Case Report

Langerhans Cell Histiocytosis Presenting With Cardiac Tamponade: A Case Report

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ABSTRACT

Background: Langerhans cell histiocytosis (LCH) is a rare disorder of the reticuloendothelial system with an unknown etiology. We herein present an LCH case with cardiac tamponade and the oral cavity involvement to raise awareness of the distinguishing features of this diagnostically challenging entity.

Case Report: This study describes a 52-year-old man who presented with dyspnea (NYHA functional class II) and bilateral pedal edema of 4 days' duration. A clinical examination revealed a large pericardial effusion with cardiac tamponade. A positron emission tomography-computed tomography scan showed a heterogeneously enhancing soft tissue lesion, 2.6×1.7×1.6 cm in size, in the right mid-submandibular region. An intraoral examination confirmed the right submandibular mass. The biopsy of the submandibular gland mass confirmed the diagnosis of LCH.

Conclusions: LCH is often diagnosed in childhood but may manifest in any age group, from infancy to adulthood. Pericardial effusion is a rare finding in this case of LCH. The rarity and the variable system involvement of LCH necessitate a multidisciplinary approach for accurate diagnosis and effective treatment. ***(Iranian Heart Journal 2022; 23(2): 142-149)***

KEYWORDS: Langerhans cell histiocytosis, Pericardial effusion, Cardiac tamponade

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Langerhans cell histiocytosis (LCH) is part of a group of histiocytic neoplasms along with Erdheim–Chester disease, Rosai–Dorfman disease, and several other disorders.[1] It arises from immature myeloid dendritic cells in the bone marrow[2] and has a variety of presentations. LCH most commonly affects children, in whom the following are most common[3]: bone lesions (68%), multiple bone lesions (19%), isolated skin disease (11%), and isolated lymph node involvement. The oral manifestations of LCH are most commonly found in the soft palate and the gingiva.[4] Cardiac involvement is relatively rare in LCH,[5] and only a few cases have been reported previously. In 1981, Pickens et al[6] described a 60-year-old woman who had pericardial effusion with histiocytosis X. In 2016, Gholami[7] described a 7-month-old girl

diagnosed with LCH and pericardial effusion. LCH is diagnosed when a biopsy sample has a positive immunohistochemistry test for S100, CD1a, and langerin. BRAFV600E mutation may also be demonstrated by immunohistochemistry.[5]
We herein describe a 52-year-old man with LCH who presented initially with pericardial tamponade, which is a rare presentation.

Case Presentation

A 52-year male diabetic patient presented with complaints of bilateral pedal edema and dyspnea on exertion (New York Heart Association [NYHA] functional class II) of 4 days' duration. His blood pressure was 80/64 mm Hg, his heart rate was 110 beats per minute and his axillary temperature was 37.4 °C. A clinical examination revealed bilateral pitting pedal edema and mild pallor. There was no cyanosis, clubbing, or lymphadenopathy. On auscultation, muffled heart sounds were heard. Electrocardiography showed low-voltage complexes (Fig. 1A). Echocardiography showed a massive pericardial effusion with early right atrial/right ventricular diastolic collapse with normal left ventricular systolic function, suggesting pericardial tamponade (Fig. 1B). Pericardiocentesis was done, and a hemorrhagic fluid was aspirated. The cytology and biochemistry of the fluid were negative for tuberculosis or any malignancy. Tumor markers such as CEA and C19-9 were negative. A computed tomography (CT) scan of the chest was done, and it showed a moderate-to-large pericardial effusion, along with a bilateral minimal pleural effusion (left>right) with the sub-segmental collapse of the underlying lung. A few atelectatic bands were found in the bilateral lower lobes, the lingular segments, and the anterior segment of the left upper lobe. An abdomen CT scan revealed an ill-defined hypodense enhancing lesion in the medial limb and the body of the left adrenal gland; in addition, adrenal metastasis or adrenal adenoma was suspected initially. Hence, a positron emission tomography-computed tomography (PET-CT) scan was done, and it showed an FDG-avid heterogeneously enhancing soft tissue lesion, 2.6×1.7×1.6 cm in size, in the right mid-submandibular region (Fig. 2A & 2B). An intraoral examination also revealed a right submandibular gland mass. A Tru-Cut biopsy of the right submandibular mass showed a diffuse proliferation of neoplastic histiocytes with eosinophils (Fig. 3A & 3B), which were p63-negative and S-100–positive (Fig. 3C & 3D), confirming the diagnosis of LCH. He was started on a steroid (prednisolone) and chemotherapy with vinblastine. His condition improved, and he was discharged from the hospital after 5 days. Echocardiography at 1-month follow-up showed the complete resolution of the pericardial effusion and improvement in the overall general condition of the patient.

