

The Confusing Picture of Boxer JKD

By Bruce Cattanach



It is clear from anecdotal evidence that kidney disease has existed in Boxers for many years but the frequency has always been low, diagnosis has been uncertain, and there has only been dubious evidence that it might be inherited. It has ‘appeared’ and ‘disappeared’ in several Boxer groups such that, with the knowledge that kidney failure can be caused by external agents, it is hardly surprising that many breeders have been sceptical about the disease having a genetic basis. Even as evidence is currently accumulating; uncertainty and confusion dominates thinking.

Here I summarise this background history as I have seen it, leading on to the more definite evidence that we have today.

Background

I have been made aware of kidney disease in Boxers a number of times over the past 30 or so years. But up until about 5 years ago, I too was not truly convinced it was inherited. I first saw kidney disease in Boxers at the time of progressive axonopathy (PA) in the early 80s. That delightful lady, Leslie Boyle, came to me seeking advice over a couple of litters that contained show age puppies that were suffering from kidney failure. The two litters were related; both were inbred on one of Leslie’s major dogs. The evidence for the condition being inherited was there, but limited, and only loosely suggested that a recessive gene might be involved. However, Leslie accepted that there was a risk that should be avoided and took it seriously enough to close the line. Sadly, she died a few years back and never learned that she had made the right decision.

No more cases appeared and I thought that this might be the end of the matter, but early in the 2000s I learned that Sweden had been picking up kidney failures in Boxers with the Swedish Kennel Club immediately banning parents from further breeding. Some of these dogs were British-bred. On enquiry, I was supplied with the pedigrees, but they showed a mixture of lines and nothing to indicate to me that the condition was really inherited. I was even less convinced when I learned that Sweden was recording kidney problems in a number of breeds at the same time. This did not sound like a genetic problem.

Not long after I was notified that a small group of American Boxers were suffering kidney problems. Obtaining the pedigrees I saw that some showed inbreeding on one notable stud dog of the day, but seeming outcrosses had also produced the disease. Again, a genetic effect seemed possible but a bit dubious, yet there was enough concern among owners that blood samples were collected and sent to Dr Lindblad-Toh at the Broad Institute to instigate a scan to find the gene; and funding was obtained in the name of one unfortunate dog, Suki – “the Suki Story” (<http://www.jdarasboxers.com/suki.htm>). The amount of material was admittedly limited but no indications of a responsible gene were detected. This event brought some further hints of kidney disease in the UK to my attention, but again a genetic effect could not be seen. However, kidney disease was clearly around as in-

ternal medicine specialist Marge Chandler of Edinburgh University was able to collect some 30 cases within a short period of time. She published a detailed paper in 2008, but, as before, the pedigree evidence did not stretch to establishing a genetic cause. Shortly after, Sheila Cartwright of Tyegarth Boxers reported early observations of Boxers suffering a range of kidney problems to Breed Council, but nothing came of this.

But finally, when a general practice vet asked me to speak to one of his clients, Sharon McCurdy, who was experiencing numbers of kidney cases in her breeding, I found I was faced with indisputable indications that the condition was indeed inherited. The evidence that gradually accumulated was as follows:

Genetics and breeding

- The first pedigrees provided by Sharon McCurdy showed close inbreeding on one dog, immediately suggesting an inherited basis with a recessive gene likely to be involved.

- This conclusion was then supported by further pedigrees presented by other breeders. All showed the same inbreeding on the same dog. A family group was evident.

- Cases were found involving the key dog’s ancestors and relatives. Inbreeding on them was producing the disease. The family group was thus much larger and it seemed that the main core of British breeding was involved.

- Cases were then detected in outcrosses to foreign dogs, seemingly disputing a recessive gene inheritance.

- As already indicated, kidney disease had been found in Boxers elsewhere in the world and when all the pedigrees internationally were considered together one found that the foreign dogs that had produced the kidney disease in the UK came from families that had produced the disease in their own countries.

- In all cases that could be studied there was therefore either inbreeding or a doubling up on the disease from both sides of pedigrees. The pedigree evidence fully supported the recessive gene inheritance and further indicated that the same gene was responsible for kidney disease in Boxers world-wide.

- There were several problems with this conclusion though. With a recessive gene, 25% of puppies in affected litters should be affected, and while we have as yet little evidence on the actual frequency, it is abundantly clear that the incidence must be much lower. For example, extensively-used males often produce no more than a single affected pup. There was also the finding that far more bitches are affected than dogs, and that age of onset is not a crucial factor for diagnosis. Further understanding of the disease itself was needed.

