

## Thymic Hyperplasia after Remission of T Lymphoma is Not Always Associated with a Relapse

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DOI: [10.36347/sjmcr.2021.v09i08.005](https://doi.org/10.36347/sjmcr.2021.v09i08.005)

| Received: 25.06.2021 | Accepted: 29.07.2021 | Published: 06.08.2021

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### Abstract

### Case Report

We suspect a mediastinal relapse of the cancerous pathology when a thymic hyperplasia occurs in patients with complete remission post chemotherapy. In this article, we report the case of a thymic hyperplasia that appeared six months after the end of chemotherapy in a 31-years-old patient followed for stage IV T-cell lymphoma treated with CHOEP chemotherapy. The PET scan (Positron Emission Tomography) objectified a complete metabolic remission with the disappearance of the thymic hyperplasia.

**Keywords:** cancerous pathology, thymic hyperplasia, chemotherapy, PET scan.

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## INTRODUCTION

Benign thymic hyperplasia can occur after the management of a cancer with chemotherapy, it can be associated with a mediastinal relapse of the cancer, but can also occur in the context of a post chemotherapy enhanced inflammation. The performance of a PET Scan could prevent benign thymic hyperplasia is a phenomenon that can occur after chemotherapy for cancer, it may be a sign of mediastinal relapse of cancer but it can also be synonymous with an inflammatory post chemotherapy syndrome; PET scan could avoid a diagnostic thymectomy.

## CLINICAL OBSERVATION

The patient is a 31 years old female, with no significant medical history. The symptomatology dates back to four months prior to the diagnosis. Bone pain with the progressive development and increase in volume of an axillary adenopathy has been described, associated with a worsening of health and a significant but unquantified weight loss, nocturnal fever and night sweats, as well as functional impotence in the two lower limbs without any sensory deficit, due to the bone pain. The performance of a biopsy of the axillary adenopathy brought to light the presence of an anaplastic T cell lymphoma with large CD30 positive cells, ANTI EMA, ALK.

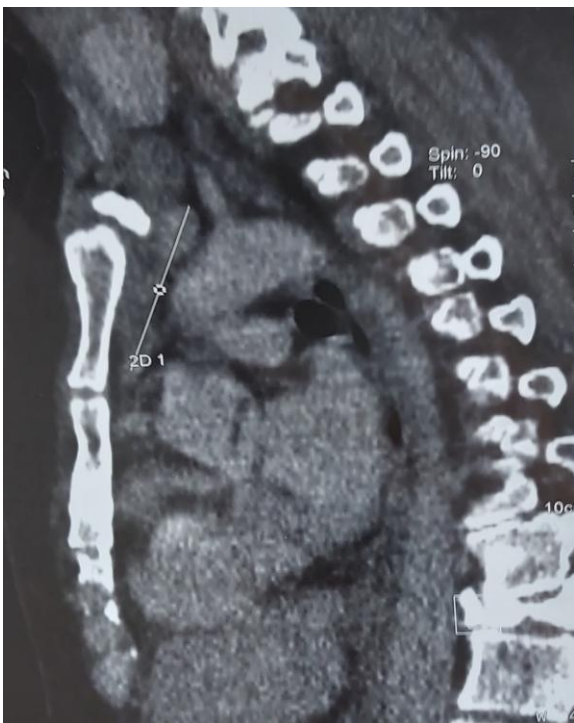
The extension assessment showed the existence of sub and supra diaphragmatic tumors, with multiple pulmonary and bone localisations, a dorsolumbar MRI showed another localisations around T5, T10, L3 and L4 without intraductal extension. The MRI showed a right sacral and left iliac localisation of the tumor as well, extended to the sacral foramina.

Therapeutically, the patient was put under chemotherapy according to the CHOEP protocol (Cyclophosphamide 750mg/m<sup>2</sup> on the first day, Doxorubicine 50mg /m<sup>2</sup> on the first day, Etoposide 100mg/m<sup>2</sup> from day1 to day3, second and third days; oncovin 1.4mg/m<sup>2</sup> on the first day; prednisone 40mg/m<sup>2</sup> from day1 to day5.