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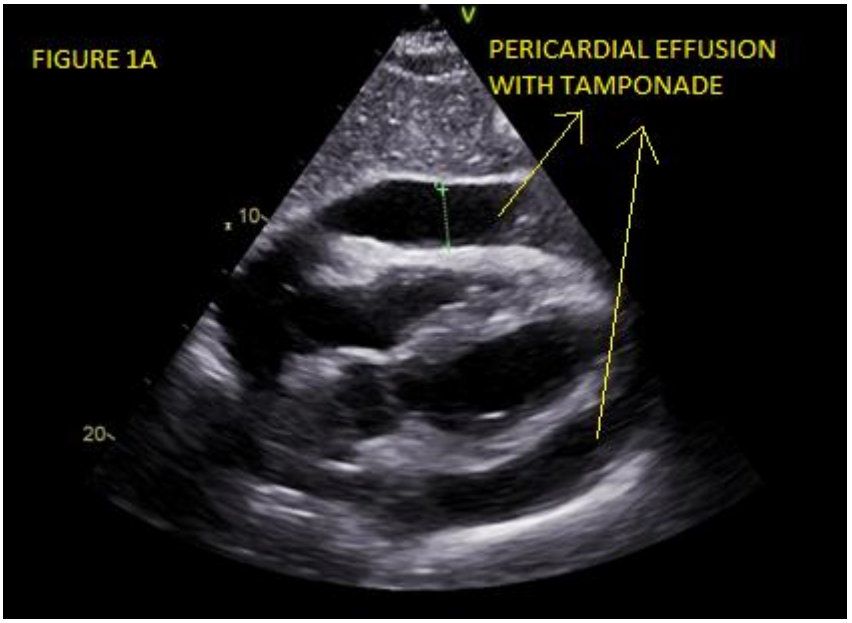

Figure 1A: The 2D echocardiographic image shows a massive pericardial effusion.

