


## CASE REPORT

### Inflammatory myofibroblastic tumor mimicking a relapse in a patient with Hodgkin's lymphoma: report of an unusual case and review of the literature

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#### Introduction

Inflammatory myofibroblastic tumors (IMT) are rare pseudosarcomatous inflammatory lesions, occurring in the soft tissue and viscera of children and young adults. Fascicles of bland myofibroblasts in a collagenous stroma mixed with prominent inflammatory cells including lymphocytes, eosinophils, and plasma cells are observed in the histological examination of the lesions. The diagnosis is generally difficult and dependent on the relative proportion of the inflammatory and myofibroblastic cells [1]. IMTs may also behave as aggressive and destructive neoplasms and are rarely associated with malignancies [2, 3]. Resection of the tumor mass, observation, chemotherapy, radiotherapy [2], and nonsteroidal anti-inflammatory drugs (NSAIDs) like celecoxib [4] are management options for IMTs. Herein, we present a rare case of IMT in a patient with Hodgkin's lymphoma (HL) in complete remission, in which IMT mimicked

#### Key Clinical Message

New PET-positive lesions in previously treated patients with lymphomatous malignancies need further investigations. Relapse, sarcoidosis and secondary malignancies are the most important differential diagnosis. Inflammatory myofibroblastic tumors (IMT) is a rare complication after treatment of Hodgkin's disease and every PET-positive lesion should be biopsied to prevent unnecessary intervention.

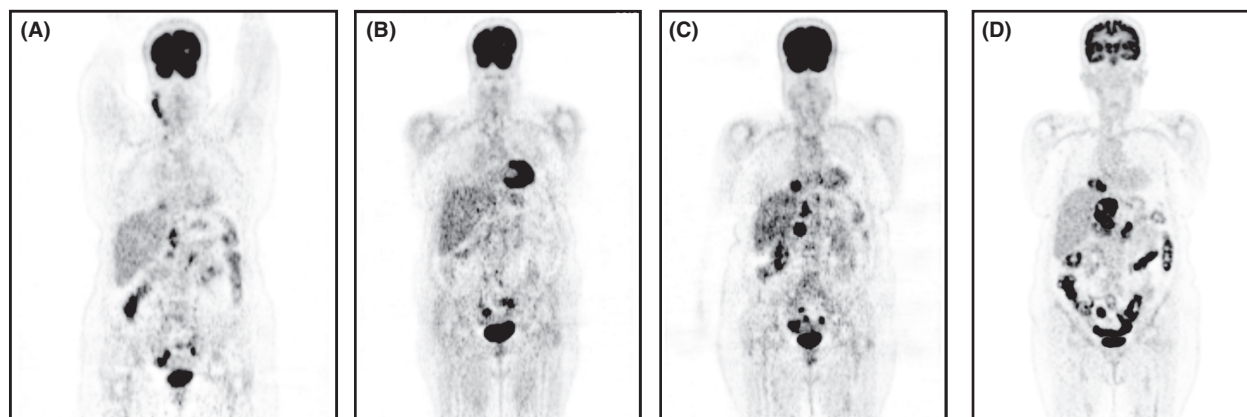
#### Keywords

Hodgkin's lymphoma, inflammatory myofibroblastic tumor, inflammatory pseudotumor, plasma cell granuloma, relapse.

HL relapse on imaging by PET and complicated the management strategy of HL due to difficulty in the histological diagnosis.

#### Case Report

A 70-year-old female patient was admitted to our clinic in April 2011 with complaints of newly noticed cervical lymphadenopathy and night sweats which began 1 month ago. Her past medical history was significant for hypothyroidism, Type 2 diabetes mellitus and dyslipidemia. Her only medication was levothyroxine sodium for hypothyroidism. At the time of admission, the vital parameters were within normal limits. The physical examination confirmed right cervical mass approximately 5 cm in diameter. The tru-cut biopsy of the mass revealed EBV-positive, mixed cellular type classical Hodgkin's lymphoma. The positron emission tomography (PET) showed multiple supra- and infradiaphragmatic malignant metabolic



**Figure 1.** PET images. (A) At the time of diagnosis; (B) complete remission after six ABVD; (C) new lesions at 11th month of CR; (D) lesions progressed despite NSAID treatment.

lymph nodes, and suspicious hypermetabolic activities in the spleen, in the antrum of the stomach, and in the wall of the rectum (Fig. 1A). Bone marrow was not infiltrated, proven by biopsy.

Our patient had stage IV disease. The Hodgkin's International Prognostic Score (IPS) was 2 (age  $\geq 45$  and stage IV disease). After six courses of ABVD (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) treatment, the PET scan in November 2011 confirmed complete remission (CR) of the disease (Fig. 1B). In the first 6 months of follow-up, the patient was asymptomatic.

