By Rob Pilsworth MRCVS

Dealing with sarcoids

Some horses are genetically predisposed to developing tumorous lesions which, left untreated, can prove fatal for the individual and risk infection of other horses

Imagine what it would be like if human malignant skin cancers were contagious. Imagine that it was possible, just by touching or spending time in the vicinity of an affected patient, that you yourself could develop the disease. Our whole attitude and approach to these tumours would be radically different. But in the horse just such a condition already exists, and yet we hardly take it as seriously as we would take any form of cancer in man, despite it being the commonest nodular skin tumour in the horse.

It was Chaucer in the 14th Century who first coined the term "familiarity breeds contempt", and my goodness isn't that the case in the equine sarcoid? Anyone who has been around horses for any length of time knows what a sarcoid is, don't they? They are just a kind of large wart, aren't they? Something that can be left alone to be dealt with further down the line. In the life of a racehorse, which is often passed from one ownership to another during its career, the 'buck' of treatment is often passed along. But these lesions should be taken far more seriously. They represent a potentially highly invasive skin cancer (*see Fig 1*), which can end in the demise of the horse, and being common and frequently ignored doesn't lessen this. So what are equine sarcoids, how do they occur and how can we get rid of them?

Figure 1 A large invasive sarcoid, now very difficult to treat. This sarcoid would have almost certainly been the size of a small finger-nail at one stage, at which point treatment would have been relatively straightforward and probably effective (Courtesy Prof. Derek Knottenbelt)

Causation

For many years it has been known that the DNA (the genetic blueprint which allows organisms to reproduce) of the cattle wart virus, bovine papillomavirus (BPV), is present in almost all sarcoids. The theory that sarcoids were the result of direct infection of the horse with the bovine papillomavirus was contentious though, for two main reasons. First, nobody could isolate the virus itself from the sarcoid, even though its DNA appeared to be present, and second, when horses were injected experimentally with BPV they developed sarcoid-like lesions at the site of injection, but these rapidly regressed and disappeared spontaneously.

We were therefore left wondering what it is that makes the difference for the horse to go on and develop full sarcoid tumours. We now probably have the answer.

It seems that certain individual horses carry genetic changes in their major histocompatibility complex (MHC) which predispose them to the development of true sarcoid tumours following infection. The MHC is a similar concept to a blood group, we all have them, and we all have slight variations in them.

It's the variation between MHC's that, for instance, determines the success or failure of organ transplantation, and is the basis of tissue matching between donor and recipient. We have now identified several discreet genetic mutations within the MHC that pre-dispose the horse to the development of sarcoid when infected with BPV, and these are to some extent heritable. In other words horses that have developed sarcoids may pass on that tendency to their offspring.

But how does the cattle wart virus get into the horse? For a long time the suspect was the common fly (Stomoxys calcitrans). Flies were implicated because of the predilection site for the development of sarcoids, usually in the thin-skinned hairless regions of the horse, where flies love to feed. Areas such as those around the eyes and mouth, the axilla (armpit) and the inside of the hind legs are predilection sites for the development of sarcoids, all regions that flies like to chew on. In the same way, sarcoids will often develop at the site of a wound. Anyone who has nursed a horse with wounds in a field in summer will know just how difficult it is to keep the wound margins free of chewing flies.

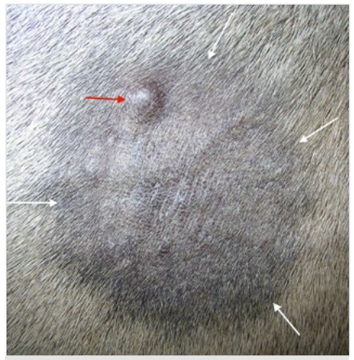

Figure 2 A small sarcoid in a yearling (red arrow). Note the area of transformation where the skin has changed colour and lost its hair coat as a result of peripheral 'seeding' of infective particles from the central sarcoid. For effective treatment all this skin has to be removed (Courtesy Prof. Derek Knottenbelt)

Experimental work has shown that flies raised in an environment containing both cattle warts and sarcoids can and do pick up and carry the virus and DNA with great ease. They then secrete these agents in their saliva for variable periods, and it is the biting flies that almost certainly introduce the BPV in the first place. In cattle, this just produces warts, which usually resolve spontaneously after natural immune challenge. In most horses, the same phenomenon occurs, but in some sarcoids develop.

Treatment

There have been many differing approaches to the treatment of sarcoids, none of them 100% effective. There are, however, now several treatment regimes available with success rates approaching 90% or above. One of the things we have to remember when evaluating any treatments for sarcoids is the fact that the horses so affected are predisposed to the development of these lesions, because of deficiencies in their immune system already described. So we can treat the sarcoids we can see with 100% effectiveness, but these horses could subsequently be re-infected by flies either with the wart virus or with material from another equine sarcoid and go on to develop further lesions. It is therefore probably simplistic to ever expect a 100% permanent cure.

One of the difficulties in treating sarcoids is the fact that they are a mixture between a tumour and an infection. Cutting them off simply doesn't work. They just grow back, often in a more menacing form. Because of the area of infected and transformed skin around the sarcoid (see Fig 2) recurrence will be inevitable and often in a far more invasive and aggressive form than the original sarcoid, so whatever treatment regime we use we need to somehow address the fact that the area of tissue around the sarcoid is infected, and to deal with this at the same time.

