CASE REPORT

Embryological Basis of Cystic Hygroma: A Case Report

Shefali Yadav[1], Nikita Gulati[2], Devi Charan Shetty[3], Saurabh Juneja[4]

Abstract

Aim: We intend to present a cystic hygroma (CH) case in a 2-year-old baby in the anterior cervical triangle, which is a rare site, as the most common site for the occurrence of CH is the supraclavicular fossa of the posterior cervical triangle.

Background: Among developmental abnormalities in the lymphoid system, CH are usually seen in the posterior neck. Lymphatic malformations are generally exhibited either at birth or before the age of 2 years. Lymphatic channels are attenuated endothelium-lined spaces devoid of any cells and smooth muscle layer. Also, morphologically distinguishing normal lymphatic channels from venules or capillaries is a challenge.

Case description: A 2-year-old female patient reported having a chief complaint of swelling in the left submandibular region for 4 days. The patient underwent surgery for CH 18 days after birth. Swelling was rubbery in texture and firm in consistency.

Conclusion: A D2-40 immunoexpression was an identifying clue for normal lymphatics in comparison to morphology. Henceforth, this can be concluded that such tumors depict at least partial differentiation of endothelial cells lining lymphatic spaces.

Clinical significance: The present article helps in illuminating the role of D2-40 in the diagnosis of lymphatic malformations, such as CH, and also highlights the embryological basis of the pathogenetic mechanism of this rare disease, which potentiates the role of various treatment modalities in pediatric cases for management considerations.

Keywords: Amorphous, Cystic hygroma, Lymphoid aggregates, Malformation.

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Background

Among developmental abnormalities of the lymphatics, CH appear in areas of lymphovenous junctions, mainly in the posterior neck region. Such lymphatic malformations are generally exhibited either at birth or before the age of 2 years, with 40–50% involvement of the dorsum of the tongue.[1,2] Mostly exemplified by single or multiple fluid-filled cystic spaces. CH arising during adult life are superficial cutaneous malformations (lymphangioma circumscriptum).[3] Approximately 50% of lymphatic malformations are seen in the vicinity of components of the lymphatic system present in the head and neck region. Worth mentioning are the lymphatic malformations of the orbit due to the endangered vision as well as the so-called "giant" lymphatic malformations.[4] Lymphatic malformations are classified as—(1) macrocystic, when they are within the level of mylohyoid muscle situated in the anterior and posterior cervical triangle; (2) microcystic, when situated above mylohyoid muscle seen in regions of the oral cavity, such as tongue, submandibular, or parotid region; and (3) mixed type.[5] Development of the lymphatic system takes place at the end of the 5th week of intrauterine life (IUL) as endothelial protuberance from the venous apparatus. The right and left thoracic ducts of lymphatic vessels connect with the venous system at the junction of the internal jugular with subclavian veins at the end of the 6th week of IUL, leading to the complete formation of lymphatics. The jugular lymphatic impediment arises as a result of failure in joining jugular sacs to join with and drain its content into jugular veins leading to lymphatic fluid accumulation. Lymphedema of the periphery, such as subcutaneous tissues, accompanies the relative overgrowth of the overlying skin along with elevation of the pads of the fingers.[6.] Association of CH cases have also been visualized among the group of genetic disorders and syndromes, such as Noonan, Roberts's, and multiple pterygium syndromes. Although CH regresses during pregnancy, still, serial ultrasounds are prerequisites for evaluation of the case and henceforth, favor individualized management options.[7] Continuous lymphedema progresses to fluid accumulation in surrounding connective tissue stroma.[8] In this case report, we hereby present a CH case in a baby of 2 years of age at the anterior cervical triangle, which is a rare site, as the most common site for the occurrence of CH is the supraclavicular fossa of the posterior cervical triangle.