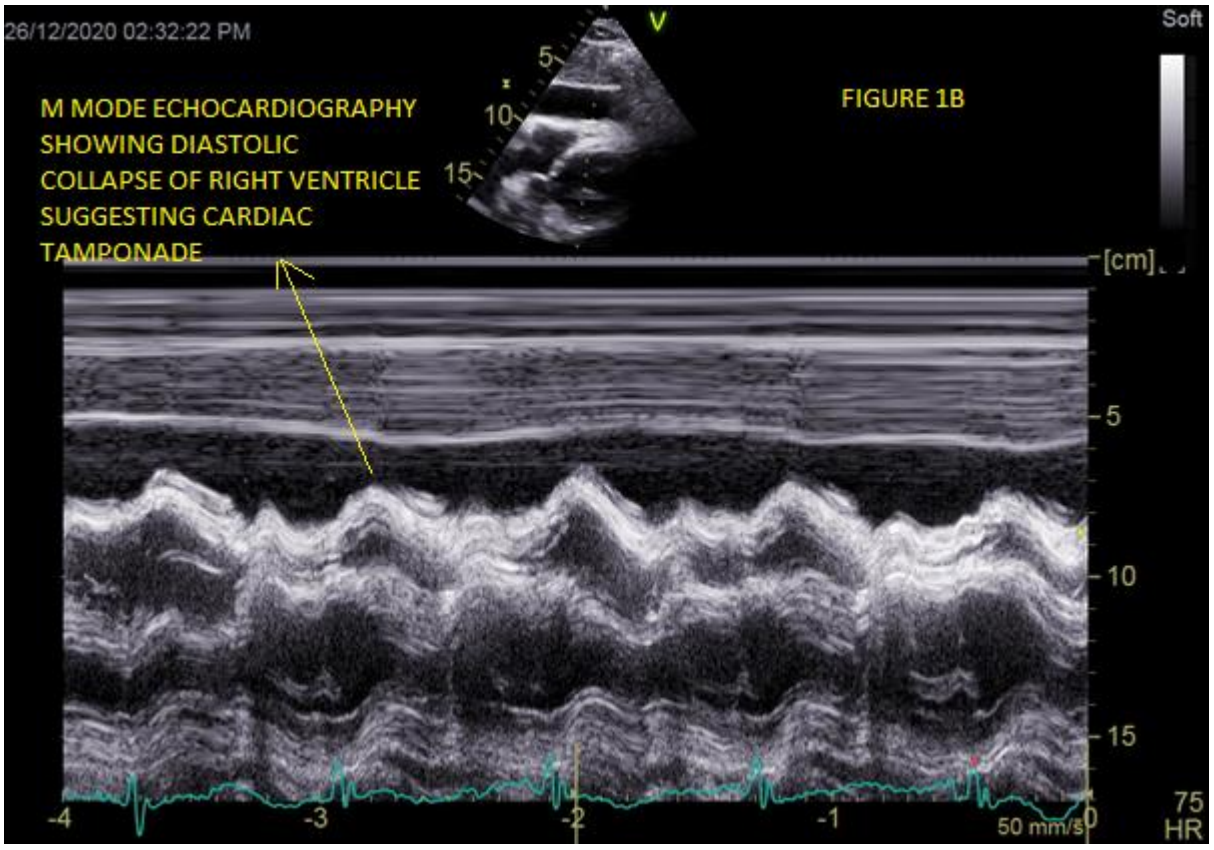

Figure 1B: The 2D echocardiographic image shows the diastolic collapse of the right ventricle, suggesting cardiac tamponade.

