



INFECTIOUS DISEASE: MINIREVIEW

Feline Injection Site Sarcomas: Data from Switzerland 2009–2014

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Summary

Feline injection site sarcomas (FISS) were first described in the early 1990s. Despite extensive research, the pathogenesis of these tumours has not been elucidated conclusively. Their appearance and the marked increase in their incidence has been mainly connected to the injection of vaccines, and it is assumed that a chronic inflammatory reaction at the injection site triggers subsequent malignant transformation. The role of alum-based adjuvants has been discussed, but is controversial. The present study of the Swiss Feline Cancer Registry (SFCR) with data from 2009 to 2014 revealed a marked decrease of the incidence of fibrosarcomas compared with the previous observation period. Notably, this drop occurred after a non-adjuvanted feline leukaemia virus vaccine was introduced in Switzerland in 2007. This observation, together with the previous findings of the SFCR, further supports the notion that alum-adjuvanted vaccines are involved in the genesis of FISS and that non-adjuvanted vaccines might be safer for cats.

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Feline injection site sarcomas (FISS) were first described by [Hendrick and Goldschmidt \(1991\)](#) who noted an increase in sarcomas at anatomical locations preferentially used for injections in cats. They related the increased tumour frequencies to the administration of rabies and feline leukaemia virus (FeLV) vaccinations. Subsequent studies reported sarcoma development following the injection of other non-adjuvanted vaccines, long-acting antibiotics, steroids or lufenuron and even after the use of non-absorbable suture material and microchip implants ([Lester et al., 1996](#); [Burton and Mason, 1997](#); [Esplin and McGill, 1999](#); [Buracco et al., 2002](#); [Kass et al., 2003](#); [DeMan and Ducatelle, 2007](#); [Daly et al., 2008](#)).

Despite extensive research, the underlying pathogenesis of this neoplastic process has not been elucidated. The most widely accepted hypothesis implies

that a chronic inflammatory reaction at the injection site triggers subsequent malignant transformation ([Hendrick and Brooks, 1994](#); [Hartmann et al., 2015](#)). The fact that alum-containing adjuvanted vaccines induce intense local inflammation has fuelled the speculation that they might be particularly linked to the development of FISS ([Hendrick et al., 1992](#); [Macy and Hendrick, 1996](#); [Day et al., 2007](#)). However, the role of adjuvants in the causation of FISS has remained controversial ([Woodward, 2011](#)). Among other studies that support the role of adjuvanted vaccines in the genesis of sarcomas ([Day et al., 2007](#); [Srivastav et al., 2012](#)), a previous analysis by the Swiss Feline Cancer Registry (SFCR) from 1965 to 2008 revealed a marked increase in the incidence of fibrosarcomas after the introduction of an adjuvanted FeLV vaccine into Switzerland in 1986. The aim of the present study was to analyse data from the SFCR from 2009 to 2014 and report on diagnoses of fibrosarcomas during this period. We

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compare the new data with the findings of the previous analysis (Graf *et al.*, 2015, 2016).

From the beginning of 2009 to the end of 2014, 21,692 feline tissues were sent for pathological examination to the laboratories contributing to the registry. Neoplasia was diagnosed in 41% (8,923) of the samples. Of these, 1,512 tumours were diagnosed as fibrosarcoma, of which 96% were in the skin/subcutis. The most prominent locations were the skin of the shoulder, flank and back area. The proportional distribution of fibrosarcomas in these areas was similar in the years 2009–2014 compared with the previous observation period, despite the recommendations by the Swiss Association for Small Animal Medicine (SVK-ASMPA) to avoid injections into the shoulder area and to use the flank or hindlimb regions instead (Swiss Association for Small Animal Medicine, 2008). Analyses of the influence of age revealed that fibrosarcomas occurred more frequently in middle-aged and older cats, with a mean age of 11 years (Fig. 1). The mean age of cats presenting with a fibrosarcoma was slightly higher compared with the 1965 to 2008 period (10.3 years), but remained stable from 2009 to 2014.

