is often sufficient without any need for other expensive and time-consuming imaging studies. Few cases may however, require additional imaging modalities such as computer tomography or magnetic resonance imaging.[1-3,5] The Characteristic sonographic appearance of CCH is that of multiloculated cystic masses with septae of variable thickness that contain solid components arising from the cyst wall or the septa. Studies correlating sonograms with the pathologic specimens have reported the solid component to correspond to clusters of abnormal lymphatic channels, too small to be resolved with ultrasound.[1,3]

The traditional treatment of choice for CCH is complete surgical excision. However, complete surgical extirpation may be difficult or impossible without sacrificing important neurovascular structures.[3-7] Where excision are incomplete, recurrence are high.[3-10] Other than surgical procedures, several approaches such as, embolization via interventional radiology, sclerosing therapy, laser therapy and psychological support have been employed to varying degree of successes in the therapy of CCH.[11-16] Multiple sclerosing agents such as bleomycin, ethanol, 3% sodium tetradecyl, polidocanol, ethibloc sulfate, OK-432 (picibanil) have been employed in children.[8,11-16] However, the ideal sclerosing agent in the pediatric population remains to be discovered.

In this study, we employed the use of the very cheap and readily available tetracycline as intralesional sclerosant in the treatment of all CCH in our centre. Our search through electronic literature did not find any study linked to the use of Intralesional Tetracycline (ILTCN) as sclerosant in cystic hygromas despite its reported successes in testicular hydrocele, renal cyst, hepatic cyst in children and in thyroid cyst.[16-22]

AIMS AND OBJECTIVES

To document our 8-years' experience with ILTCN as a primary treatment modality for CCH.

MATERIALS AND METHODS

This prospective study commenced in May 2014 and is still ongoing. This study had approval of the hospital ethical committee in accordance with the Helsinki Declaration of 2010. All patients had informed consent directly where achievable and where otherwise from parent/care giver. Sonographic evaluations of the masses with B-mode and Doppler interrogation using Toshiba Nemio XG 7.5MHz – 10MHz transducer were done in recumbent or semi-recumbent positions. Ultrasounds to document the sonographic characteristics of the masses were performed by two consultant radiologists. All patients with sonographic confirmed cystic hygroma had laboratory evaluation of their pack cell volume, full blood count, platelet and bleeding time done prior to recruitments into the study to ascertain their suitability for the procedure.

In preparation for drainages, ultrasound scan to identify a point where as many locules as possible can be entered were performed. Sizes 16G-18G cannula or spinal needle were employed for the drainages. The needle placements under aseptic technique were guided by the two consultant radiologists with a consultant surgeon and a paediatrician always in attendance. All patients had the cysts aspirated to the lowest achievable. Where necessary, the needle was re-introduced to break more locules for aspiration without exiting the site of primary entry. The cannular was left in situ and preparations of tetracycline (100mg/ml) were injected as the cannular was been gently withdrawn to allow for injection into nearly all drained locules.

On complete cannular withdrawal, a gentle pressure is maintained with a finger at the entering point while the apparently flabby mass is gently squeezed to allow for good spread of the sclerosant.

No patients had more than 10mls injected per course. Repeat injections of TCN were performed at an interval of 3-4 weeks where necessary after drainage of remnant locules as described above. Resolution was defined as complete disappearance of the cyst or reduction of the cyst(s) to near immeasurable volume on sonography.

All patients were followed up in the clinic by the surgeon and the paediatrician to document resolution and possible complications. The minimum follow up of patients included in this presentation is three years.

RESULTS

Eleven patients comprising of 7 males and 4 females aged between 1- 14 years (Table 1) who CCH treated with ILTCN sclerotherapy at our centre under ultrasound guidance between 2014 and 2019 are presented. Other than disfiguring swelling (Figure 1A & 1B), all but two patients were asymptomatic. The two symptomatic patients presented with mild respiratory and swallowing difficulties that resolved spontaneous with drainage. CCH location and the resultant compressive effect on vital structure as airways or oesophagus were the reason for symptomatic presentation rather than cyst sizes.