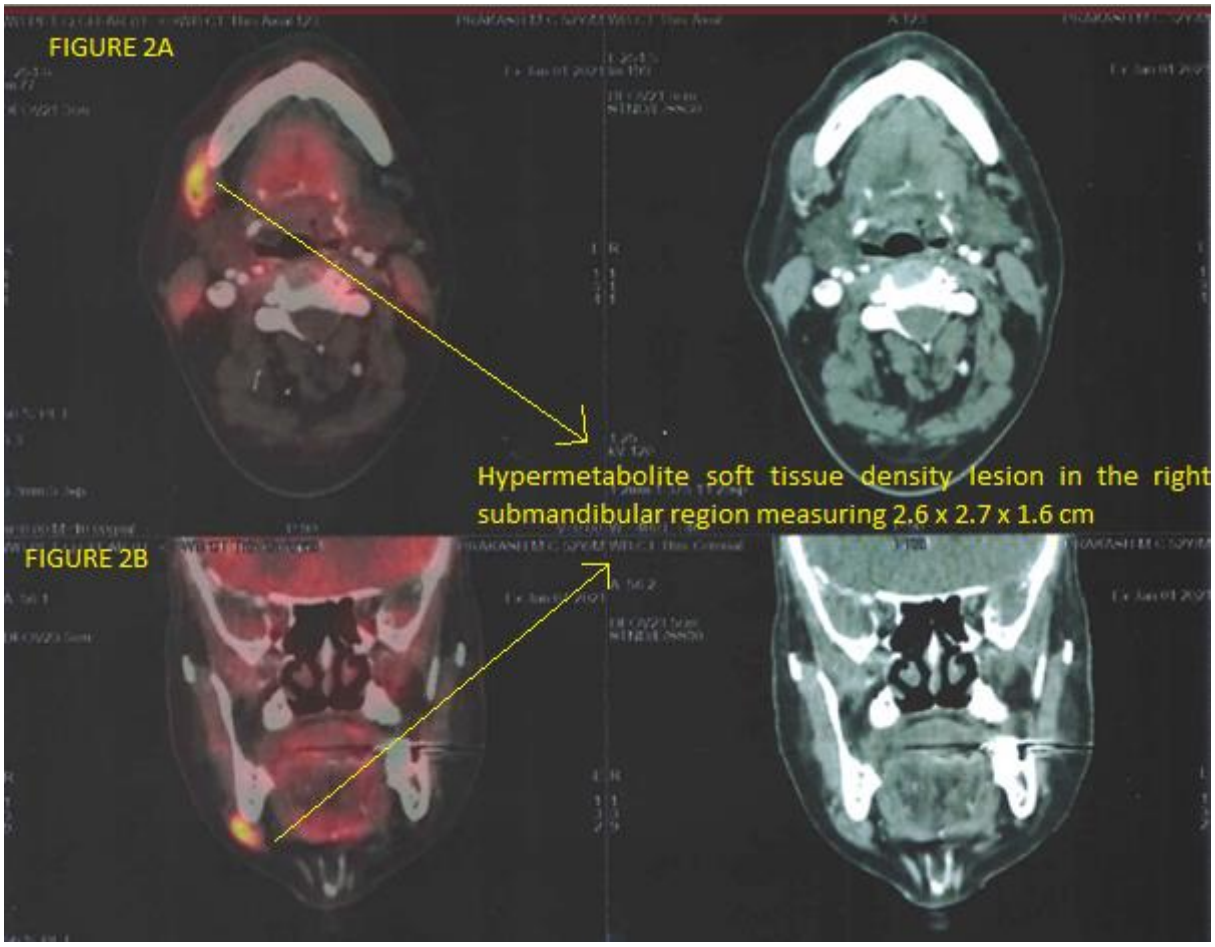

Figure 2: The FDG positron emission tomography image shows a hypermetabolic soft tissue density lesion in the right submandibular region, 2.6x2.7x1.6 cm in size,

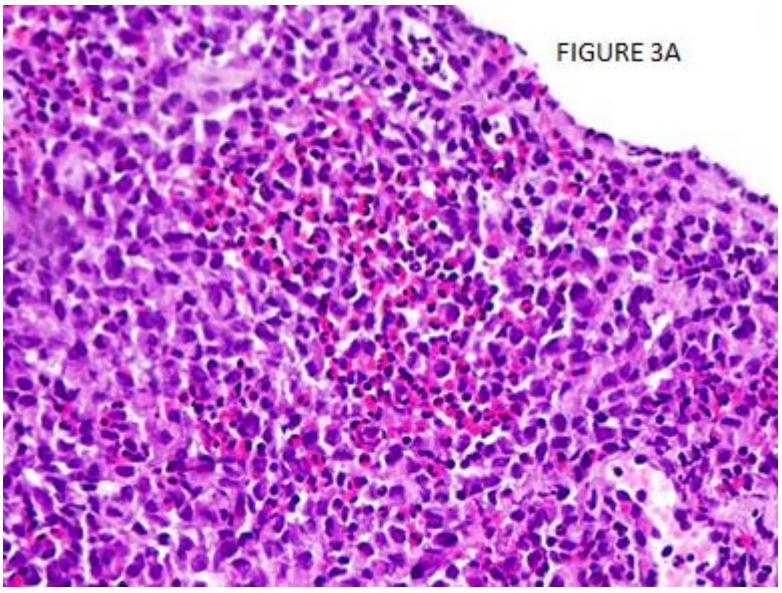

Figure 3A: The Tru-Cut biopsy of the lesion shows the diffuse proliferation of neoplastic histiocytes with eosinophils (H&E=x200).

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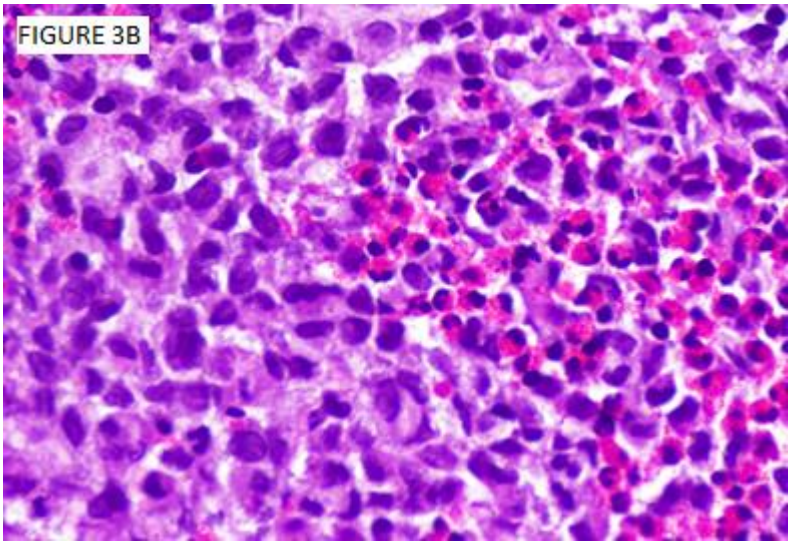

Figure 3B: The image shows sheets of histiocytes, a few with intranuclear grooves and interspersed eosinophils (H&E=x400).