Twelve percent of the whole patient population examined from 2009 to 2014 were entire male, 38% neutered male, 13% entire female, 31% neutered female and 6% of unknown sex. These proportions did not appreciably change over those years. As many as 4.7% of all entire males, 5.6% of neutered males, 5.1% of entire females and 6.8% of neutered females presented with a fibrosarcoma, thus confirm-

ing the previously reported slight, significant differences in sex/neutering status risks (Graf *et al.*, 2016).

Multiple regression analysis revealed that no breed had significantly higher odds of developing a fibrosarcoma compared with the European shorthair cat (odds risk [OR] = 1). However, in concordance to the previous analysis spanning the years 1965–2008, several breeds had significantly lower odds ratios (Fig. 2) (Graf *et al.*, 2016). It remains open as to whether this effect is related to genetic differences or is due to differing vaccination practices.

Data from 2009 to 2014 revealed that the very high relative diagnostic frequency of fibrosarcoma in the beginning of 2000 (20% of all tumours) began to decrease markedly from 2010 to 2014 (11%) (Fig. 3). In absolute numbers, fibrosarcoma diagnoses decreased from 282 in 2009 to 160 in 2014 (Supplementary Table 1), while the overall submissions to the contributing pathology laboratories remained stable.

There are no official statistics about the cat population in Switzerland, only estimated numbers from the pet food industry are available. These estimates ranged between 1.3 and 1.5 million cats for recent years and there are no indications of major changes in the population size (European Pet Food Industry, 2016).

FISS develop most frequently at injection sites. Several studies indicate an influence of the vaccine adjuvant alum, which is added in order to trigger the immune response when an inactivated

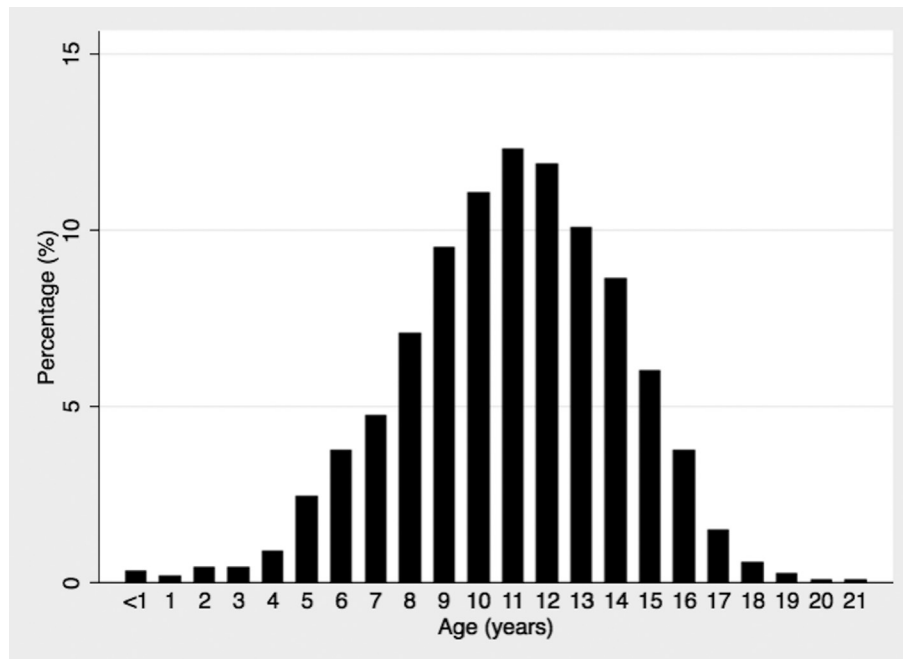


Fig. 1. Age distribution of cats on development of fibrosarcoma (2009–2014).

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