The disease

- The kidney disease has most typically been seen in young, juvenile Boxers (less than 3 years of age). Hence the inclusion of the term ‘juvenile’ in naming the disease.
- For diagnosis in Sweden and America, detailed histo-pathology has been the absolute requirement to define what is known as ‘renal dysplasia.’ Hence the name they use, juvenile renal dysplasia (JRD), or renal dysplasia (RD).

- Other names for the disease, such as progressive nephropathy, chronic renal failure, Ask-Upmark syndrome, polycystic kidney disease, and others have also been applied simply to describe what was found on pathology.

- In the UK, diagnosis has been based simply on symptoms and standard blood and urine analyses, but with the critical rider that there must be family evidence of the disease being inherited. Hence, application of the broad, non-specific name, juvenile kidney disease (JKD) to denote the inherited kidney disease we find in Boxers.

- With seemingly different diagnoses, it has not been clear to researchers in the past whether there were several different kidney diseases within the breed or only one with different expressions or effects.

- However, as all these conditions appear to be occurring within the same family groups, an important conclusion from the pedigree studies is that most, whatever their diagnostic names, are merely manifestations of the single kidney disease we here call JKD.

Different disease manifestations

- JKD is found far more frequently in bitches than in dogs, the difference possibly being as great as 10 : 1. How could this be? JKD commonly leads to urinary tract infections (UTIs) such that UTIs commonly signal developing JKD. The urinary tract is much shorter in bitches and therefore more prone to infection than in dogs. The incidence of detected kidney disease is therefore expected to be higher in bitches than in dogs.

- Limited studies have suggested that the age of onset of JKD may actually be much earlier in dogs than bitches and may also be more severe, such that affected individuals may be ‘lost’ as fading puppies. The cause of death of such dying pups is seldom investigated but several dying male pups of suckling age have been found, with subsequent kidney pathology, showing damaged kidneys. JKD may therefore be responsible for some fading puppies. If males are more likely to die early (and be missed as fading puppies), it follows that most later-occurring cases (juvenile or older), which are the actual diagnosed cases, will be bitches.

- JKD has also been detected following stress, notably in bitches during pregnancy or following caesareans, when deaths attributable to JKD have been diagnosed. Again, as with UTIs, this enhances JKD detection in this sex.

- JKD has tended to be defined by its early, juvenile age of onset. The consequence has been that later onsets of kidney failure (at 5 or more years of age) have been attributed to other causes and old age itself, rather JKD. However, JKD has recently been convincingly diagnosed by pathology in older Boxers showing indications of kidney failure. There is therefore the possibility, or even expectation, that some individuals with mild degrees of JKD may go through their full lives without disease detection.

- All of the above occurrences will contribute to the observed shortage of affected cases relative to the 25% expected, but a major factor is the structure and function of the kidney itself; it has spare or reserve capacity such that damage cannot easily be detected. In fact over 70% of the capacity of the kidney must be knocked out before any symptoms of kidney failure appear. This immediately suggests that if JKD damage is not substantial, affected dogs will not experience the actual disease. In total therefore, a first effect may occur in fading puppies, notably in males; a variable degree may occur in juveniles; but at later ages the disease may only occur when triggered by UTIs or other stress events, or even old age; and it is almost certain that severe damage is never reached in many dogs, such that those with minor levels of effect may be symptom-free and live outwardly normal lives until dying from other causes. It is therefore essentially expected that the frequency of JKD cases will be less than the 25% expected with a recessive gene. Genetically affected but outwardly healthy dogs will exist in our breeding populations.

Summation

It is clear from the above that JKD has been with us for years but has been largely unnoticed because of its partially hidden nature. Here, I have addressed only the biological reasons on how JKD is largely missed, focusing on the difficulties of recognising and understanding the disease and its expression. Much of the background evidence is limited; there is a need for research upon the disease itself. And, to this end, a UK specialist in internal medicine has agreed to help the breed with this difficult disease. The aim is to seek hard evidence that some fading puppies may have JKD and also older, post-juvenile dogs. Both aspects will require UK breeder cooperation in providing the needed material, and to this end appeals have already been placed in the media requesting the help of breed clubs and individuals. The results will not only aid a better understanding of the disease but provide essential information for the operation of valid scans to find the responsible genes that are running in Norway, Sweden, and America. Here is the chance for breeders to obtain answers for the many problems they see with JKD.

Information Source

All available pedigrees are to be found on the www.boxerjkd.com website together with breeding guidelines based on currently available information. The pedigrees are being updated as released by owners. References and links to published work are also provided, as also basic information on the disease, its diagnosis and treatment.