Table 1: Showing the patients ages, sexes, location and numbers of scleretherapy injections for complete resolutions amongst patients who have been followed up for at least 8month.

S/N	Sex	Age	Size	Location	Sclerotherapy
1	M	4years	large	Right side	Twice
2	F	12years	large	Right side	Once
3	F	14 years	Big	Right side	Twice
4	M	2years	Big	Left	Once
5	F	5years	Large	Right	Twice
6	M	1.5years	Large	Right	Once
7	F	3years	Large	Left *	Thrice (had residual solitary mass}
8	M	3years	Large	Right > Left	Once
9	M	7years	Large	Right	Once
10	F	2years	Large	Left	Once
11	F	4years	Large	Right supra-clavicular*	Once

* Obstructive features with some breathing difficulties

NB: Size classification here, Big = 5cm - 10cm & Large = >10cm

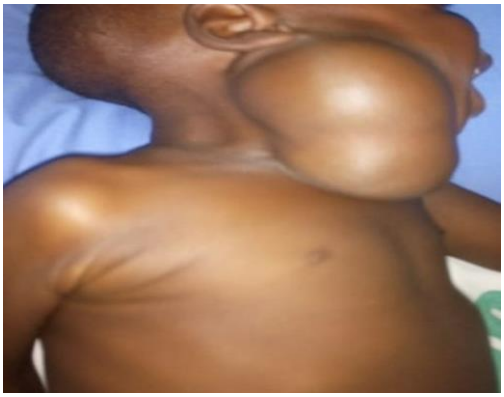

Figure 1A: Photograph of a 4-year-old boy with right Cervicofacial cystic hygroma.
Note the disfiguring effect. About 850mls of lymphatic was drained

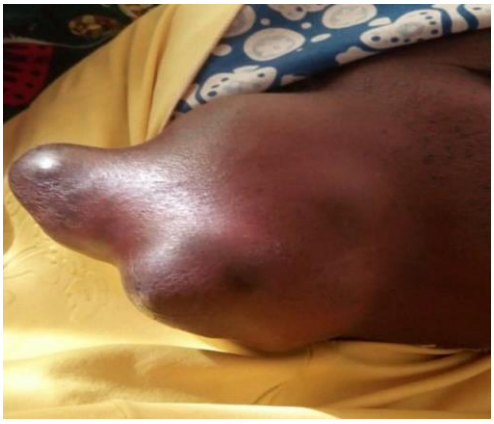

Figure 1B: Photograph of a 14--year-old lady with long standing giant lobulated facial cystic hygroma thought to be parotid gland tumour prior to ultrasonography. About 1800mls of lymphatic fluid was drained from this mass. sclerotherapy. *About 1800mls of lymphatic fluid was drained prior to sclerotherapy*

The sonographic appearance common to all the CCH in this study was a characteristic non-vascular multiloculated cystic mass with septa of variable thickness that contains solid components in some instance (Figure 2A & B). All drainages and sclerotherapy procedures were performed on outpatient basis without any observable complication other than minimal pain. No local or regional anesthesia was used. However, in some anxious children where cooperation was difficult, procedure were done under mild sedation.

The drained volume of fluid from CCH ranged between 60mls – 1,800mls. The average volume of ILTCN injected was 5mls. The volume of cysts was a function of the cyst gross size. The more the volume of fluid contained in the CCH, the more the patient disfigurement.

Eight (8) out of eleven (11) patients (80%) had complete resolution of CCH with a single dose of ILTCN, two patients achieved complete resolution with two courses and only one patient had three courses to achieve complete resolution of the cysts. The only patient who had 3course of ILTCN had a residual small echogenic solid nodule measuring15.9mm by 14.7mm (Figure 2A &B) recommended for excision biopsy. However, because of the direct proximity to the carotids vessels, excision was avoided.

