Feline injection site sarcomas – the old and the new

Feline injection site sarcomas are rapidly growing mesenchymal tumours that develop in sites where vaccines and other medications are administered. They are locally invasive tumours with a low-moderate metastatic rate. Tumour recurrence is very common and outcome improved when tumours are small at diagnosis and amenable to aggressive surgical excision. Multimodality therapy is often recommended however the precise role of radiation therapy and chemotherapy requires further investigation. Guidelines for feline vaccination have been developed in light of the potential for injection site sarcoma development at the site of vaccination.

Key words: Feline injection site sarcoma, feline vaccine-associated sarcoma, chemotherapy, radiation therapy, surgery, feline vaccine.

Introduction

Feline injection site sarcomas were historically referred to as ‘vaccine-associated sarcomas’ following their initial links to vaccine administration in the early 1990s (Hendrick & Goldschmidt 1991, Kass et al. 1993). Although these tumours most commonly develop following vaccination, in recent years similar tumour development has been identified in cats following the injection of non-vaccine related foreign material such as antibiotics, steroids, meloxicam and microchip implantation (Kass et al. 2003, Daly et al. 2008, Munday et al. 2011, Martano et al. 2012). This has lead to the preferred nomenclature of ‘feline injection site sarcoma’.

How vaccines and other foreign material contribute to sarcoma development is not yet fully understood. Chronic inflammation likely plays a major role, however it is well accepted that the aetiology of feline injection site sarcomas is complex and multifactorial (Martano et al. 2011).

Incidence

An accurate indication of the incidence of feline injection site sarcomas in the UK is very difficult to determine. It is clear, however, that the disease is uncommon with an incidence of 1 case of feline injection site sarcoma/5000 feline vaccination visits suggested in one recent study. (Dean et al. 2013). Given the low incidence of feline injection site sarcomas, and their occasional development following the injection of non-vaccine related foreign material, cats should continue to receive necessary vaccines and injections particularly when the risk/incidence of disease is higher than that of sarcoma development.

Presentation

Feline injection site sarcomas are generally rapidly growing masses that develop at sites commonly used for injection (such as the interscapular region). Any mass that develops in a region that has been used for injection (even if the most recent injection was months or years prior) should be treated with suspicion. Feline injection site sarcomas are generally fast growing and infiltrative. Achieving an early diagnosis is of great importance as small injection site sarcomas are more likely to be successfully treated with surgical excision.

Diagnosis

Cytology is useful for the diagnosis of approximately 50% of feline injection site sarcomas. The relatively low diagnostic yield of this procedure is likely related to the mesenchymal nature of the tumours as mesenchymal tumours tend to exfoliate less well for cytology. Fine needle aspirate cytology is recommended as the first step in the diagnostic process for cats with masses that appear in sites commonly used for injection. Fine needle aspirate cytology should not be delayed as these tumours should not be delayed as these tumours are more successfully treated when small at diagnosis and amenable to aggressive surgical excision.

If cytology and/or the clinical presentation is suspicious of feline injection site sarcoma biopsy is recommended. Wedge or punch biopsy is recommended and both are generally uncomplicated to perform. Wedge and punch biopsies are types of incisional biopsy. Incisional biopsy is preferred to excisional biopsy for injection site sarcomas.
because of the highly infiltrative nature of the tumours. Biopsy should be performed at sites that do not extend the surgical margin required to remove the tumour (i.e. avoid the edges of the tumour). Keep in mind also that the centre of the tumour can contain larger amounts of necrotic tissue which may complicate diagnostic yield. Given the challenging nature of treatment of feline injection site sarcomas, referral at the point of cytological suspicion or histopathological confirmation of feline injection site sarcoma may be elected.

Excisional biopsy is an attractive option for pet owners in the hope that it will minimise procedures for the patient and expense for the owner. Unfortunately, this is rarely the case for feline injection site sarcoma. Recurrence rates are extremely high when surgical margins are minimal and where the (often interscapular) anatomy makes successful revision surgery very challenging. Excisional biopsy for the diagnosis of suspected injection site sarcoma is therefore not recommended. It increases the number of procedures for the patient and negatively impacts survival times. Achieving a diagnosis prior to treatment significantly improves the chances of a successful outcome for the injection site sarcoma patient.

