

The challenges of diagnosing soft tissue sarcomas

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Abstract

Soft tissue sarcomas a rare group of cancers that can affect various parts of the body, although the vast majority occur on the extremities where they may present as a slow growing painless mass. The symptoms of soft tissue sarcomas are very much dependent upon the area of the body that is affected. The rarity of the condition, as well as the subtle nature and varied symptoms patients present with can add to the diagnostic challenge and lead to delays in diagnosis. The purpose of this article is to identify the factors that influence delays in diagnosis and the impact of this on the prognosis of the condition.

Keywords: soft tissue sarcoma, diagnosis, challenge, delay, prognosis

الملخص:

سرّكومة الأنسجة الرخوة هي مجموعة نادرة من السرطانات التي يمكن أن تصيب أجزاء مختلفة من الجسم، وإن كانت تعتمد أعراض سرّكومة . غالبيتها تحدث في أطراف الجسم حيث قد تظهر كتلة صلبة غير مؤلمة تكبر بشكل بطيء ندره حالات الإصابة بهذا السرطان إضافة إلى الأعراض . الأنسجة الرخوة بشكل كبير على المنطقة المصابة من الجسم الغرض من هذا المقال هو تحديد العوامل التي . الطفيفة والمتنوعة للإصابة يُمكنها أن تزيد من صعوبة التشخيص وتأخره . تؤدي إلى التأخر في التشخيص وتأثير ذلك على التنبؤ بالحالة

سرّكومة الأنسجة الرخوة، التشخيص، التحدي، التأخر، التنبؤ: الكلمات الدالة

1. Introduction

Soft tissue sarcomas are an uncommon group of tumours, representing around 1% of adult and approximately 7-15 % of paediatric malignancies.¹ The annual incidence in Europe is estimated to be around 4-5/100,000.² Soft tissue sarcomas are of mesenchymal origin and can occur anywhere in the body, however around 60% are found on the extremities³Most sarcomas are thought to occur spontaneously with no clear aetiology however, a few are associated with other conditions such as Li Fraumeni syndrome and Neurofibromatosis. Sarcomas most commonly occur in the middle age group, although there are certain sarcomas that are more common in children such as Rhabdomyosarcoma, Osteosarcoma and Ewings tumours. Rhabdomyosarcomas are the most common form of soft tissue sarcomas in children.⁴

Symptoms of soft tissue sarcomas are dependent upon the area of the body affected, but typically they can present as a painless mass. Usually these masses are slow growing and symptoms, if any, are the result of compression or invasion of normal structures, and therefore vary considerably depending on the location of the lesion. For example, orbital sarcomas may cause proptosis, intra-abdominal sarcomas may cause abdominal fullness, constipation, back pain, or early satiety. Genitourinary soft tissue sarcomas can cause haematuria. Malignant tumours tend to be larger than benign lesions.⁵ When soft tissue sarcomas occur below deep muscle fascia they can be difficult to identify early and they often become very large before being detected.

MRI is the gold standard for diagnosing soft tissue sarcomas, however as access to MRI is often limited, ultrasound is a reasonable initial investigation.⁶ CT can be useful for the investigation of abdominal sarcomas and CT chest is important for detecting metastasis. Tissue biopsy is essential for a precise histological diagnosis. Once all the imaging and samples are available, ideally the diagnosis should be made via a multi-disciplinary team of surgeons, pathologists, oncologists and radiologists.

Surgical excision with wide margin of normal tissue is the mainstay treatment, however consideration needs to be taken regarding minimising loss of normal tissue which could result in an unacceptable loss of function. Furthermore, wide margins may not be feasible due to proximity with key organs and in such situations, patients may be offered adjuvant chemotherapy. Some paediatric tumours are treated with chemotherapy prior to surgery whereas adult sarcomas have a low sensitivity to chemotherapy and radiotherapy, and so these therapies are generally used in the palliative setting.⁷