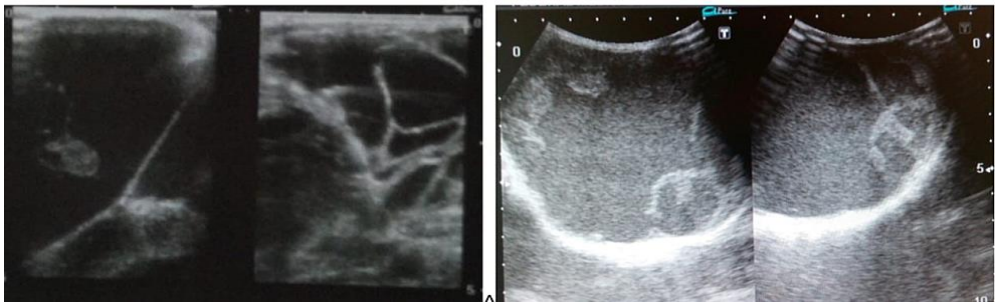

Figure 2A: Sonogram of two different patients showing multiloculated cystic hygromas prior to drainages. *To the left is the sonogram the right infra-auricular cervicofacial cystic hygroma in a 4years old boy. Note some echogenic*

solid components along the septae. To the right is sonogram of a neglected cystic hygroma in a 14-year-old lady thought to be parotid gland tumour prior to ultrasonography.

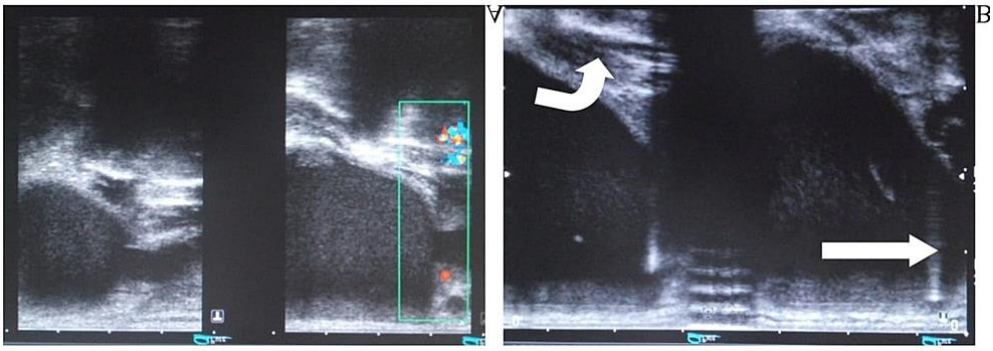

Figure 2B: B-mode and colour Doppler sonograms showing cystic hygroma compressing the carotid vessels. Note the Compressed carotid vessels (curved arrow) and the position of the draining needle (straight arrow).

There was no recorded case of adverse reactions other than pain at the site of injection which rarely persisted beyond 30mins.

We have followed up all patients for a minimum of 3years, and some patient has had a follow up of about 9 years with no observed case of recurrence thus far.

DISCUSSION

Complete surgical excision remains the ideal treatment for CCH in many centres. However, complete surgical excision may be impossible without sacrificing or injuring some important adjoining structures.[6-10] The reported recurrence rates after apparent complete excision and partial excision is about 10-27% and 50-100% of cases respectively.[6-10] Aside issues of recurrence with incomplete excision, morbidity and mortality, surgery may be associated with complications such as wound infection, haemorrhage, hypertrophied scar and lymphatic discharge from the wound.[6-10] In Ameh & Nmadu[10] series involving 41 children surgically managed for CCH, 5 died and 4 had recurrence. Several other studies recorded similar surgical outcome.[6-9]

In resolving the foregoing surgical challenges, there is a gradual conversion towards sclerosant therapy but the ideal sclerosing agent in the pediatric population remains to be discovered. Sclerotherapy with bleomycin and OK-432 have shown good responses. The latter showing more satisfactory response and lesser complications than the former.[11-15] Kuwabara, et al[12] successfully performed an in utero sclerotherapy of a giant cystic hygroma using OK-432 in a fetus at 26 weeks. The risk of systemic toxicity, pulmonary complications, local necrosis or pain has been described with bleomycin.[11-13] Unlike bleomycin and OK-432, not much is documented in the literature on TCN use in the treatment of CCH employed in this study. However, several studies have reported the success with TCN sclerotherapy in testicular hydrocele, fistula, hepatic cyst, renal cysts and thyroid cysts.[16-22] In all such studies, to

the best of our knowledge, no adverse effects related to ILTCN were reported. We therefore assumed TCN may have a good therapeutic safety as intralesional sclerosant in children.

