Regional Malignant Mesothelioma experience

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Introduction

Malignant mesothelioma is an aggressive form of cancer usually occurring as a result of exposure to asbestos. Malignant mesothelioma is the primary neoplasm of the pleura, but it may also involve other organs. The prognosis has slightly improved due to recent developments in the systemic therapies, but it is still relatively poor with a median survival of around 2.8 months [(1)]. As the survival from malignant mesothelioma is limited there is a need for a timely, effective and well organised assessment of patient with suspected malignant mesothelioma. Multidisciplinary Team approach forms an important aspect of cancer care and has been part of the NHS Cancer plan. There is evidence that a well-structured multidisciplinary team (MDT) may result in improved cancer outcomes and better decision making regarding the management plan and treatment options [(2)]. In fact, a systematic review suggested that MDT approach can influence the clinical decision-making but concluded that there was insufficient evidence regarding their effect on the outcomes [(3)]. Nevertheless, a

specialist malignant mesothelioma MDT has been recommended by the UK Department of Health's 2007 Mesothelioma Service Framework [4]. The role for the mesothelioma MDT is to review radiological and histopathological evidence to support the diagnosis, to make recommendations regarding the treatment and encourage research trials recruitment.

In 2020 we established a regional Malignant Mesothelioma MDT covering the region of East Yorkshire, North Yorkshire, North Lincolnshire and Goole. This area is covered by our tertiary thoracic surgical and oncology services. There is one large teaching tertiary referral hospital and 5 smaller district general hospitals with the population covered close to 2 million including both urban areas with historical port industry and rural areas. In this report we will describe regional malignant mesothelioma MDT from the perspective of effectiveness of making the diagnosis and treatment recommendations.

Methods

A retrospective review of patients who were discussed at the regional malignant mesothelioma MDT was undertaken. The patients had assessment for history of asbestos exposure, co-morbidities, performance status. They also underwent radiological imaging including a chest radiograph, computed tomography of the thorax, thoracic ultrasound and when appropriate positron emission tomography (PET) scan. When applicable, patients underwent pleural fluid sampling and pleural biopsy (radiological or surgical). The demographics, investigational aspects and the therapeutic decisions were reviewed together with the patients' survival outcomes.

Results

Between 03/12/2020 and 24/11/2022, 150 (32 female) patients were discussed at the Regional Malignant Mesothelioma MDT meetings. Their mean age was 74.9 years (range 41 years to 89 years). Of those patients 41 did not have mesothelioma. In 29 patients a radiological diagnosis of malignant mesothelioma was made and in 80 patients a histological diagnosis of malignant mesothelioma was confirmed. The mean time from symptoms to presentation at the regional Malignant Mesothelioma MDT was 31.2 days (range 1 to 69 days).

Of those patients who underwent biopsy, 50 patients had a Video Assisted Thoracoscopic surgical (VATs) pleural biopsy, 25 had image guided either computed tomography (CT) or ultrasound guided biopsy. In 5 patients with omental mesothelioma histological diagnosis was confirmed through a laparotomy or an image guided biopsy. Histological results revealed that 52 patients had epithelioid malignant mesothelioma, of which 5 had omental epithelioid malignant mesothelioma, 17 patients had sarcomatoid malignant mesothelioma, 7 patients had biphasic malignant mesothelioma of which 1 had omental malignant mesothelioma. In 4 patients, desmoplastic malignant mesothelioma was diagnosed.

Overall survival for all patients was 10.3 months (range from 2 days to 1166 days). Following the Regional Malignant Mesothelioma MDT, 67 patients were offered best supportive care approach due to their poor performance status and their comorbidities profile. The survival in patients receiving a best supportive care approach was 8 months (rage from 2 days to 1008

days). In the group of patients receiving a best supportive care approach, 28 had a radiological diagnosis of malignant mesothelioma. Their mean survival was 6.6 months (range 2 to 1008 days). At the time of the analysis all of those patients were dead. 39 patients who received a best supportive care approach had histological diagnosis of malignant mesothelioma. 19 of those patients were assessed for systemic anticancer treatment (SACT) and were either deemed not fit for SACT or declined the treatment.

Mean Survival from the time of discussion at the Regional Malignant Mesothelioma MDT to death was 8.6 months (range 2 days to 1008 days). One patient who was diagnosed with epithelioid mesothelioma on 24/02/2022 was still alive in March 2025. For 23 patients with epithelioid mesothelioma median survival from the time of discussion at the Regional Malignant Mesothelioma MDT to death was 11.2 months (range 39 days to 1008 days). For 16 patients with other types (11 sarcomatoid, 3 biphasic, 1 desmoplastic) the mean survival from the time of discussion at the Regional Malignant Mesothelioma MDT to death was 5.2 months (range 38 days to 726 days).

37 patients received SACT and their mean survival was 12.3 months (range 63 to 1166 days). The SACT included chemotherapy or immunotherapy. 17 patients had Nivolumab/Ipilimumab of which 2 patients were still alive since 2022. 20 patients had chemotherapy Carboplatin/Pemetrexed or Cisplatin/Pemetrexed and 5 patients received palliative radiotherapy. Surgery followed by SACT was undertaken in 6 patients all of whom were diagnosed with an epithelioid malignant mesothelioma. Two of those patients were still

alive; one was diagnosed on 23/08/2023, one was diagnosed 23/06/2022. For the other patients who underwent surgery, their survival was as follows: 1 patient survival of 331 days, 1 patient survival of 449 days, 1 patient survival of 522 days, 1 patient survival of 966 days.