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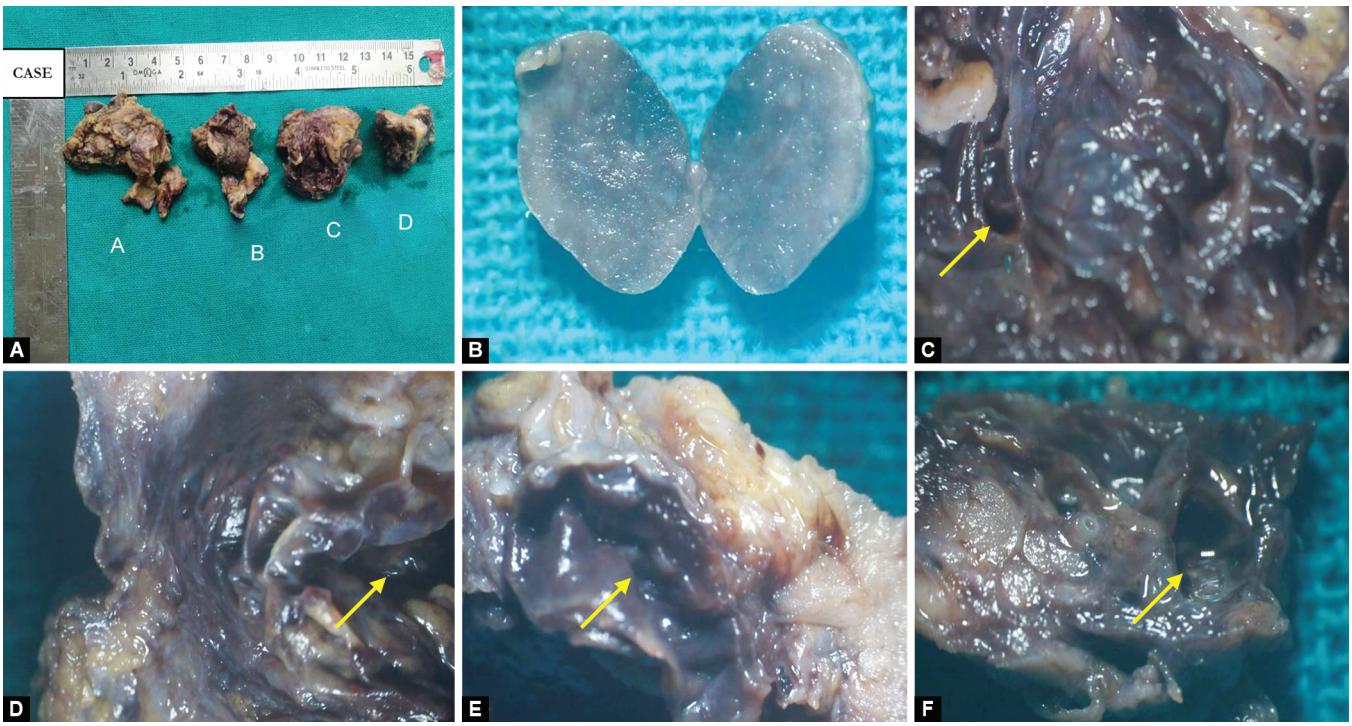
Patient consent statement: The author(s) have obtained written informed consent from the patient's parents/legal guardians for publication of the case report details and related images.

