***Case report***

**INFAMMATORY MYOFIBROBLASTIC TUMOR IN A NIGERIAN CHILD: A RARE PRESENTATION- CASE REPORT AND REVIEW OF LITERATURE**

**ABSTRACT**

**Background**

An inflammatory myofibroblastic tumor (IMT) is a rare neoplasm composed of myofibroblastic and fibroblastic spindle cells accompanied by inflammatory cells, including lymphocytes and eosinophils. It is predominantly found in children and adolescents. The IMTs found in the head and neck region account for 14 to 18% of extra-pulmonary IMTs [lungs being the most commonly affected regions]. On account of its ambiguous clinical presentation, an IMT needs to be differentiated from other infectious, granulomatous, autoimmune, and neoplastic lesions on the basis of histopathologic findings and immunohistochemical analysis. The mainstay of care for localized tumors is a surgical resection; however, for advanced disease, the line of care is not well defined. Spontaneous regression has also been reported in some people. Chemotherapy regimens result in an overall response rate of approximately 50% based on retrospective data.

**Case presentation**

An 8-year-old male who presented with a history of generalized body swelling, which progressed to weakness of both lower limbs and later inability to walk, with associated urinary and fecal incontinence of about 8 months duration. However, 5 weeks before presentation, developed cough, difficulty with breathing, progressive weight loss, and drenching night sweats. An initial diagnosis of disseminated tuberculosis was made, but this was changed following a histology report of an inflammatory myofibroblastic tumor (IMT). Further treatment was not done as the child passed on.

**Conclusion**

IMT is a rare tumor that is easily misdiagnosed. This case report contributes significant clinical insight into the presentation and diagnosis of a rare tumor, IMT, in a low-resource tertiary healthcare setting. Its importance lies in highlighting the non-specific features at presentation and possible treatment approaches in the context of limited diagnostic infrastructure. Additionally, the case offers valuable information on the management of IMT, thereby informing clinicians practicing in similar environments. Furthermore, the report enriches the global data pool on IMT presentations, especially in African populations, where literature on such cases remains scarce.

Key words; IMT, inflammation,tumor

**INTRODUCTION**

Inflammatory myofibroblastic tumour (IMT) is an ultra-rare sarcoma that has been classified as a neoplastic disease of intermediate biological potential, given the low risk of recurrence and metastatic potential.1 It is known by several names, including pseudosarcoma, epithelioid inflammatory myofibroblastic sarcoma and inflammatory pseudotumor.2 IMT usually arises in the lungs (most common site) or the abdominal soft tissues of children and young adults, although a wide anatomic distribution and a broad age range have been documented, with a low prevalence ranging from 0.04% to 0.7%, affecting mainly younger individuals.3,4 Though rare in the maxillofacial region, it has been reported in the epiglottis, endolarynx, parapharyngeal space, maxillary sinus, orbits, submandibular region, and oral cavity.1,5 The etiology and pathogenesis of IMT are not fully established, however, some risk factors have been described, including smoking, trauma, chronic inflammation, autoimmune diseases, and IgG4-related disease. 1,6 Some hypotheses suggest an abnormal immunological response to viruses or antigens (Human Herpesvirus-8, Human Immunodeficiency Virus, and Epstein-Barr virus are mostly implicated), however, the cause remains largely unknown. 7-9 Histologically, myofibroblasts are cells of mesenchymal origin, having ultrastructural characteristics in common with fibroblasts and smooth muscle cells. It is characterized by spindle-shaped cells with inflammatory cells in the connective tissue. Its biological behavior is largely undefined and considered benign; however, recurrences and metastasis have been documented in some studies.1 Myofibroblastic differentiation in sarcoma represents a source of long-standing debate. The only mesenchymal malignancy that explicitly refers to “myofibroblastic” differentiation is the so-called low-grade myofibroblastic sarcoma.10   When malignant behavior is present, less than 5% of cases have metastasis, and of all the cases, 8–18% may have malignant transformation. 2

The identification of recurrent *ALK* gene rearrangements has greatly contributed to the understanding of this rare mesenchymal tumor. ALK is a receptor tyrosine kinase first identified as a component of the nucleophosmin (NPM)-ALK fusion oncoprotein, which is aberrantly expressed in anaplastic large cell lymphoma (ALCL).11 Importantly, it should be noted that *ALK* rearrangement is far less common in adults than in children and young adults with IMT.12 A variation in tumor biology could be the basis of these differences between these two age groups. Kinase fusions play a critical role in the biology of many IMTs and have been reported in about 80% of these tumors.13 It can be further divided into the more common pulmonary variant and the less common extra-pulmonary variant. The pulmonary variant occurs more commonly in children and young individuals and has a more benign clinical course. The extra-pulmonary variant affects older individuals [after the 2nd decade] and has a more aggressive clinical course.14,15