The reported overall median survival in our cohort of patients was 7.9 months. For patients with epithelioid malignant mesothelioma who received SACT, median survival was 12.8 months. For patients with epithelioid malignant mesothelioma who received best supportive care form of treatment had reported median survival of 7.8 months. For patients with sarcomatoid malignant mesothelioma the median survival was 3.6 months. For all patients receiving SACT the median survival was 12.4 months. For all patients receiving best supportive care the median survival was 6.4 months. For patients with a radiological diagnosis of malignant mesothelioma the median survival was 3 months.

Discussion

Our experience revealed that by setting up a regional malignant mesothelioma MDT we were able to provide a standard approach to managing patients with this condition. The decision about management of the patients with malignant mesothelioma was made by a core group of experts in manging this condition including respiratory physicians, thoracic surgeons, medical and clinical oncologists, histopathologist, radiologists, specialist cancer nurses and palliative care team. Through this approach the patients had access to all the modalities of potential therapies for malignant mesothelioma. The MDT was able to identify patients who could potentially be treated with specific therapeutic modalities. This was of particular

importance in the context of deciding on systemic anticancer treatment options or in a small, selected group of patients', on surgical interventions.

Our experience revealed that the patients who had a radiological diagnosis of malignant mesothelioma had overall poor survival around 3 months. This reflected the fact that the patients were not fit to undergo investigations to confirm the diagnosis histologically. This was related to their poor performance status and related co-morbidities. Those patients were not fit to be considered for any therapeutic options. Current therapeutic options for systemic treatment of malignant mesothelioma include a combination of immunotherapy agents or chemotherapy agents such as pemetrexed in combination with cisplatin (6-9). NICE, provided guidelines for the use of immunotherapy agents Nivolumab with Ipilimumab for untreated unresectable malignant pleural mesothelioma [6]. This was supported by the findings of studies such as Checkmate 743, which showed survival benefits of (Nivolumab/Ipilimumab) compared to chemotherapy (Platinum/Pemetrexed) for patients with epithelioid malignant mesothelioma and more importantly for those with non-epithelioid malignant mesothelioma where the overall survival benefits were more pronounced with observed overall survival of 18.1 for immunotherapy compared to 8.8 months for chemotherapy group [7, 8]. Our findings confirmed that patients with sarcomatoid malignant mesothelioma when appropriately selected had similar outcomes to those reported in large studies when treated with immunotherapy. Those survival benefits were also similar for patients with epithelioid malignant mesothelioma who received systemic anticancer treatment.

In the context of malignant mesothelioma surgery may be considered in a small, selected group of patients [10, 11, 12, 13, 14]. However, there are limitations of surgery as described by the findings of MARS study, which reported high morbidity associated with extra pleural pneumonectomy [12]. There is, however, potential role for decortication or pleurectomy [13, 14]. In our cohort of patients, a small number of carefully selected patients underwent surgery in the form of pleurectomy or decortication. Those patients had epithelioid malignant mesothelioma, were generally fitter with good performance status and had less co-morbidities. Surgery according to the current recommendations was part of the multimodality treatment [15]. Those patients underwent careful assessment including systematic investigations combined with the decision from the multidisciplinary team composed of respiratory physicians, thoracic surgeons, radiologists, histopathologists and oncologists.

Based on our experience we can come out with some suggestions and observations. Patients with radiological diagnosis of malignant mesothelioma had shorter survival around three months, mainly related to their poor performance status and co-morbidities profile. Patients with sarcomatoid malignant mesothelioma should be carefully assessed as immunotherapy as this form of treatment may result in better outcomes in this group of patients. Patients with epithelioid malignant mesothelioma had overall better outcomes and they should be carefully evaluated with regards to treatment options including systemic therapies or multimodality treatment approach including potential surgery. Finally, surgery in selected patients is an option but the patients should be carefully evaluated, and the procedure should

be undertaken by a thoracic surgeon who has significant experience in performing those procedures. The MDT approach allowed for a standardised care for all patients with malignant mesothelioma through our region. In order to improve the structure of the malignant mesothelioma MDT an active pre-MDT screening of the cases was introduced, which allowed to assure that all the required information such as imaging and histology samples were available. The communication between the MDT and the referring teams was standardised allowing for all the relevant information at the time that the patients were discussed. We observed increased number of image guided biopsies to be undertaken, reflecting interventional radiology team experience. Our histopathology team developed expertise in diagnosing malignant mesothelioma and provided a reference to the local hospitals' teams. The oncology team developed expertise in the use of systemic treatments including immunotherapy in the context of malignant mesothelioma. Finally, close links were established between our cancer specialist nurses and the local malignant mesothelioma patients support group allowing for the patients to have access and support. In conclusion the regional malignant mesothelioma MDT has provided a standardised approach to managing patients with this condition therefore providing care based on expertise of many specialists involved in the patients care.

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