A case-control study of Feline Injection Site Sarcoma in the UK

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Background and Introduction

Feline Injection Site Sarcoma (FISS) are a group of clinically aggressive neoplasms that occur at distinct anatomic locations used for the administration of injections.

These tumours have previously been referred to as vaccine-induced or vaccine-associated injection site sarcomas. Some epidemiological studies performed in the United States have indicated that vaccination (against rabies & FeLV) may be a risk factor for tumour development[1-3]. The potential association between vaccination and FISS is unclear, but FISS may represent the most serious adverse event following the vaccination of cats. Recently other injections such as lufeneron have also been implicated in the development of these tumours.

To date there has been no extensive epidemiological study of FISS in cats in the UK.

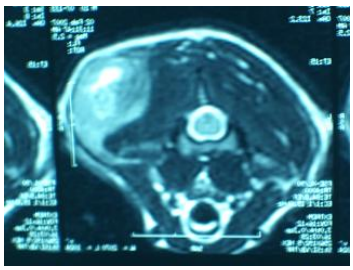

Fig 1. MRI scan of a cat with a FISS dorso-lateral cervical spine

Hypothesis

The main hypothesis is that: **vaccination, drug administration or local trauma is associated with the development of feline injection site sarcomas**

Aims

1. To reach a consensus on the histological diagnosis of FISS in cats in the UK, that can be used as the case definition for the study
2. To identify risk factors for the development of FISS in cats in the UK

Histopathology consensus for case definition

Objective: To form a consensus of expert opinion on the histological features of FISS and determine the case definition for the case-control study.

Methods:

•Five leading veterinary pathologists in the United Kingdom were recruited to the study.

•50 slides were examined by each of the histopathologists including:

- 30 feline injection site sarcoma (FISS),
- 13 soft tissue sarcomas (STS)
- 7 fibrosing panniculitis (FP)

• Pathologists were blinded to the original diagnosis, and to the anatomical location from which the sample was taken

• Each pathologist awarded a score (adapted from Couto[4]) for each slide and then made a final diagnosis of FISS, STS or FP.

Results

The discordant slides (21/50 when ≥ 1 pathologists disagreed) were discussed at round table meeting

An interim set of major and minor criteria were developed for FISS.

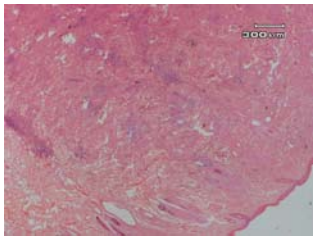

Fig 2 – Marked inflammation, aggregations of lymphocytes, cellular pleomorphism and necrosis are all histopathological characteristics of a FISS lesion (H&E, x300)

Completing the consensus

•30 of the original 50 slides are to be re-examined by each of the histopathologists :

- 20 feline injection site sarcoma (FISS),
- 10 soft tissue sarcomas (STS)

•Pathologists will blinded to the original diagnosis, and to the anatomical location from which the sample was taken.

• Each pathologist will each slide using a new scoring system and then make a final diagnosis of FISS, possible FISS or STS.

Based on these findings a final set of criteria will be developed and used as the case definition for the case-control study.

Case-control Study

Objective: To examine the relationship between putative risk factors and the likelihood of FISS development.

Definitions:

Case: a cat with a tumour that meets all of the histopathology criteria of a FISS

Control: a cat without a FISS that is from the same defined population as the cases.

Defined population: the cats attending the veterinary practice that submit histopathology samples to the collaborating laboratories.

Sample size calculations

A sample size of 960 (192 cases and 768 controls in a 1:4 design) would be sufficient to be 80% confident of detecting a significant (P <0.05) two-fold increase in risk, assuming 10% primary exposure (e.g. FeLV vaccination) in the control group.

To allow for non-response, loss to follow-up and exclusion of cases and controls after data collection, we will aim to increase the sample size by 30% to 250 cases and 1000 controls for a total sample size of 1250.

Fig 3. A cat with a FISS in the interscapular region

References: 1. Kass et al, *JAVMA* **203**:3 396-405(1993), 2. Gobar et al JAVMA **220**:10 1477-1482, 3. Kass et al *JAVMA* **223**:9 1283-1292, 4. Couto et al, *Vet Pathol* **39**:33-41(2002),

Methods:

Recruitment of cases

• Cases are identified at the five collaborating pathology services

• Questionnaire is distributed to the owner of the FISS case

• Medical records are obtained from the practice.

• Histopathology of all cases will be reviewed by the pathologists using the histopathology criteria for inclusion/exclusion to the study as appropriate.

Recruitment of controls

• Veterinary practice who regularly submit diagnostic samples to the histopathology collaborators were invited to participate in the study.

• Each control practice will be required to recruit a maximum of 5 controls during the course of the study.

• Each time a case is recruited to the study, 4 different control practices are randomly selected to recruit a control

• Questionnaire is randomly distributed to a client that owns a cat over the age of 5 years

• Medical records for the control are obtained from the practice.

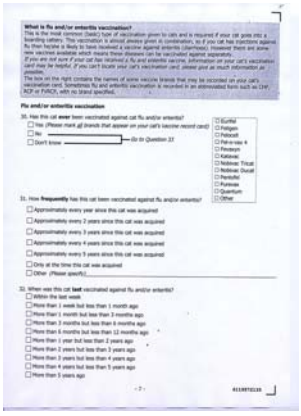

Fig 4. A page of the questionnaire concerning vaccination

Results

Since the case-control study was initiated:

Cases

• 48 cases have been identified by the collaborating pathologists.

• 27 RVS have agreed to participate in the study to date, one RVS has declined.

• 9 completed questionnaires have been returned

Controls

•108 questionnaires have been distributed to RVS

•30 completed questionnaires have been returned

•163 practices have agreed to become control practices

Reminders are being sent 4-8 weeks after initial contact has been made.

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