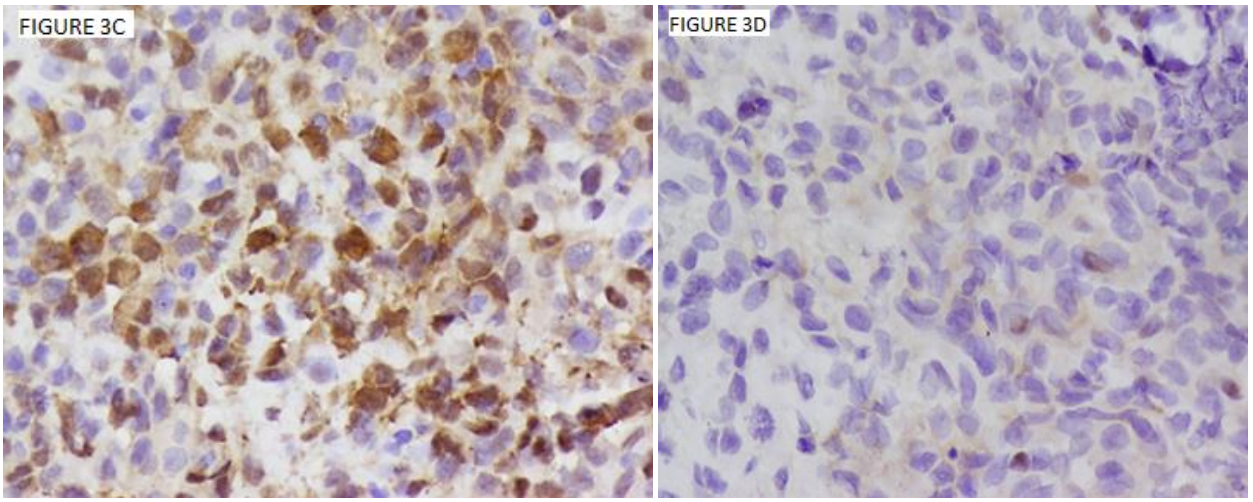

Figure 3C & 3D. The images show the immunohistochemistry profile of the tumor cells: S-100–positive (3D) and p63-negative (3D) (monoclonal Ab=x400).

DISCUSSION

LCH is a rare disorder of the reticuloendothelial system with an unknown etiology.[2] It was earlier thought to be derived from epidermal Langerhans cells but is now known to be a clonal disease of myeloid dendritic cells. LCH can affect individuals of any age, but it inflicts mainly children aged between 1 and 4 years.[8] The diagnosis of LCH is established by evaluating clinical and radiographic findings and confirmed by histopathological and immunohistochemical studies.[5] Histologically, the nuclei of LCH cells are irregular with prominent folds and grooves; additionally, there are fine chromatin and indistinct nucleoli. On electron microscopy, cytoplasmic structures known as “Birbeck granules” are visualized. The characteristic immunophenotype of LCH includes the expression of CD1a, the S100 protein, and langerin in Langerhans cells.[5] The clinical manifestations are varied, with bone involvement being the most common (80%),

followed by skin and nervous, pulmonary, hematopoietic, and hepatobiliary systems.[9]

Pericardial effusion is an abnormal accumulation of fluid in the pericardial cavity. Pericardial effusion is an important finding because it can cause high pressure, which adversely affects cardiac function, a condition termed "cardiac tamponade". Symptoms in the patient are dependent on the amount of the fluid.[10] Pericardial effusion is a rare manifestation of LCH, and we wish to discuss this rare entity with the help of this case.

