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Nodular histiocytic hyperplasia: A rare incidental finding that can be potentially misdiagnosed as malignancy

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Abstract
Introduction: Nodular histiocytic hyperplasia is a rare benign condition that occur most commonly in body cavities such pleura, peritoneum, pericardium and in hernial sacs. Morphologically, it comprises nodular florid proliferation of histiocytes which can mimic malignant neoplasms such as metastatic carcinoma and mesothelioma. Therefore, it is essential to recognize this entity to prevent a potential diagnostic pitfall.
Aim: To familiarize pathologists with a rare entity to prevent a potential diagnostic pitfall.
Material and Methods: A case of inguinal hernia sac with incidental nodular histiocytic hyperplasia was studied for detailed histopathological examination and expression of immunohistochemical markers.
Results: Running a wide panel of immunohistochemical stains revealed that the proliferative cells are positive for the histiocytic markers CD68 and CD163 but negative for epithelial and mesothelial markers.
Conclusion: Nodular histiocytic hyperplasia is a benign condition characterized by proliferation of histiocytes that were believed previously to be of mesothelial origin. It is essential to recognize this entity as it can be potentially misdiagnosed as a malignant neoplasm.

Keywords: Nodular histolytic hyperplasia, hernial sac, CD68, CD163

Introduction
Nodular histiocytic hyperplasia is a benign condition characterized by proliferation of histiocytes. It was first described by Rosai and Dehner in 1975 [1]. They reported 13 cases of hernial sacs with florid proliferation of cells that were believed to be of mesothelial origin. Later on, this condition has been reported to occur in other sites such as peritoneum, pleura, pericardium, lung parenchyma and urinary bladder [2, 3]. It is hypothesized that the condition occurs as a reactive process as a result of irritation by trauma, tumor or inflammation [4]. In 1998, Ordonez *et al*. described four cases originating in pleura, hernial sac and urinary bladder with similar proliferation of cells that were reactive with the histiocytic marker CD68 [2]. Therefore, the term nodular histiocytic hyperplasia rather than nodular mesothelial hyperplasia was proposed. The florid proliferation of histiocytes can be deceiving and mimicking malignancy. We are presenting this case to familiarize pathologists with this rare entity to prevent a potential diagnostic pitfall.

Case presentation
A 39 year old male patient presented with intermittent lower abdominal pain for one year duration. Physical examination revealed right inguinal swelling. The patient diagnosed to have indirect inguinal hernia for which open mesh repair was performed. Histopathologic examination of the hernia sac revealed multiple fragments of fibroadipose tissue lined by mesothelial cells. Some fragments show proliferation of cells arranged in diffuse sheets and nodules (Fig 1A). The cells have abundant pale cytoplasm and oval shaped nuclei, with occasional cells having nuclear grooves while others show lobulated appearance of the nuclei (Fig 1B, 1C). No nuclear atypia, necrosis or atypical mitotic figures are identified.

By Immune peroxidase stains, the proliferative cells are strongly diffusely positive with the histiocytic markers CD68 and CD163 (Fig 2A, 2B) but negative with epithelial markers (Cytokeratin AE1/AE3 and EMA), mesothelial markers (Calretinin and WT1), Langerhans cell markers (CD1a and S100), myeloid marker (Myeloperoxidase) and dendritic cell markers (CD21 and CD23). The proliferative index (Ki-67) is very low. Based on the morphological and immune histochemical findings, the diagnosis of nodular histiocytic hyperplasia was rendered.

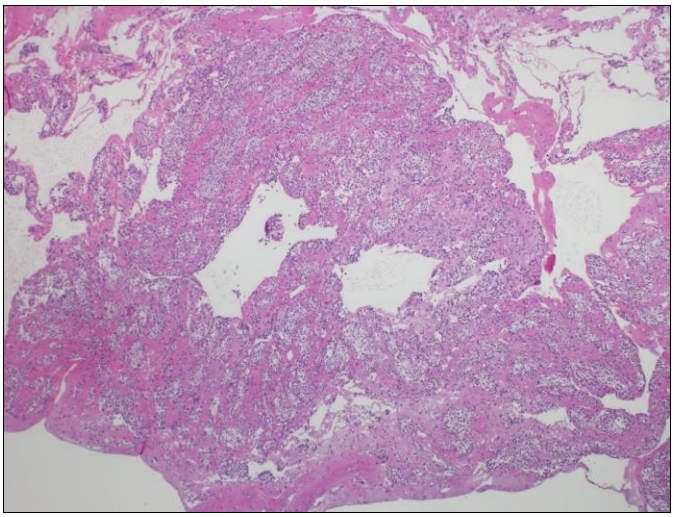

Fig 1A: Photomicrograph depicting nodular proliferation of cells within the wall of hernial sac (Hematoxylin & Eosin stain, x40)