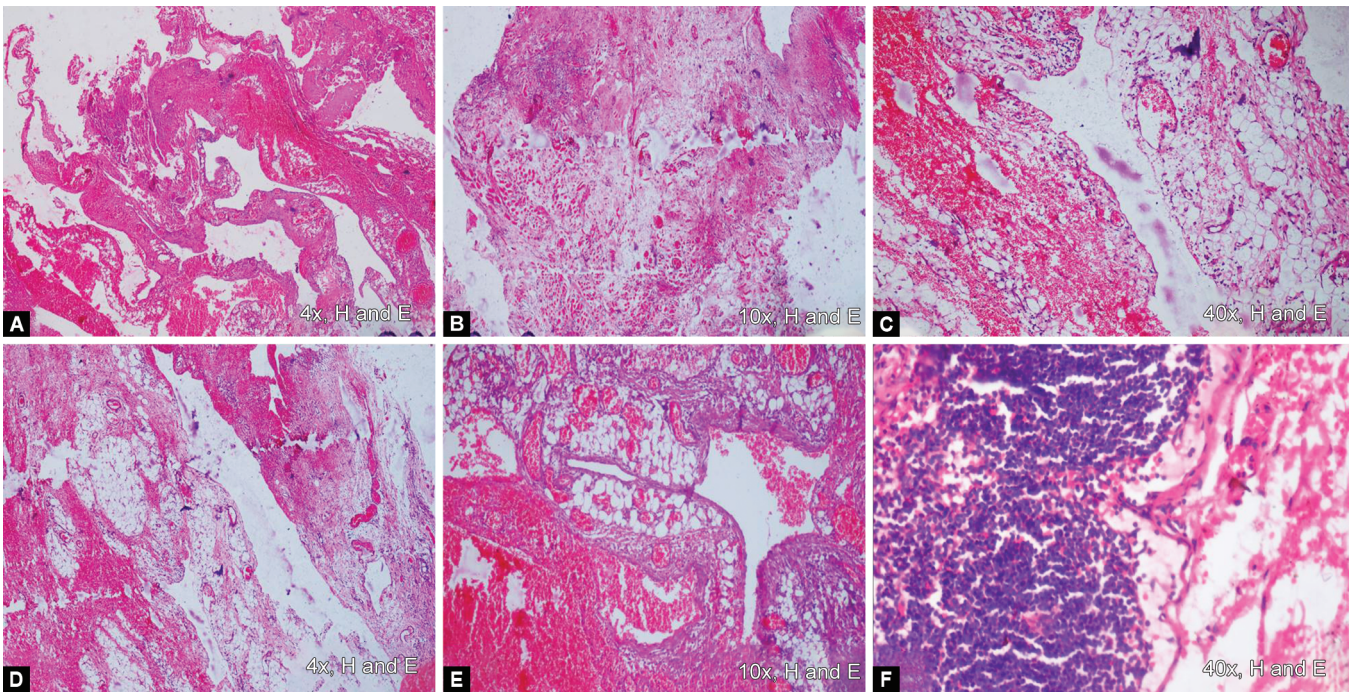
Case Description

A 2-year-old female patient reported a chief complaint of swelling in the left submandibular region since 4 days. The patient underwent surgery for CH 18 days after birth. Extraoral examination revealed swelling in the left submandibular region extending from the midline to the angle of the mandible. Swelling was rubbery in texture and firm in consistency. Left side submandibular and sublingual lymph nodes were palpable. Based on previous history and clinical details, CH was given as a provisional diagnosis.

Excisional biopsy was done, and the gross specimen, along with stereomicroscopic examination (Fig. 1) revealed multiple cystic spaces of varying shapes and sizes filled with brownish material. Histopathological examination revealed fibrocellular connective tissue stroma consisting of multiple dilated, thin-walled sinus-like spaces filled with eosinophilic acellular material (Figs 2A and B). Sinuses were surrounded with flat endothelial cell layers (Fig. 2C). Multiple small to large, intertwining cavernous spaces resembling



Figs 1A to F: (A) Gross examination revealed four soft tissue specimens measuring 4.8 × 4.5 × 3 cm in their greatest dimension, brownish yellow in color, with focal cystic, and hemorrhagic areas; (B) Stereomicroscopic examination showed multiple small cystic spaces filled with secretory material; (C, D, E, F) (C to F) Stereomicroscopic examination showing well-circumscribed lesion consisting of multiple interconnecting cystic spaces along with hemorrhagic areas



Figs 2A to F: (A) Fibrocellular stroma containing multiple sinusoidal spaces along with hemorrhagic areas (H and E, 4×); (B) Cystic wall containing fibrous tissue (H and E, 10×); (C) Fibrous stroma showing large sinusoidal space filled with amorphous eosinophilic material along with areas of hemorrhage and adipose tissue (H and E, 40×); (D) Fibrocellular stroma showing multiple sinusoidal interconnecting spaces along with hemorrhagic areas (H and E, 4×); (E) Fibrous and adipose tissue in the cyst wall (H and E, 10×); (F) Fibrous tissue consisting of aggregates of lymphoid cells (H and E, 40×)