The causes of pericardial effusion are varied and include viral, bacterial, fungal, and protozoal infections, as well as autoimmune disorders, neoplastic diseases, metabolic causes, and drug-induced etiologies.[11] Mild pericardial effusions are generally asymptomatic. Moderate-to-severe pericardial effusion symptoms include dyspnea, tachypnea, coughs, low-grade fevers, and increased heart rates. The prognosis of pericardial effusion depends on the underlying cause. It is particularly poor in cases of effusion due to neoplastic infiltration but much better in cases of viral/idiopathic effusion. For the patient presented here, we performed a complete blood count, a chest X-ray, and electrocardiographic and echocardiographic studies, which helped confirm the diagnosis of pericardial effusion and rule out more common causes. Pericardiocentesis was also done, and hemorrhagic fluid was aspirated. The cytology and biochemistry of the fluid were negative for tuberculosis or any malignancy. Tumor markers such as CEA and C19-9 were also negative. A chest CT scan revealed a moderate-to-large pericardial effusion, along with a bilateral minimal pleural effusion (left>right) with the sub-segmental collapse of the underlying lung. An abdomen CT scan illustrated a hypodense enhancing lesion in the left adrenal gland. Adrenal adenoma or metastasis was suspected; hence, a full-body PET-CT scan was obtained. We found a soft tissue lesion in the right mid-submandibular region, 2.6×1.7×1.6 cm in size (Fig. 2A & 2B). An intraoral examination also revealed a right submandibular gland mass. A Tru-Cut biopsy of the right submandibular mass showed the diffuse proliferation of neoplastic histiocytes with eosinophils (Fig. 3A and 3B), which were p63–negative and S-100–positive (Fig. 3C & 3D), confirming the diagnosis of LCH. The patient was started on a steroid (prednisolone) and chemotherapy with vinblastine. His condition improved, and he was discharged from the hospital after 5 days. Echocardiography at 1-month follow-up showed the complete resolution of the pericardial effusion and improvement in the overall general condition of the patient.

The existing literature presents only a few previous cases of LCH with pericardial effusion, with only one of those cases involving a submandibular mass. In 1981, Pickens and Rosenshein[6] described a 60-year-old woman diagnosed with LCH and pericardial effusion. She had non-pruritic maculopapular rashes on her body and submandibular masses for several months. A skin biopsy specimen confirmed LCH. In addition, Pickens and Rosenshein detected a large pericardial effusion in their patient. Gholami[7] described a 7-month-old girl with skin rashes, lymphadenopathy, bone lesions, and pericardial effusion.

The case described here presented an interesting scenario. The patient was an adult, and LCH is very rare in adults. Furthermore, he presented with pericardial effusion. In this case, pericardiocentesis was performed to reduce the respiratory symptoms, but later on, steroids reduced the pericardial fluid and resolved his symptoms after the diagnosis of LCH was confirmed. If respiratory distress is observed in patients with LCH, the physician should consider

pericardial effusion, and a chest X-ray and an echocardiographic examination should be performed. Patients with LCH should have long-term follow-up care to detect late complications from the disease or the treatment.

CONCLUSIONS

The rarity and variable system involvement of LCH necessitate a multidisciplinary approach for an accurate diagnosis, an effective treatment, and an uneventful follow-up. Pericardial effusion in LCH, which is an unusual presentation, should be considered when the patient experiences respiratory distress. Awareness of the oral manifestations of LCH with pericardial effusion may aid clinicians greatly in reducing morbidity and mortality associated with this debilitating condition.

Learning Objective

LCH is classified as inflammatory myeloid neoplasia of an unknown origin. LCH is a multisystem disease. Cardiac tamponade is not commonly reported in the literature. We herein presented a rare case of symptomatic pericardial disease as the first clinical presentation of LCH at a usual age. Among the extraskeletal manifestations of LCH, cardiovascular involvement is often asymptomatic and, thus, under-diagnosed. Nonetheless, it is linked to poor prognosis. This is why a cardiologist should always look for cardiovascular involvement when a new case of LCH is diagnosed. Accordingly, knowledge regarding LCH is essential to allow for prompt diagnosis and management.

Conflict of Interest

The authors report no financial relationships or conflicts of interest regarding the content herein. The paper is not under consideration elsewhere. None of the contents of this paper has been previously published. All the authors have read and approved the manuscript. There is no association with any industry. No honoraria, grants, or other forms of payment were given to anyone to produce the manuscript. Each author listed on the manuscript has seen and approved the submission of this version of the manuscript and takes full responsibility for the manuscript. The authors will also transfer the rights of the article to the journal upon publication.

Decelerations

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Ethical Approval

Institutional ethics committee clearance was taken for the study.

Informed Consent

Written informed consent was taken for the procedures involved and for the publication of anonymized data.

Consent for Publication

Consent was obtained from the patient for the publication of anonymized data.

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