**Pathology**

Injection site sarcomas are often described as a type of fibrosarcoma however other sarcoma types are also reported including rhabdomyosarcoma, osteosarcoma and chondrosarcoma. Characteristics of aggressive biological behaviour such as marked nuclear and cellular pleomorphism, increased tumour necrosis, high mitotic activity and the presence of peritumoural inflammation are common on histopathology (Henrick & Brooks 1994). Macrophages may contain aluminium hydroxide if used as vaccine adjuvant (Morrison et al. 2001). One study reporting 59% of feline injection site sarcomas to be high grade tumours (Phelps et al. 2011).

**Clinical Staging**

Feline injection site sarcomas are locally invasive with a low–moderate metastatic rate (approximately 20–28%, Hershey et al. 2000, Phelps et al. 2011). For this reason recurrence tends to be of greater concern than metastasis. Reported sites of metastasis vary but commonly include lungs and/or lymph nodes (Hershey et al. 2000). Haematology, biochemistry, FeLV/ FIV status and urinalysis are recommended for evaluation of the general health of the patient prior to treatment. Evaluating the general health is useful to better manage the patient medically, to better evaluate risks and to provide prognostic information to the pet owners prior to expensive or invasive procedures.

Thoracic imaging is recommended to evaluate for metastatic disease. Left lateral, right lateral and ventrodorsal thoracic radiographs tend to be the most practical method of evaluating for pulmonary metastases in general practice. Where referral is an option for the patient, CT of the thorax is preferred. CT has greater sensitivity at detecting smaller metastatic lesions and the benefit of evaluating the depth of the tumour to assist with surgical planning (Figure 1).

Feline injection site sarcomas are generally much larger than they appear on physical examination. One study evaluating the utility of CT for injection site sarcomas showed the size of the tumours on CT to be approximately double what was measurable on physical examination (McEntee & Page 2001). Either CT or MRI prior to surgery can improve anatomical understanding of the extent of the tumour for the surgeon and, improve the likelihood of a successful surgery (McEntee & Page 2001, Rousset et al. 2013).

Abdominal ultrasound is sometimes performed prior to treatment to better evaluate the general health of the patient prior to invasive treatment. Theoretically, abdominal metastases are more likely when the tumour is on the caudal half of the body (e.g. hind limbs). In cases where CT of the thorax is performed for clinical staging the CT may be extended to include the abdomen in order to evaluate for metastases or other concurrent disease.

**Treatment**

The best outcome for feline injection site sarcoma patients is associated with complete surgical excision performed by a specialist soft tissue surgeon (Hershey et al. 2000). Investigation and referral early in the disease process has the potential to be of great benefit. The role of radiation therapy and chemotherapy is less well understood and early discussion with a medical oncologist is recommended. In some cases chemotherapy and/or radiation therapy may be offered in addition to surgery depending on clinical staging results, pathology results and geographic availability of treatment modalities.

Surgical excision of injection site sarcomas is complicated by the infiltrative and invasive nature of the tumours. Wide surgical excision offers the best chance of cure. Several studies have also shown that longer survival is expected when a complete excision is achieved at the first surgery (Hershey et al. 2000, Phelps et al. 2001). A surgical margin of 2-3cm laterally and one fascial plane deep was, historically, recommended. Unfortunately, incomplete margins were common and recurrence rates high with this method (Hershey et al. 2000). One study reported tumour recurrence rates of approximately 19% in cases where complete excision was achieved and 69% when excision was incomplete (Giudice et al. 2010).

The high rate of recurrence prompted investigation of a larger surgical dose. One recent study reported lateral margins of 5cm and deep margins of two fascial planes or bone (Phelps et al. 2011). In this publication nearly all (97%) cases were histologically reported as complete excisions. Extending the surgical dose significantly improved the likelihood of a successful surgery. Unfortunately, some tumours with complete excisions reported on histopathology still recurred. Local recurrence rates of 14% were reported and the overall median survival time was 901 days.

This aggressive surgical method appears to offer a better outcome than more conservative surgical excisions (Figures 2–4). The pattern of recurrence suggests that close ongoing monitoring for recurrence