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8year old male who presented to us in a chronically ill state. Before presentation, he had developed generalized body swelling which progressed to weakness of both lower limbs and later inability to walk, with associated urinary and fecal incontinence of 8 months duration. He also developed a chronic cough at the same time, and received some oral medications in a health facility. However, as symptoms persisted, he resorted to traditional remedies and took a water-based herbal concoction for 3 months, with no significant improvement. He returned to the same health facility where a chest x-ray done revealed pleural effusion, which was drained and commenced on anti-kochs medications, which he had taken for 5 months, with resolution of cough, fecal and urinary incontinence, and regained milestone (standing with support).

5 weeks before presentation in our facility, he developed a cough, difficulty with breathing, and progressive weight loss. Cough was productive of yellowish, non-bloody, and non-foul-smelling sputum, with associated chest pain and drenching night sweat. He developed a fever while on admission. On examination, he was chronically ill-looking, severely pale, with grade 3 digital clubbing, significant axillary, submandibular lymphadenopathy, dyspneic, tachypneic, and bilateral pitting pedal edema up to the knee. On chest examination, there was asymmetrical flattening of the right upper lung zone, reduced chest expansion on the right, reduced air entry and vocal fremitus, with dull percussion notes over the right lung zone. The abdomen was markedly distended, and the liver was 8cm below the right coastal margin, firm, non-tender, and ascites was present. There was marked muscle wasting, grade 2 power in lower limbs and grade 4 in upper limbs, with reduced tone in upper limbs, increased tone in the lower limbs, and ankle clonus present. A diagnosis of disseminated tuberculosis (pulmonary, Pott's disease) with suspected drug-resistant tuberculosis was made. He received blood and blood products, intravenous antibiotics, antifungal, anti-tuberculosis drugs, pyridoxine, prednisolone, and corrected deranged electrolytes. He also had chest tube insertion done for drainage of pleural effusion.

A complete blood count showed leukocytosis (19,000), neutrophilia (81%), repeat was 4300 and 74% respectively, ESR-10mm/hr. Electrolytes showed hyponatremia (132) and acidosis (17) and were corrected; retroviral screening was negative. Chest x-ray showed right lung collapse with a pleural effusion. Ferritin 720.81ng/ml (normal range 10-150ng/ml). Gene expert test- negative for tuberculosis. Lactate dehydrogenase 325u/L (normal range 110-295u/L). Bone marrow aspiration (BMA)- normal. Liver function test- GGT 122(normal range <55U/L) and ALP 229 (normal range 0-211 U/L), albumin 23 (32-55g/L), total protein 49 (67-82g/L). Peripheral blood film (PBF) and bone marrow aspiration (BMA) were both normal. Bone marrow biopsy reported a gelatinous transformation of the marrow.

Chest CT scan done showed- a large paravertebral mass from T6 down to the abdomen, displacing the thoracic aorta anteriorly and to the left, displacing the right pleura, causing a collapse and displacement of the right lobe anteriorly, and significant bilateral pleural effusion. Pulmonary nodule (1x0.8cm) is seen in the anterior segment of the left upper lobe, with multiple para-aortic nodes in the abdomen displacing the aorta anteriorly; Diagnosis- a lymphoma with pleural and abdominal extension, and distant metastasis (bone, pulmonary).

Tru-cut biopsy of the right intrathoracic mass revealed a neoplastic lesion composed of spindle cells admixed with cells of eccentric nuclei and brightly eosinophilic cytoplasm, myxoid background with mixed inflammatory infiltrates comprising lymphocytes, plasma cells, and histiocytes. There are hyper- and hypo-cellular areas, thin and thick-walled blood vessels, and golden-brown pigmented areas, all within the lesion. Vessels with thrombus formation, adjacent lining tissue, and skeletal muscle are seen. No mitosis or necrosis seen- Diagnosis –mesenchymal neoplasm, probably an inflammatory myofibroblastic tumor was made. Immunohistochemistry was advised for a definitive diagnosis, but could not be done due to financial constraints.

On account of the new diagnosis, the caregivers were counselled and treatment options explained extensively. However, further care was not done as the child passed on.