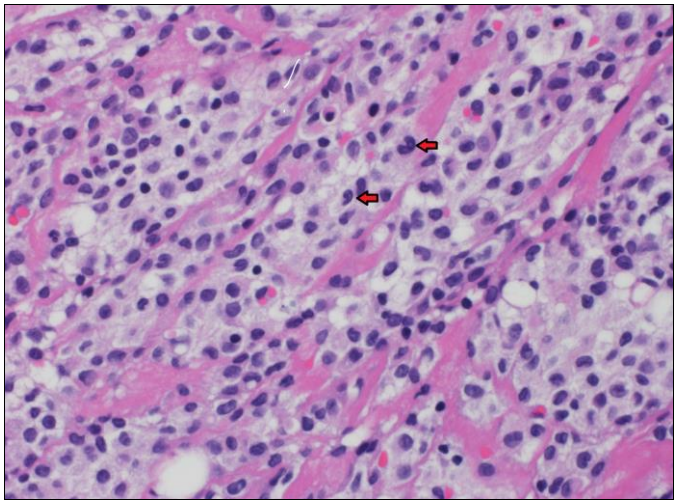

Fig 1B: the cells have abundant pale cytoplasm and the nuclei have different shapes, some exhibit marked lobulation with metamyelocyte-like appearance (red arrows) (Hematoxylin & Eosin stain, x400)

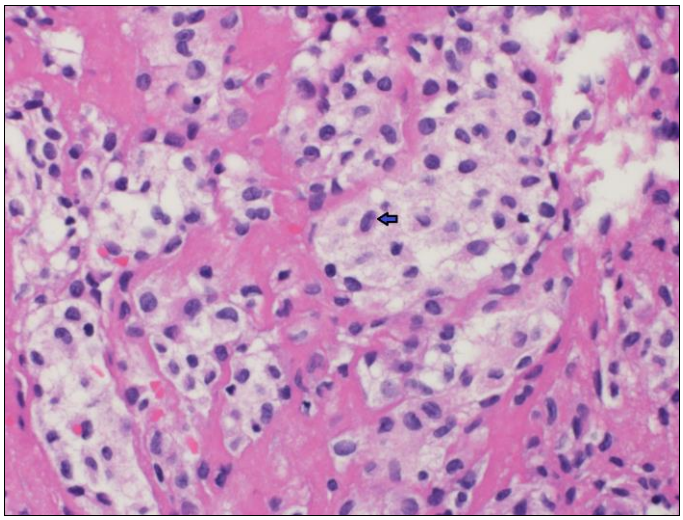

Fig 1C: few cells have nuclear grooves (blue arrow) (Hematoxylin & Eosin stain, x400)

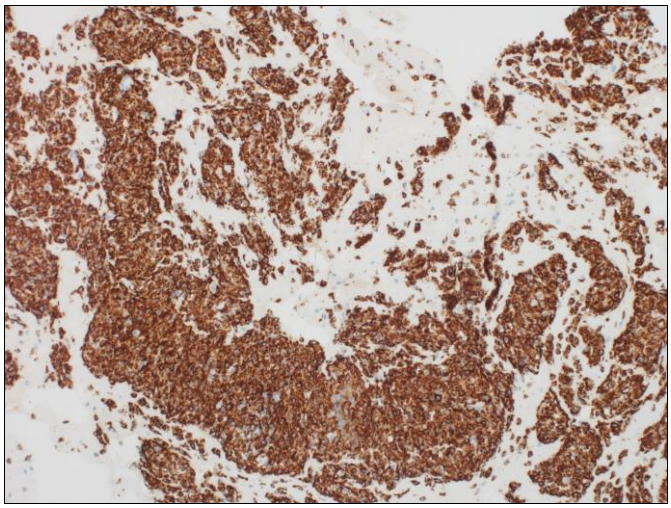

Fig 2A: the cells are immunoreactive for CD68 stain

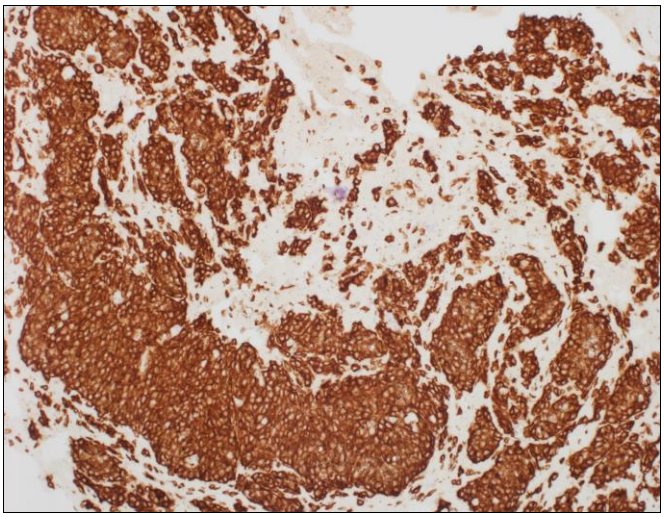

Fig 2B: the cells are also immunoreactive for CD163 stain

Discussion

This condition is important to recognize for three reasons:

1. It represents a reactive proliferation of histiocytes that have unusual nuclear morphology. The histiocytes in this condition can have nuclear grooves which could be mistaken as Langerhans cell [1]. The nuclei can also have lobulated appearance mimicking metamyelocytes [1]. Therefore, it is essential to differentiate this condition from other diseases such as Langerhans cell histocytosis and chronic myeloid leukemia.
2. The histiocytic proliferation is sometimes so florid that a malignant diagnosis such as mesothelioma or metastatic carcinoma would be seriously considered [1-5]. This can be deceiving, so it is important to recognize this entity in order not to misdiagnose this reactive histiocytic proliferation as malignancy, which may result in unwarranted therapy.
3. In previous reports, the proliferative cells had been described to be mesothelial in origin based on the morphologic appearances [1]. However, the diffuse reactivity of these cells for CD68 and CD163 immune histochemical stains in our case as well as in other reported cases, confirms their histiocytic nature [2].

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