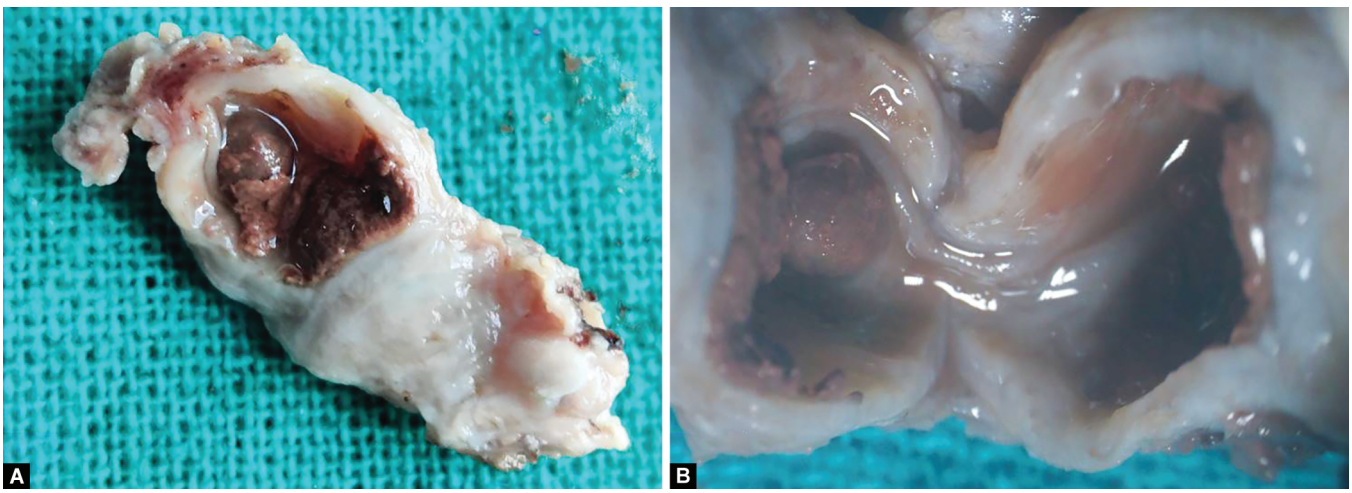
lymphatic channels in loose fibrocellular connective tissue stroma were appreciable (Figs 2D and E). The connective tissue stroma is composed of thin bundles of collagen fiber bundles associated with fibroblasts having spindle to oval nuclei along with lymphatic spaces lined by thin, attenuated endothelium having flat nuclei. The lymphatic spaces are filled with eosinophilic amorphous material containing lymphocytes, red blood cells (RBCs), and a few eosinophils. Scattered lymphoid aggregates found in the form of germinal follicles were also evident (Fig. 2F). Deeper connective tissue stroma shows adipocytes and muscle bundles having normal architecture surrounding the sinusoidal spaces (Fig. 2E). Masson's trichrome staining (Figs 3 to 6) confirmed the presence of smooth muscles in the fibrous lymphatic walls, which is a characteristic feature of CH. D2-40 immunohistochemistry was done to confirm the presence of lymphatic channels, and continuous linear expression was observed, confirming the presence of lymphatics. Hence, the final diagnosis of CH was given. Recurrence of a similar swelling was again reported on the right region of the neck. Gross (Fig. 3), as well as histopathological examination (Fig. 4), again revealed similar macroscopic and microscopic details as that of the previous biopsy.

Discussion

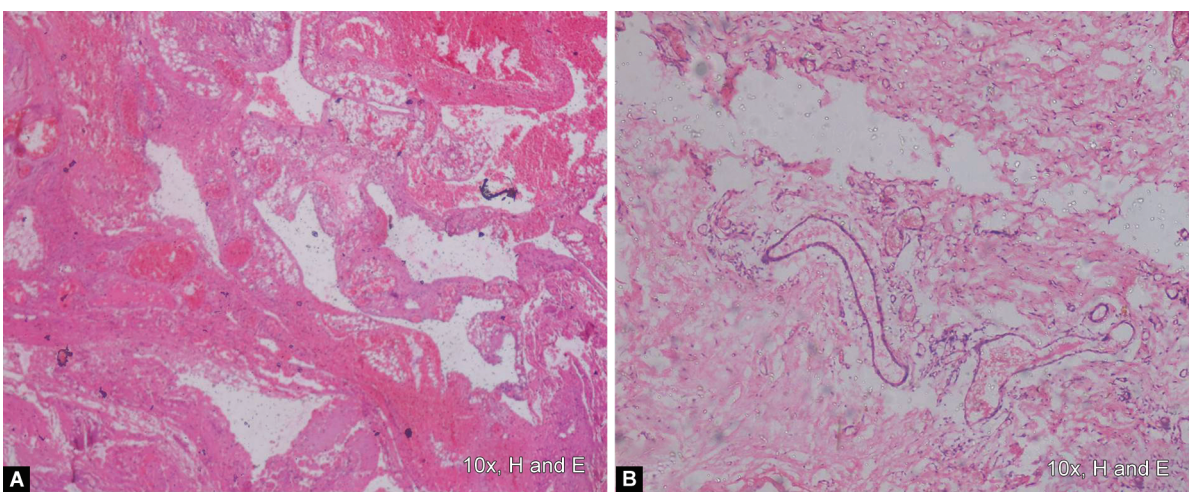
Lymphatic vessels are attenuated endothelium-lined channels lacking RBCs and smooth muscle layer. Morphologically distinguishing normal lymphatic spaces from venules or capillaries is a challenge. D2-40 immunopositivity assists in delineating flattened channels or endothelial lined spaces containing lymphocytes. Discerning microvessels is illustrated with the assistance of biomarkers, such as CD105, CD31, and CD34; however, none of them are peculiar for lymphatics. Lately, innumerable specific antibodies for illustration of lymphatics have been recognized, such as podoplanin, vascular endothelial growth factor receptor-3, D2-40, Prox1, etc.[9] D2-40 proves to be a highly sensitive as well as specific biomarker of lymphatic in normal tissues. Henceforth, it could be culminated that such tumors depict at least partial differentiation of endothelial cells lining lymphatic spaces.[10]