DISCUSSION

IMT was first described in 1939 by Brunn and his colleagues when it occurred in the pulmonary region. 10 The overall prevalence of IMT is 0.04–0.7%. It is usually seen in children and adolescents aged between 2 and 16 years old. IMT is divided into the more common pulmonary variant and the less common extra-pulmonary variant. The pulmonary type occurs more commonly in children and young individuals and has a more benign clinical course. The extra-pulmonary variant affects older individuals [after the 2nd decade] and has a more aggressive clinical course.  14,15  It has also been reported in the neonatal age group. The index child was an 8-year-old, which falls into the pulmonary variant as seen from the history and examination findings; however, the clinical course did not appear benign, as some clinical features appeared like the extra-pulmonary variant, known to have an aggressive course. In contrast, some other studies have found IMT located in other sites, including the umbilicus, jaw, brain, and the axilla, which were not found in the index child. The symptoms presented by patients depend primarily on the primary site of the IMT. At the time of diagnosis, patients typically present with a painless mass, often remaining completely asymptomatic until the mass reaches a size that causes complications.16 Symptoms may present as pain, and approximately 20% present with symptoms of generalized malaise, fever, and weight loss 17, and some of these findings were part of the presenting complaints of the index patient. Based on the duration of illness, our index child had a clinical feature suggestive of a chronic inflammation, which is a known risk factor for IMT, though viral screening was not done. In contrast, Neuhauser et al had positive EBV results in some patients with splenic IMT. It is also important to note that a negative viral screening does not preclude the possibility of a previous asymptomatic viral exposure.  Despite its classification as a benign or locally aggressive tumor, IMT can exhibit unpredictable behavior, necessitating careful diagnosis and management. 18

The radiological presentation of IMTs is diverse. On imaging, multiple masses in one anatomic region may be seen and may vary from an infiltrating lesion to a well-delineated lesion, with different proportions of inflammatory and fibrotic components in the mass. This finding is in keeping with the reported child, where several nodes were found in both the thoracic and abdominal areas. Variable attenuation can thus be noted on the CT scan, with persistent and delayed contrast uptake, in the fibrotic component of the IMT. Magnetic resonance imaging may show low signal intensity on T1- and T2-weighted images owing to fibrosis, along with restricted diffusion.19 Biologically, IMTs can induce inflammation with leukocytosis, neutrophilia, and elevation of C-reactive protein and erythrocyte sedimentation rate, and all these were evident in the laboratory investigations of the index child. 20 Historically, IMTs were considered to arise as a result of an exaggerated reactive or reparative process to tissue injury. IMTs in the liver’s portal area can cause elevated levels of γ-glutamyl transferase (γGT), alkaline phosphatase (ALP), aspartate transaminase (SGOT), and alanine transaminase (ALT), indicating obstructive cholestasis, however, only GGT and ALP were found to be elevated in the index child.21,22 Additionally, imaging may suggest a mass present at certain sites; however, histological diagnosis is the mainstay in making a diagnosis of IMT. For the index case, a CT scan suggested a lymphoma, but the histologic analysis aided the final diagnosis, thereby preventing a misdiagnosis and wrong management, as in the case of this child, who was previously managed for disseminated tuberculosis, until we had a histology report.

IMTs can be treated by surgical excision, curettage, steroid therapy, radical surgery, and radiotherapy.5 The mainstay of treatment is surgical resection, with a recurrence rate as high as 60%, but complete resection significantly reduces this probability to around 2%. Recently, surgical excision has been supplemented with CO2 laser light.[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5670301/#bib0020) Radiation, chemotherapy [cyclosporine, azathioprine, methotrexate and cyclophosphamide], ALK molecular targeted therapeutic drugs [crizotinib], and steroid therapy are used when the tumours are invasive, non-resectable, recurrent, show signs of malignancy/metastasis, or when surgical margins are positive.[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5670301/#bib0020) In addition, NSAIDs are being suggested as a treatment option because of their anti-inflammatory and antiangiogenic effects.5 The use of NSAIDs resulted in tumor regression in older children, whereas others reported no response to NSAIDs.At the time of initial diagnosis, the index child was given steroids, and this could have contributed to some clinical improvement. However, with the new diagnosis of IMT, the child was scheduled for surgery and chemotherapy, but passed on before receiving any treatment.

CONCLUSION

IMT continues to be a diagnostic rarity and often surprises clinicians histologically, although the diagnostic features frequently become more apparent in hindsight. A multidisciplinary approach is crucial for managing IMT. Since recurrence is possible, prolonged follow-up and close monitoring can facilitate early detection.

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