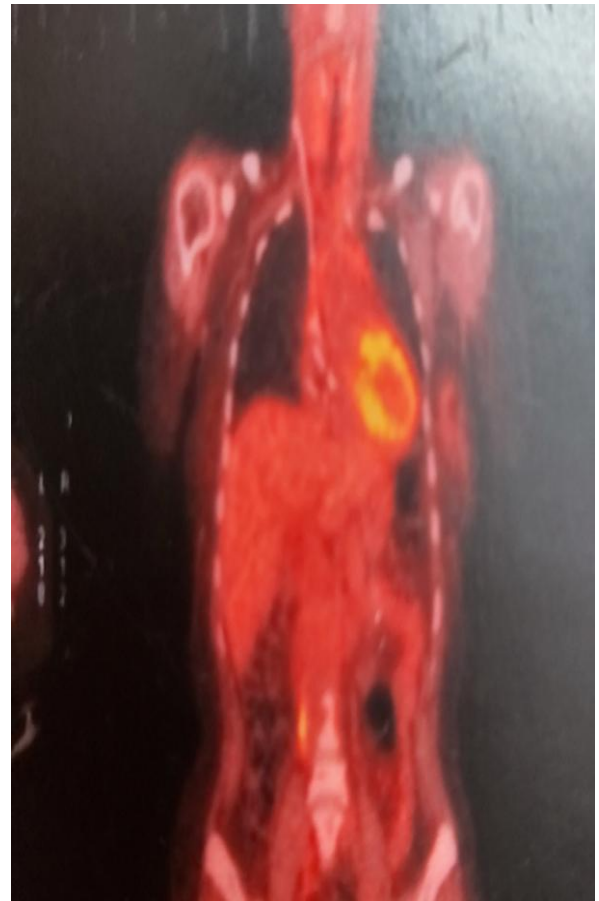
Clinical improvement is noticed from the second cycle of chemotherapy, when the patient resumes walking without assistance, an MRI is performed for reevaluation post chemotherapy shows the disappearance of any previous tumoral lesions but with the persistence of lytic lesions on T5 and T10.

At the end of the six chemotherapy cycles; the patient regained autonomy and showed no clinical signs, including no bone pain or tumoral syndrome. The MRI check up showed the same aspect that has been described after the fourth cycle of chemotherapy.

The patient remained under surveillance through a clinical, biological and radiological examination, using a neck, chest, abdomen and pelvic CT scan. At this time, the PET scan was not available in our structure. The biological assessment was programmed every three months and the radiological assessment every 6 months. Six months after the end of the treatment, the clinical examination of the patient is normal and the biological assessment doesn't show anything associated with a potential relapse. However, the CT scan shows a quadrilateral antero superior mediastinal structure, clearly contoured of homogenous density without calcifications, molding the adjacent structures without a mass effect measuring 53x23x55mm (Fig 1) This structure is associated with a thymic hyperplasia. After 3 months of surveillance, this thymic hyperplasia persists, a PET scan is performed and shows the fixation of the  $^{18}\text{F}$  FDG with a  $\text{SUV} = 2.5$  (Fig 2), thus eliminating the possibility of a malignant origin of the hyperplasia, suggesting a complete remission. The surveillance with a PET scan three months afterwards confirms the complete remission and the disappearance of the thymic hyperplasia (Fig 3). Currently, 20 months have passed after the end of the treatment, and the clinical examination doesn't show anything particular. Biologically, there is no inflammatory syndrome and the PET scan is still ruling in favor of a complete remission.



**Fig 1:** CT scan shows a quadrilateral antero superior mediastinal structure, measuring 53x23x55mm



**Fig 2:** TEP scanner objectifying the thymic hyperplasia with  $\text{SUV} = 2,5$



**Fig 3:** TEP scanner after 1 year objectifying disappearance of thymic rebound

## DISCUSSION

The thymus is a lymphoid organ lying in the middle of the mediastinum, it is a lymphoid gland involved in the immune system but also in the

production and maturation of T cells in the fetus [1], normally, it has a triangular shape [2]. In adults, the thymus eventually undergoes hyperplasia due to stress, tuberculosis or for instance the interruption of corticosteroids, this could also be due to other conditions; after treatment, this thymic hyperplasia is reversible and the organ returns to its normal size [3].