Our experiences spanning about 9 years period have shown TCN to be effective and relatively very safe as intra-lesional sclerosant in the management of CCH. We have not recorded any adverse effect or complications thus far.

When compared to other sclerosants, TCN is not only very cheap but it is also readily available even in the remotest settlement.

Despite the nearly 100% success rate of TCN sclerotherapy for CCH in this study thus far, we are not unmindful of the small population base and teeth discoloration, a known complication of TCN in children. We therefore suggest adequate parental counseling and the need for longer follow up to adequately establish its safety because of the largely children population involved.

So far, none of our patients had recorded any complication beyond transient local pain probably because only one (1) and maximum 3 doses of intracavitory and not systemic TCN administration were used to achieve complete resolution in our study.

The high success rate we recorded in this study may not be unconnected to our techniques of draining as many locules of the multiloculated CCH before infusing ILTCN. Multiloculated CCH with septae of variable thickness and solid components as in (Figure 1-3) may present some sclerotherapy challenges. Therefore, we suggest for effective therapy as many locules as possible may need to be drained and injected since unbroken locules may persist and be mistaken for failed therapy or recurrence. We made this assertion base on our experience in this study where only one child had 3 courses ILTCN injections (the maximum in our study). This is unlike in Hall, et al[14] and Ogita, et al[15] studies where the children respectively received as many as 5 and16 maximum numbers of injections of OK-432. We are not unmindful of homogeneity of black population used in our study. Hence, we were unable to exclude racial factor contributing to the success.

Most sclerosing agents used in the treatment of CCH more often than not require more than two courses.[11-15] We achieved complete resolution with a single injection ILTCN in about 80% (7 out of 11patients) and nearly 100% with maximum 3 injections of TCN. It is probably TCN is more effective than bleomycin and OK 432 as sclerosant in CCH or our techniques of draining as many locules as possible and then inject TCN preparations into the drained locules gave better outcomes. The Sharif et al[12] report of a case of complete resolution with single session of bleomycin sclerotherapy as against multiple sessions reported by several authors may lay credence to the later.

In Thomas, et al[18] studies with doxycycline as sclerosant, 87% of patients (28 of 32) had excellent or moderate response with an average of 2.8 treatments (range, 1-7 treatments). This success rate is much lower than an average of a single treatments course with TCN in our study (80% complete resolution with a single course).

The cost of 1-3 courses of TCN sclerotherapy is more than 40 times cheaper than the costs of surgery in our centre. Therefore, we opine that since drainage and sclerotherapy is several time cheaper than surgery and it's relatively free of morbidity and mortality, it should be consider as first line in the management of all children with CCH while surgery should be reserved for cases recalcitrant to sclerotherapy. However, more studies employing different races and longer follow up will be required to validate overall efficacy and safety of TCN sclerotherapy in CCH.

CONCLUSION

Sclerotherapy with IL-TCN is simple, effective, readily available, and safe treatment option for CCH that is more than 40 times cheaper than surgery. Therefore, it can be considered as a first line treatment of choice in CCH while surgery should be restricted to only cases where incomplete resolution occurred with sclerotherapy. We suggest for effective therapy, as many locules as possible of a multiloculated hygromas may need to be drained and injected with sclerosant since unbroken locules may persist and be mistaken for failed therapy or recurrence.

DISCLOSURE

This work receives no financial support or funding of any kind either private or public source.
This article was previously presented as a meeting abstract at the 2019 ARIN Annual Scientific Meeting on August 1, 2019. It is however not under consideration for publication.

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