

Clinical Features, Management & Outcomes of Patients with Thymoma and Thymic Carcinoma in a Multi-Centre UK Series



THE NATIONAL ONCOLOGY TRAINEES
COLLABORATIVE
FOR HEALTHCARE RESEARCH



INTRODUCTION

Thymic carcinoma and thymoma are rare entities accounting for less than 1% of adult cancers [1] and are associated with poor prognosis [2, 3]. Masaoka staging is widely accepted, and for patients with stage III & IV disease the 5-year survival is between 30-50% [1]. Surgical resection forms the mainstay of treatment. Poor prognosis in the advanced setting is often related to the inability to remove tumours due to infiltration into surrounding organs [1]. Consequently, adjuvant radiotherapy is recommended for stage II-III disease and adjuvant chemotherapy recommended in stage IV disease [2].

The evidence on which this guidance is based, is at best level III evidence, outlined within the ESMO guidelines for this condition, although the mainstay of evidence is focused on early disease [4]. A recent Cochrane review confirmed that most patients worldwide with advanced disease are treated with a Cisplatin-based regime of chemotherapy in addition to surgery and/or radiotherapy [1]. The extent to which current UK practice reflects this guidance is unclear, with no recent case series from multiple centres within the UK describing the presentation, management and clinical outcomes for this form of rare tumour, although single site data has been presented [5, 6]. Although there are data series available from other countries [2] and data registries [9], the types of treatments offered within the NHS and patient outcomes have not been evaluated in the era of personalised medicine.

We present here a large case series of patients with thymoma and thymic carcinoma drawn from six major cancer centres across the north of England and Northern Ireland. This unique dataset has been generated by the National Oncology Trainees Collaborative for Healthcare Research (NOTCH), a collaborative trainee-led initiative that provides a vehicle through which rare cancer diseases can be studied across multiple UK centres.

METHODS

Patient population

Three hundred and thirty two consecutive patients presenting with thymoma, thymic carcinoma or thymic carcinoid between 2008 – 2018 at six cancer centres in the north of England and Northern Ireland. Participating centres were Leeds Cancer Centre, the Northern Centre for Cancer Care, Clatterbridge Cancer Centre, The Christie Hospital, Northern Ireland Cancer Centre and Sheffield Cancer Centre. Patients were included if aged 18 years or above at diagnosis, with thymoma, carcinoid tumours or thymic carcinoma on histology, or with radiologically or clinically diagnosed thymoma or thymic carcinoma where biopsy was not possible or non-conclusive. Patient records were also required to be available for inclusion into the project.

Study design

Study concept, design and delivery were overseen by NOTCH. Patients were identified within each centre via local searches within the Somerset MDT database and chemotherapy prescribing databases. All patients were diagnosed or treated within the timeframe from November 2008-November 2018.

Medically trained investigators extracted data, this was crosschecked for accuracy prior to submission.

Governance

Study approval was granted by each individual participating centre, either as an audit project (Leeds Cancer Centre, the Northern Centre for Cancer Care, Clatterbridge Cancer Centre, The Christie Hospital, Northern Ireland Cancer Centre) or as service review (Sheffield Cancer Centre).

Table 1: Outcomes & treatments for patients according to stage specifically in thymoma

Tumour stage	Total number of patients	Primary treatment modality					Numbers receiving adjuvant therapy	Number of patients living with recurrence	Number of patients deceased
		Surgery	Radiotherapy	Chemotherapy	Surveillance	Supportive care			
I	70	68	0	0	1	1	12	0	5
II	109	106	0	2	1	0	54	4	11
III	34	26	2	6	0	0	22	2	11
IV	20	5	2	13	0	0	7	7	5
Unknown	13	7	1	2	0	3	5	2	5

Table 2: Outcomes & treatments for patients according to stage specifically in thymic carcinoma

Tumour stage	Total number of patients	Primary treatment modality					Numbers receiving adjuvant therapy	Number of patients living with recurrence	Number of patients deceased
		Surgery	Radiotherapy	Chemotherapy	Surveillance	Supportive care			
I	5	4	0	1	0	0	2	0	1
II	14	12	0	1	0	1	9	2	3
III	15	8	1	6	0	0	10	0	9
IV	25	3	3	17	1	1	4	7	14
Unknown	3	1	1	1	0	0	0	1	1

RESULTS

A total of 332 patient records were reviewed across the participating NOTCH centres outlined above. The typical distribution seen epidemiologically in other countries (usually 2:1 Female: male) did not seem to be represented in our cohort, with 167 male patients and 163 female. Average age at diagnosis was 60 years (range 25 – 88 years).