Conclusion

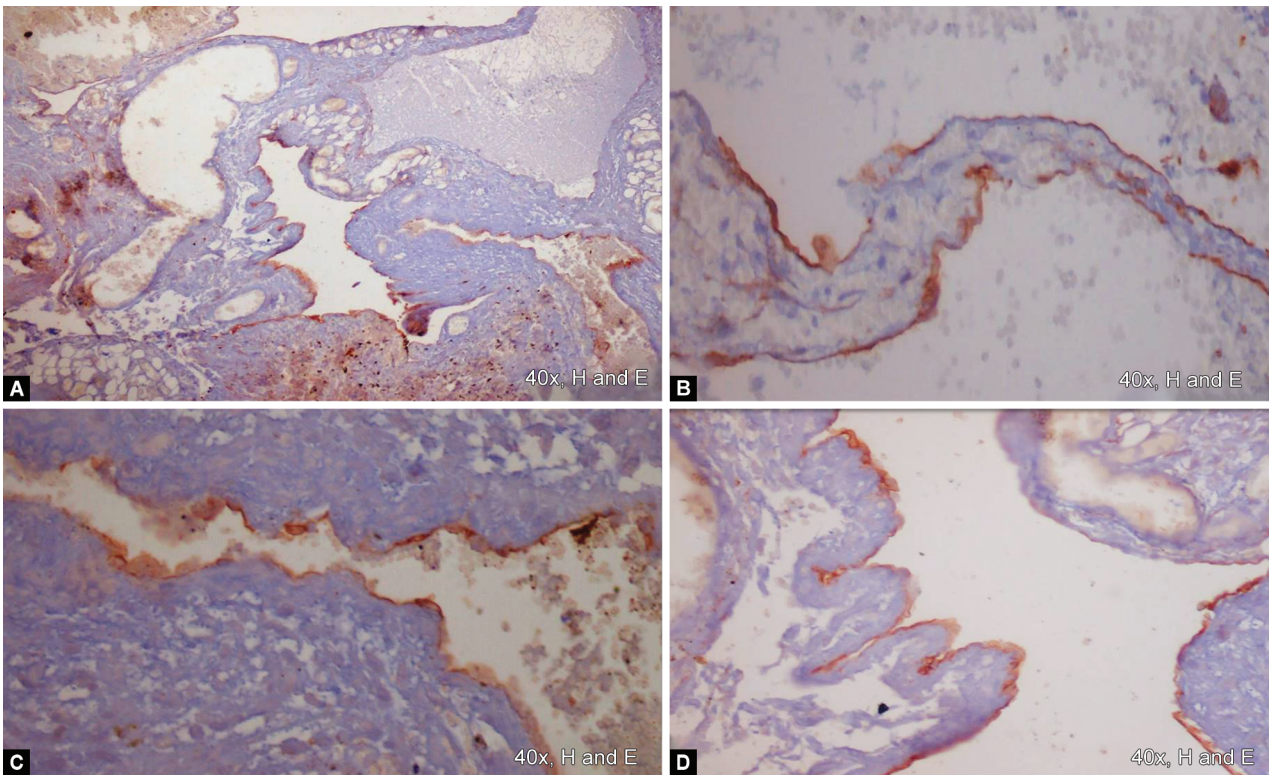
The immunohistochemical assessment indicates a probable role of smooth muscle and thereby is suggestive of the fact that the lymphatic malformation vasculature is either prematurely advanced