However, at the eleventh month of CR, the PET imaging in October 2012 revealed newly formed multiple hypermetabolic lymphadenopathies in the abdomen and in the mediastinum (Fig. 1C). A tru-cut biopsy of the retroperitoneal lesion was performed, and malignant cells were observed; however, no specific diagnosis could be made histologically despite immunohistochemical stains.

We continued to follow our patient without treatment, as disease relapse could not be demonstrated and she was completely asymptomatic. She was re-evaluated 3 months later by PET scan, which reported partially progressed supradiaphragmatic lymph nodes, new hypermetabolic celiac and retrocausal infradiaphragmatic lesions. We did not start any treatment, and we followed up our asymptomatic patient with regular imagings.

Re-evaluation by PET scan 4 months later showed progressive disease in the abdomen. Another tru-cut biopsy from the same retroperitoneal area was performed, and IMT was diagnosed.

## Results

The lymph node tru-cut biopsy showed large atypical spindle cells with inflammatory cells around, including

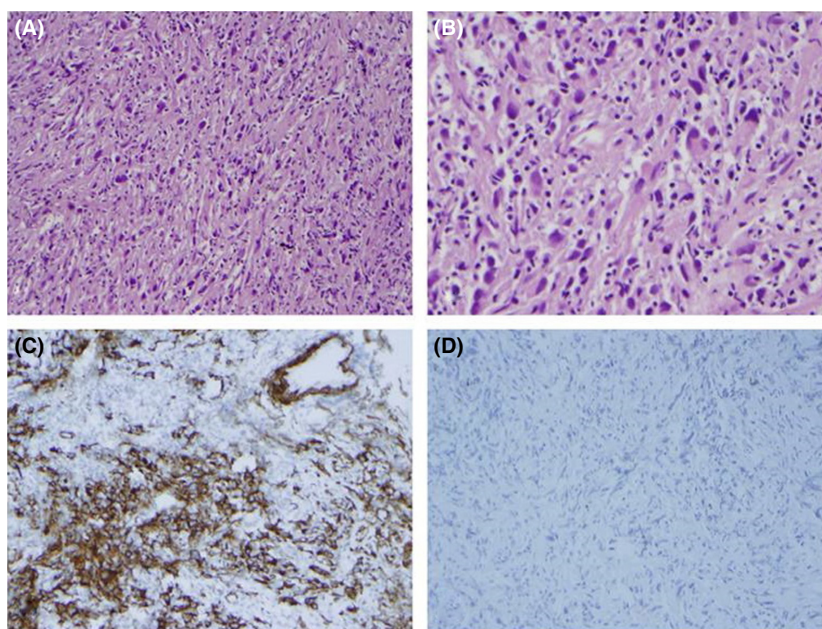
numerous histiocytes and small lymphocytes. It was considered as a soft tissue tumor with focal area of fibrosis. No Reed–Sternberg cells or its variants were observed in the specimen (Fig. 2A and B).

The large atypical cells were positive for smooth muscle actin; focally positive for vimentin; and negative for CD30, CD15, CD35, CD117, CD163, CD3, CD20, synaptophysin, chromogranin, desmin, pankeratin, ALK-1, HHV-8, CD138, EBV-LMP, e-cadherin, TTF-1, and CD34. Many histiocytes were stained positive for CD163. Mib-1 proliferation index was around 15–20%, and it was positive in atypical spindle cells (Fig. 2C and D). The small lymphocytes were mostly positive for CD3 and negative for CD20, Pax5, CD23, CD21, and CD57. The diagnosis of inflammatory myofibroblastic tumor was made according to the morphological and immunohistochemical features of the specimens.

## Treatment and Outcome

Widespread distribution of the tumor made complete surgical resection an impossible treatment option. Our patient was asymptomatic, and she had no complaints. Celecoxib 200 mg/day (100 mg b.i.d.) was administered for the treatment of inflammatory myofibroblastic tumor [4–6]. After 3 months, minimally progressed right paracardiac lesion (4.5 cm in diameter) and progressed right paracaval lesion (6.5 cm in diameter) were reported in the PET scan. She remained asymptomatic till December 2013.

In December 2013, she complained of pain in right shoulder. Weight loss (8 kg in 2 months), night sweats and loss of appetite accompanied her pain. PET scan in January 2014 revealed progressed pathological lymph nodes in the mediastinum and in the abdominal region near celiac trunk (Fig. 1D). An ultrasound assisted tru-cut



**Figure 2.** Effaced lymph node architecture with atypical myofibroblastic cells, lymphocytes, and histiocytes (A, H&E, 100X). (B) Higher magnification highlights myofibroblastic cells (B, H&E, 400X). By immunohistochemistry, the myofibroblastic neoplastic cells are positive for smooth muscle actin (C), and negative for CD30 (D, 100X, each).

biopsy of the lesion in the hilar area of liver was performed in March 2014. Pathological and immunohistochemical evaluation was totally consistent with previous diagnosis of inflammatory myofibroblastic tumor.

