

Thymic findings before and after autologous stem cell transplantation for severe systemic sclerosis: a retrospective study using computed tomography in the pre- and post-transplantation setting

Sir,

Referring to the recent publication by Colaci *et al.* (1) we would like to report our experiences in this field and especially on thymic alterations after autologous stem cell transplantation. The underlying pathogenesis of systemic sclerosis (SSc) is still a matter of discussion but alterations of the immune system definitely play an important role. Studies on incomplete thymus involution in patients with SSc raised the suspicion that thymus abnormalities might be associated with an increased risk for autoimmune diseases (1-4).

Resetting the “immunologic clock” by autologous stem cell transplantation (aSCT) is a promising therapeutic option and more and more positive data have been published during the last years (5-8). Aim of this study was to evaluate thymic alteration in SSc patients before and after aSCT.

Patients underwent non-enhanced chest-CT in the pre- and post-transplantation setting. CT examinations were carried out at suspended end-inspiratory volume from apex to base on a multidetector CT-scanner (SOMATOM Sensation 16/64 or 128 Siemens, Germany). Images were reconstructed with a 12×512 matrix, thus allowing good image quality. Thin collimation (<2 mm) was used and the axial scans were reconstructed 5.0 mm slice thickness, by an increment of 1.2. All images were reevaluated by an experienced chest radiologist with >18 years of experience on this diagnostic field and reviewed at a mediastinal window.

We used the following criteria for definition of an abnormal thymus in accordance to the above mentioned work (1):

- length and/or thickness >13 mm for diffuse enlargement or
- length >7 mm for multinodular thymic enlargement

Additionally, we measured the thymic attenuation in Houndfield units (HU) using adequate regions of interest (ROIs). Thymic size was estimated length x width in mm² regarding the slice with the

Table I. Demographic data of patients analysed. There were no significant differences between those patients with and without incomplete thymus involution.

	All patients	Pts. with normal Thymus	Pts with abnormal Thymus	p-value
% (n)	100 (28)	42.9 (12)	57.1 (16)	n.s.
Age in years, median (range)	41 (19-57)	43 (22-57)	39 (19-53)	0.071
Disease duration in years, median (range)	1.75 (0.5-7)	1 (0.5-6)	2 (0.5-7)	0.563
Scl70 + in % (n)	71.4% (20)	66.6 (8)	75 (12)	0.629
mRSS at time TX (range)	18.5 (2-35)	21 (3-32)	15.5 (2-35)	0.157
Male	42.9 (12)	41.6 (5)	43.8 (7)	0.912
Female	57.1 (16)	58.3 (7)	56.3 (9)	0.912
Pulm. fibrosis in % (n)	96.4 (27)	91.6 (11)	100 (16)	0.429
Renal manifestation in % (n)	7.1 (2)	0 (0)	12.5 (2)	0.204
Heart manifestation in % (n)	42.9 (12)	50 (6)	37.5 (6)	0.508
Response to TX	92.9 (26)	91.7 (11)	93.8 (15)	0.832
Relapse	17.9 (5)	16.7 (2)	18.8 (3)	0.887

TX: autologous stem cell transplantation; mRSS: modified Rodnan skin score.

largest expansion. All statistics were performed by Chi-square test or Wilcoxon using SPSS 22[®]. A p-value <0.05 was considered significant.

Altogether we evaluated 28 SSc patients (16 female, 12 male) with a median age at transplantation of 41 (range 19-57) and a disease duration of 1.75 (0.5-7) years, that were transplanted for SSc between 2001 and 2012 and all have had a chest-CT scan within 3 months before transplantation. Most of the patients as well as the treatment protocols are included in our clinical papers that were published during the last years (2, 3).

57.1% (n=16) of the evaluated patients showed incomplete involution of the thymus at baseline, with 10 patients showing hyperplastic and 6 nodular thymus. If we exclude those patients who were <25 years or even <30 years at the time of transplantation, still 14/25 (56%) or 10/21 (47.6%) showed an incomplete involution. Comparing those patients with or without incomplete thymus involution, there were no significant differences between these two groups regarding epidemiologic data or response to treatment (Table I).

In all 16 of the patients with incomplete involution follow up CT scans were available, showing a non-significant reduction of the thymic surface (311.9 mm² vs. 254.8 mm²; p=0.234) and density (17.4HU vs. 3.9HU; p=0.127) over the median follow up period of 11 (2-48) months.

In summary, more than half of the patients considered for transplantation for severe SSc showed incomplete involution of their thymus by means of CT scan measurement. Colaci *et al.* found in only 12% of their 200 examined SSc patients abnormalities of the thymus, using the same methods of evaluation (1).

This very high percentage in our group is most probably explained by the negative selection of very ill patients considered for transplantation. This goes in line with previous reports of abnormal enlarged thymus especially in patients with progressive disease (1). Transplantation leads to a downsizing of the thymus. This was surprising as we expected rather an enlargement of thymus tissue due to development of new, naive T-lymphocytes after autologous stem cell transplantation. Nevertheless this downsizing can on the other hand be interpreted as reduction of auto-aggression and thus response to treatment. This observation should be part of a further examination including immune reconstitution after autologous stem cell transplantation.

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