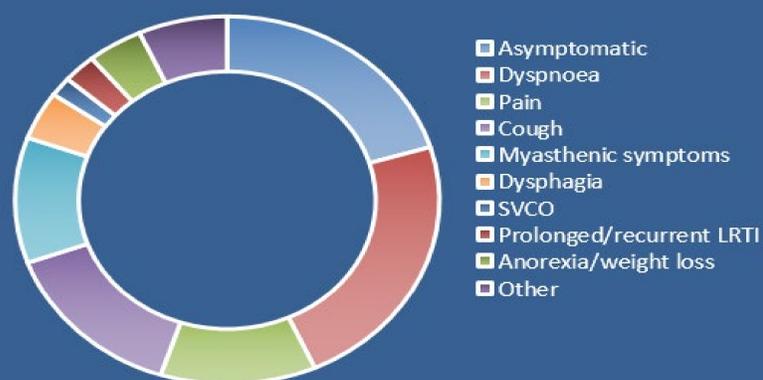
Of this population, 250 had confirmed thymoma, 74 had thymic carcinoma and seven had carcinoid tumours affecting the thymus gland. In total from the participating centres, 55 patients were from Belfast, 47 from Sheffield, 93 from Manchester, 31 from Liverpool, 32 from Hull, 49 from Leeds and 25 from Newcastle Upon Tyne.

Forty-nine patients were stage 4 at diagnosis, 52 were stage 3, 124 stage 2 and 75 were stage 1 (see Table 1 for full breakdown by tumour type). Most patients received surgery as initial therapy (249), only 60 had upfront chemotherapy, and eight had upfront radiotherapy alone. One hundred and twenty patients received adjuvant radiotherapy; this is noted to be significantly lower than the combined number of stage II & III patients. Only fifteen patients received best supportive care at diagnosis.

Of those with distant solid organ metastases, the median number of metastatic sites was 1 (range 1-6). Five patients had three or more sites of metastatic disease. The most common chemotherapy regimen first line in the stage IV setting was Platinum & Etoposide which 28 patients received, other first line regimens included Platinum & Taxol (2 patients), Cisplatin, Etoposide & Epirubicin (EPE- 2 patients) and Cisplatin, Doxorubicin & Cyclophosphamide (CAP – 1 patient). This suggests the majority of UK practice is in keeping with the ESMO guidelines, which recommend CAP or Platinum & Etoposide doublet as preferred first line therapy [4]. Second line chemotherapy options included those above, and Pembrolizumab (1 patient), Sunitinib (1 patient) and Vincristine, Adriamycin & Cyclophosphamide combination (VAC – 1 patient).

Associated paraneoplastic syndromes were present in 100 patients; predominantly this consisted of myasthenia gravis (58 patients). Interestingly, only 34% of patients had immunoglobulin testing confirmed from their medical records despite hypogammaglobulinemia being a well-recognised associated syndrome, this suggests lack of uptake of the ESMO international [4] recommendations for all patients to be tested at diagnosis.

Percentage of patients reporting symptom (%)



SUMMARY

This project has highlighted the scope of UK practice for patients presenting with thymomas and thymic carcinomas within the UK. As described above, the epidemiology in our population did not seem to reflect the internationally recognised distribution according to gender. The rate of paraneoplastic syndromes was as expected in comparison to available data [8, 9]. Current UK practice correlates with the ESMO guidelines in terms of systemic therapies, although there was a discrepancy between the number of stage II & III patients combined (176) versus the amount of patients receiving adjuvant radiotherapy (120).