One mg/kg (60 mg for our patient) daily oral methylprednisolone was initiated, and celecoxib was stopped. Even though patient's appetite and general condition had initially improved, no tumoral regression was determined in CT scans and the IMT was progressively worsened after tapering the steroid dose. Our patient died in May 2014, due to progressive IMT-induced systemic inflammatory response, septic shock, and multiorgan failure.

## Discussion

Inflammatory myofibroblastic tumors are rare pseudosarcomatous inflammatory lesions and occur in the soft tissue and viscera of children and young adults. The diagnosis is difficult, and less is known about treatment for these patients. The co-occurrence of the lymphoid malignancies and IMTs is a rare and troublesome entity due to its potential to complicate the management of the disease.

Only six patients with NHL were reported in the literature. In one case, the patient was first diagnosed with IMT and treated with corticosteroid, and then she was diagnosed with central nervous system lymphoma in the follow-up [7]. Another patient was described to have

NHL and IMT of the spleen synchronously [8]. Other four cases were diagnosed with IMT after having been treated for NHL. IMT was removed surgically in two cases [9, 10], whereas no data about the treatment were available for the other two cases [2, 11].

Two cases with Hodgkin's lymphoma were reported in the literature. The first one was a 60-year-old male patient, diagnosed with HL and IMT synchronously and, treated with surgical resection [12]. The second one was published by Howman-Giles et al., a 16-year-old male patient with Hodgkin's lymphoma, who received chemotherapy and radiotherapy in the lung field. They stated that the patient developed IMT in the radiotherapy field 16 months after the completion of the treatment. Similar to our case, the IMT lesion was PET-positive and the diagnosis could not be made by the first two CT guided biopsies. The diagnosis was made after the resection of the tumor, which also constituted the treatment of IMT [3].

The relapses are unusual following surgical intervention, and thus, complete surgical resection of IMTs is the preferred treatment whenever it is possible [2]. However, the surgical resection may be inappropriate in many patients due to widespread disease. Applebaum et al. reviewed their cases regarding the hypothesis that NSAIDs are antiangiogenic for IMTs by interfering with vascular endothelial growth factor (VEGF) signaling via cyclooxygenase 2 (COX-2) inhibition and reported that IMT

specimens were positive for the mediators of angiogenesis, VEGF and COX-2 [13]. Our case had widespread disease at the time of diagnosis of IMT, and we could not resect the tumor mass. The results of chemotherapeutic treatment were conflicting [2], and we were not in favor of chemotherapy under the circumstances. Considering the results of selective COX-2 inhibitors, we started celecoxib treatment.

Chavez and Hoffman published a case report on a 52-year-old female patient with multifocal IMT of the lung, who was treated with surgery but relapsed two times and then, who did not respond to corticosteroid therapy. She was administered 200 mg celecoxib PO BID, and at the second year of the treatment, the CT scans showed completely resolved lung nodules. They also reported nine cases of 10 who achieved CR with NSAIDs [4]. Additionally, Shatzel et al. published detailed clinical course of a 28-year-old female patient with partially resected mesenteric IMT, who was effectively treated with prednisolone and celecoxib therapy [14].

Our case had many facets like the old age of the patient, past history of ABVD chemotherapy, and the difficulty in the histological diagnosis of IMT mimicking HL relapse in PET scans. We could find only a single case similar to our patient, who had IMT in the radiotherapy field after HL treatment, which was surgically resected [3]. Our patient, after being treated for HL, did not receive any radiotherapy, and at the eleventh month after completing chemotherapy, the PET findings were consistent with the relapse of HL. Only after the second biopsy, the IMT diagnosis could be made. As the tumor was unresectable due to its widespread distribution, we preferred celecoxib treatment. The disease was progressive; we rebiopsied the lesion, and the original diagnosis was reconfirmed in a different institution. Unfortunately, as she did not respond to NSAID therapy and to subsequent steroid treatment, the systemic inflammatory response syndrome related to progressive inflammatory myofibroblastic disease occurred and she died of septic shock and multiorgan failure.

Current guidelines do not recommend following patients in CR with PET/CT or any imaging. We should state that we have first started to use PET/CT frequently in our practice since 2010. Follow-up of our case with consequent PET scans might be accepted as an over-use.

To summarize, even though co-occurrence of IMT with other malignancies is a rare entity; similar to other benign causes of PET positivity like sarcoidosis [15], IMT should be considered in the differential diagnosis of suspected recurrence of HL on radiological studies or FDG uptake in HL cases. Histological verification should be performed in order to prevent diagnostic errors and not delay appropriate management and further therapy.

## Authorship

BF, CT, TSA, EST, and ARU: followed the patient. MÖ: evaluated pathology specimens. BF, MÖzb, and EST: wrote the manuscript.

## Conflict of Interest

None declared.

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