Hyperplasia of the thymus is very common in children but may also occur in young adults [4]. In the latter, it is mostly associated with autoimmune diseases such as Sjogren's syndrome [5] or systemic lupus erythematosus [6].

Before chemotherapy, the thymic lodge is usually empty, raising fears of a relapse in the event of a post-chemotherapy thymic hyperplasia. Thymic rebound is a well-described phenomenon, especially in pediatric oncology, mostly in patients who have undergone chemotherapy for lymphoma, especially non-Hodgkin lymphoma, it can occur in post-chemotherapy [7].

Taner and al reported that 20/56 (36%) children followed up for malignant hemopathies in complete remission presented an asymptomatic thymic hyperplasia that is not associated with a relapse of their condition, thus the qualification of a thymic rebound [8].

Thymic rebound was also described several months after the end of a chemotherapy treatment for an ovarian cancer and has been diagnosed as a benign thymic hyperplasia after the performance of a thymectomy through a manubriotomy [9].

In the majority of cases, patients show no clinical signs of thymic rebound. [5] As is the case of our patient. Post-chemotherapy CT scan surveillance uncovered this asymptomatic thymic hyperplasia.

PET scan represents a useful tool that allows in many situations to eliminate false positives. The 18FDG uptake in thymic hyperplasia doesn't exceed a maximal SUV of 4 [10]. Which has been previously set by Ferdinand and Hamberg as the pathological threshold for thymic fixation to PET scan [11, 12].

PET Scan is a strong diagnostic tool that made the differentiation between a benign thymic hyperplasia and a lymphoma relapse easier. A 2012 study on a pediatric population followed up in oncology for lymphomas showed and confirmed the strong contribution of PET Scan in thymic rebounds [13], The results showed that an SUV greater than 3.4 is associated with a high risk of relapse, however, if the SUV is less than 3.4, it is a thymic rebound or a normal thymus. The PET Scan of our patient has objectified a thymic uptake of 2.5, ruling out a pathological hypermetabolism associated with an early relapse. It has

been suggested in many studies that the anatomopathological study of the thymus could be indicated if we suspect a relapse of the hemopathy if the thymic hyperplasia is associated with an increased thymic uptake exceeding the maximal SUV that has been set by Ferdinand and Hamberg of 4.

J. Margery and T. de Revel reported the case of a post chemotherapy thymic rebound of a Hodgkins lymphoma, with intensification and bone marrow autograft. The lymphoma's relapse was suspected with the progressive growth of a thymic mass with an SUV affinity of 6.8. The anatomopathological study ruled out the recurrence of the lymphoma and a thymic rebound was diagnosed. The thymic compartment returned to its normal size and form after a year [8].

Thymic rebound was discussed in patients treated with immunotherapy. Justin Mencil and al described in 2019 and for the first time a thymic hyperplasia case in two patients treated with a double immunotherapy using Nivolumab and Ipilimumab for a stage IV metastatic melanoma. The first patient developed an enlargement of the thymic compartment 9 months after the beginning of the immunotherapy. The benign character of the mass could not be confirmed only with imaging so anatomopathological study has been performed and it led to the diagnosis of a thymic rebound. In the case of the second patient, PET SCAN was enough to confirm the diagnosis of a thymic rebound 8 months after the start of the immunotherapy management.

I'd suggest adding a word about the spontaneous resolution and the management of the thymic rebound.

## CONCLUSION

The occurrence of a mass in the thymic compartment after chemotherapy may be confusing in the distinction between a thymic rebound and a mediastinal relapse of the former cancer; Moreover, 18FDG uptake in PET SCANS with an SUV limit of 4, confirms the benign character of the thymic mass. Therapeutic abstention is often the treatment of choice for the management of thymic hyperplasia because it usually evolves favorably without any treatment resulting in spontaneous resolution in only a few months.

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