The clinical subtype of the soft tissue sarcomas appears to be one of the most important factors in predicting treatment failure, therefore the role of initial surgery and accurate biopsy is crucial.⁸ The 5 year survival varies depending on the grade of the lesion, with lower grade lesions having higher survival rates of 90% and less than 50% for the high grade sarcomas.⁹ There is variability in cancer survival among different countries, for example there is a lower cancer survival in Denmark and England compared to other European countries.¹⁰ Many other factors affect the prognosis including, the subtype and dissemination of the disease, the malignancy grade, comorbidity of the patient and tumour size with larger tumours having worse outcomes.¹¹

2. What causes the delay?

Delays in diagnosis is a challenging problem in many cancers. Delays in diagnosis can be attributed to various aspects of the process from patient recognition of symptoms, to medical professional failing to identify and manage the condition including inappropriate intervention of a suspected benign condition.



i) Patient factors

Patient delay occurs when patients fail to identify their symptoms as serious or suspicious of cancer and the reasons for delay in presentation by patients are complex and multifactorial. Lack of awareness of the cancer is considered a key factor in delayed presentation, especially if the symptoms are atypical.¹²

The Anderson model¹³ reports different forms of delay patients can experience; patients can have appraisal delay which is the time taken for the patient to recognise that the symptom is an illness whereas behavioural delay is the delay on acting on the thoughts and the physical action of seeking professional help. The process of patient appraisal is not as linear as originally proposed and research suggests the process continues during and after seeking professional help.

Lack of awareness regarding cancer and sinister symptoms can lead to a delay in the patient seeking medical attention. As well as lack of knowledge regarding cancer symptoms themselves, this includes misconceptions about the risks of developing cancer or effectiveness of treatment which can all contribute to patient delay.¹⁴ Evidence suggests there are many other patient factors that are known to cause late presentations such as the patients age, ethnicity, socio-economic and cultural circumstances.^{15 16}

ii) Doctor factors

Primary care delays occur when there is a failure to recognise or appropriately investigate or manage soft tissue sarcomas. In many parts of the world the role of primary care is a gatekeeper function in accessing secondary care services, therefore primary care physicians play a crucial role in identifying and managing cases appropriately. The majority of patients presenting with cancer symptoms to primary care will have a diagnosis other than cancer and identifying those who have malignancy and not missing a potential cancer can be challenging.¹⁷ The skill of primary care physicians is filtering those at risk and those who simply present with self-limiting problems.

There are large differences in diagnostic delays pertaining to different cancers. In particular the primary care delay tends to be shorter for cancers where there are palpable or physical symptoms, such as breast cancer, and melanoma.¹⁸ The early detection of cancer in primary care can be challenging, particularly as patients often present with non-specific symptoms.¹⁹ The subtle symptoms patient with soft tissue sarcomas can present with can contribute to the delay as patient may have vague symptoms which do not quickly raise the alarm for sinister pathology. Another factor contributing to the medical professional delay in diagnosis is the rarity of the condition as an average GP will see 1 case in 24 years of practice.²⁰ The variability in presentation of soft tissue sarcomas means that should a primary care physician

be unfortunate to encounter another case of sarcoma it may be a very different presentation, even if it affects the same organ.

Inappropriate referral to the incorrect speciality also adds to the delay and may result in a worse outcome for the patient. Due to the rare presentation of soft tissue sarcoma, inappropriate surgery may be performed under the assumption that the lesion is benign, with lack of adequate surgical margins.²¹ Biopsy is key in the management of soft tissue sarcomas, however performing the biopsy can be dangerous and should ideally be performed by experienced sarcoma experts.²² There is a risk of seeding along the biopsy tract, as well as risk of a false negative result if the specimen is taken from the incorrect part. Adequate interpretation of the biopsy is needed, and ideally an experienced pathologist should be used, however given the rarity of the condition this can be challenging.²³

iii) The use of cancer pathways – a help or hindrance?