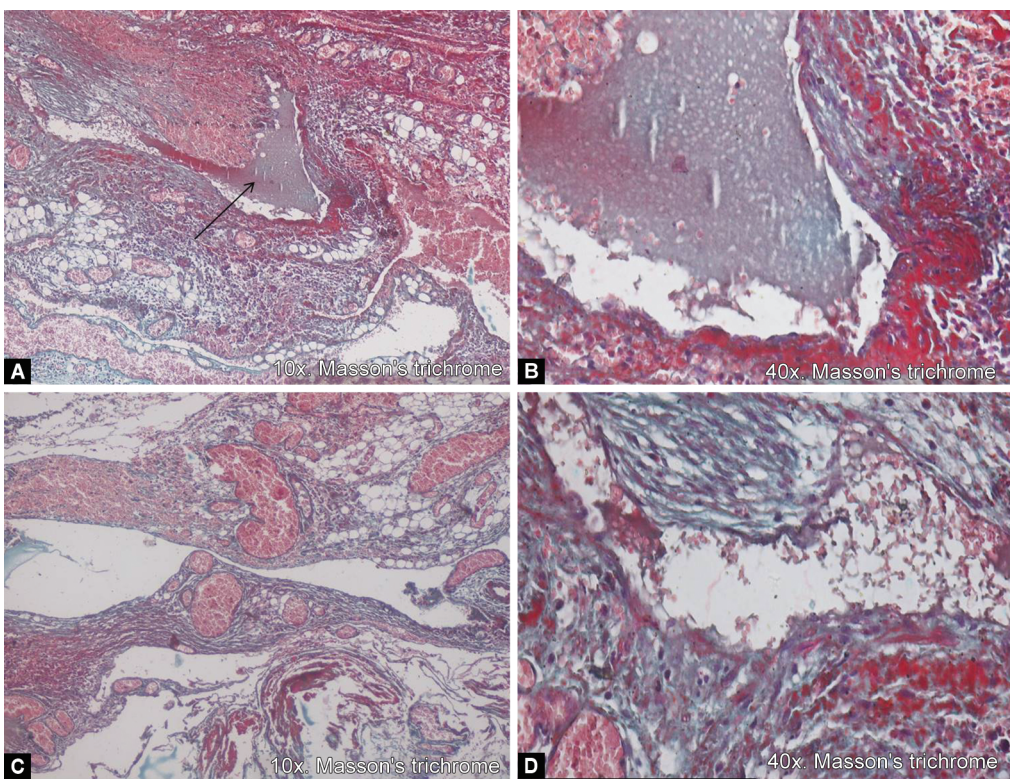
Figs 3A and B: Stereomicroscopic examination of the excisional specimen shows well-defined large cystic space filled with clear fluid-like material suggestive of secretory material



Figs 4A and B: (A) Fibrocellular stroma showing multiple large sinusoidal spaces admixed with areas of hemorrhage and adipose tissue (H and E, 10×); (B) Loose fibrillar stroma showing large cystic space along with vascular space engorged with RBCs (H and E, 10×)



Figs 5A to D: (A and C) Immunohistochemistry using antibody for Podoplanin (D2-40) displays positivity throughout the sinusoidal spaces suggestive of lymphatic channels (IHC, 10x) (B and D) Large lymphatic channels lined by flat cells showing strong immunoreaction with antibody Podoplanin identifying them as lymphatic endothelium (IHC, 40x)



Figs 6A to D: Masson's trichrome staining reveals greenish amorphous material in the large cystic material suggestive of lymph and the presence of smooth muscle lymphatic vessel wall

in collecting vessel phenotype or arrests in its remodeling phase. Surgical Intervention includes the entire excision of the tumor, being the ultimate treatment choice for CH. Among superficial lesions, excisional modality can be accomplished with minor difficulty.

Clinical Significance

Complex CHs might necessitate the role of multiple operative strategies and are not achievable without impairing adjacent vital structures. Among all nonsurgical modalities, few of them can be used, such as serial aspiration, incision as well as drainage, radiotherapy along with the injection of numerous sclerosing agents. The present article highlights the significance of the pathogenetic mechanism in the appropriate treatment planning of pediatric cases in routine practice.

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