Various countries have adopted cancer pathways in order to improve cancer outcomes including Spain, Denmark and UK. In the UK the 2-week-wait referral pathways for primary care are urgent cancer referral pathways which require priority and investigation within 2 weeks of referral. There is evidence to suggest there is significant variability in which general practices use the urgent referral pathways for suspected cancer and consequently the accuracy of their patient selection for urgent referral varies considerably.²⁴ There is an association between the low use of urgent referral for suspected cancer in general practices and increased risk of death among patients with cancer.²⁵ For some cancers, there is evidence that the use of the pathway is associated with a shorter time to diagnosis and treatment, although the size of the effect varies by cancer site. The use of cancer patient pathways in for suspected sarcoma in Denmark, have resulted in a reduction in time before referral to first appointment for all patients and accelerated the diagnostic process.²⁶

However, such referral pathways can be problematic as they have been criticised for describing common high-risk presentations of cancer and neglecting those who present as low risk, or unusual atypical symptoms. Patients presenting with vague symptoms are likely to have later diagnosis as the symptoms may not fit into the urgent referral criteria.²⁷ Furthermore, referral guidelines for some cancers may not be helpful in detecting patients with early symptoms and some studies have found that referral pathways prioritise those with a history of more advanced disease.

3. The effects of a delayed diagnosis

Studies have shown that delays in diagnosis can be important, but the impact of such delays varies considerably depending on the type of cancer. In particular the effect on prognosis is incredibly difficult to quantify due to the lack of trial evidence.²⁹

Given that the size of a soft tissue sarcoma is a prognostic factor it would be sensible to predict that an earlier diagnosis would result in a better outcome, assuming that the lesion

would have been smaller when detected. Research on the symptom duration and prognosis has demonstrated variable results including evidence of increasing, decreasing and having no impact on survival.³⁰⁻³²

Sarcomas unlike other forms of cancer are incredibly variable and as the prognosis is very much linked to the type of sarcoma, it is likely that this contributes to the difficulties in establishing a relationship between diagnostic delay and prognosis.

4. Discussion

In countries with strong primary healthcare systems, primary care physicians are typically the first point of contact for patients, making early recognition of cancer symptoms crucial. This can be a challenging task particular for cancers such as sarcomas which are considered harder to suspect as the patient may present with vague symptoms. The vast majority of patients presenting to primary care with vague and non-specific symptoms will have a non-malignant diagnosis. Many countries choose to adopt a cancer - pathways which can be helpful but may not be useful for detecting symptoms of early cancer. There is evidence to suggest that the use of risk assessment tools may be beneficial in encouraging primary care physicians to think about referrals which may lead to earlier diagnosis.³³ It is important to recognise the limitations with any set of clinical pathways or risk assessment tools.

Although there is some debate regarding the effect of diagnostic delay on the outcome of cancers, there is no doubt that prompt investigation and appropriate management of cancers improves the patients experience. Delays can have an untoward effect on the patient's mental health, both through the increased anxiety prior to diagnosis as well as concerns about whether the delay will affect the prognosis.³⁴ Furthermore there is little doubt that the size of the sarcoma can affect the surgical options, with greater loss of function and potentially increased cosmetic impact with larger lesions.

5. Conclusion and Recommendation

Soft tissue sarcomas can be challenging to recognise and patients may present with vague symptoms. Efforts to support the diagnostic process and considering using risk assessment tools may lead to an earlier diagnosis. Furthermore, using clinical audit and root cause analysis can be useful as a shared learning experience.

Further research on the factors influencing early detection of soft tissue sarcomas is needed, as this will allow for targeting of therapies and interventions. For example, with regards to breast cancer it has been recognised that older women have a more of a delay in diagnosis, so a campaign specifically targeting this population can be useful.³⁵

There are many public health campaigns on the common cancers and understandably so.

The rarity of soft tissue sarcomas contributes to the reduced awareness of the condition. Patient and doctor education is key, as well as public health campaigns which are useful in highlighting red flag symptoms and lead to an increased diagnosis of cancers.³⁶ Finally, further research is needed to examine the benefit of wider access to currently restricted investigations such as endoscopy, CT/MRI and the impact this would have on sarcoma outcomes.

In conclusion, although sarcomas are a rare group of cancers, understanding the various factors that influence diagnostic delay will guide research and future interventions which is essential to improve the diagnosis and management of the condition.

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