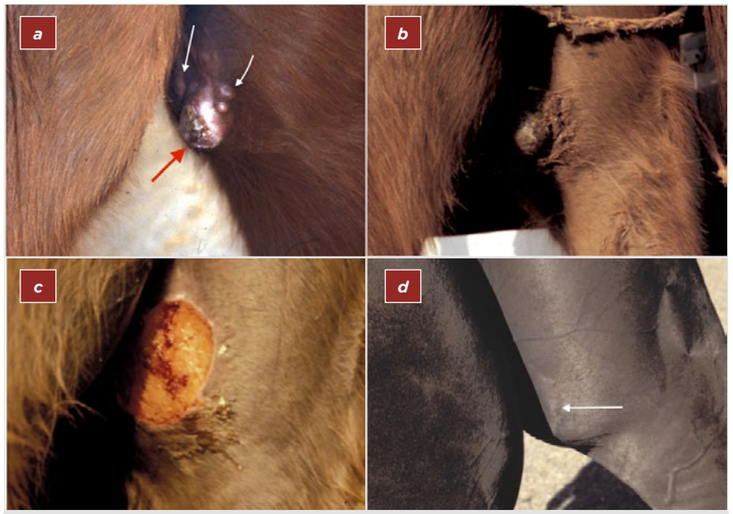

Figure 3 A horse with a large multi-locular sarcoid on the inner side of the thigh (red arrow, 3a). Note the small satellite sarcoids developing around the main lesion (white arrows). Following treatment with the topical cytotoxic drug AW4, the sarcoid has died, in association with the zone of infected skin around it, even though the cream was not applied to this region. Once the skin has sloughed, the wound heals without the need for sutures (figure 3c), leaving minimal scarring (figure 3d)

Effective Treatment Methods

1. TOPICAL CYTOTOXIC DRUGS

Certain chemicals, when applied to the surface of a sarcoid, will diffuse into the tumour and kill it. By doing so, they also often seem to expose the BPV DNA more fully to the host's immune system, and the dead sarcoid, plus a wide margin of tissue around it, sloughs off (*see Fig 3*).

Professor Derek Knottenbelt OBE, recently retired from the Liverpool University School of Veterinary Medicine, researched an old 'patent remedy' cream that he first encountered when he worked with a veterinary practitioner, Jack Walker, in the Cotswolds. Jack was the last in a line of veterinary Walkers who had learned from their fathers, not by attending college, stretching back over 300 years. He was much in demand with the practice's sarcoid cream, travelling far and wide to treat cases, for the simple reason that it worked. Derek continued to investigate and modify this cream, now in its fifth generation, and called AW5. This medication contains a mixture of potentially highly toxic chemicals, and so is only available on bespoke prescription tailored to the individual case, to veterinary surgeons, not directly to members of the public. Details can be found on Professor Knottenbelt's website http://www.equinesarcoid.co.uk.

One of the things clinicians notice when using this cream is that although the cream is only applied directly to the sarcoid itself, the eventual 'slough' includes a wide margin of previously 'healthy' skin (*Fig 3*), which almost certainly also contained the infective material of sarcoid.

The cream is not suitable in all situations. It results in a large 'slough' and this can be dangerous when the sarcoid occurs for instance near the eye or over a joint, so individual cases always have to be assessed on their merits.

2. LASER REMOVAL

Whilst simply cutting off sarcoids appears to be pretty ineffective, the removal of the lesion and an area of surrounding skin with the use of a cutting laser has proven to be successful in a large number of cases. Richard Payne at Rossdales Veterinary Hospital in Newmarket was among the first to use this technique in a large number of horses in the UK, and published the results of treatment on almost 100 horses, showing a success rate at 18 months from treatment of 83%. The beauty of laser resection is that the horse ››

most often does not require a general anaesthetic (*see Fig 4*), and has a very limited 'down time'. This is normally a week of walking exercise, after which normal training can resume. Obviously sarcoids in the vicinity of tack, such as in the axilla or around the girth, will require a longer period removed from training to allow full healing, but this procedure results in very little loss of training days, minimal scarring, and, when correctly done, low recurrence rates. The bad news of laser resection is that as lasers have become increasingly available in equine practice, some clinicians are carrying out the procedure without adequate skill or training, or removal of a sufficient margin around the lesion. This has resulted in cases of recurrence of the tumour in a much more aggressive form, as is always the case with sarcoid, usually for someone else to have to deal with, and this has diminished the perceived success rate for the procedure.

3. ELECTRO-CHEMOTHERAPY

For many years it was known that injection of sarcoids with cisplatin (an anti-cancer drug developed for humans) resulted in regression of the sarcoids, but success rate was not universally high. Cisplatin is an oily mixture, it doesn't like to mix with tissues and to be successful has to be injected in to every part of the sarcoid to produce its necrotizing effect. More recently it has been shown that treating the sarcoid tumours with electric current pulses following injection of the Cisplatin massively increases the kill rate to the sarcoid cells, and rates of remission at four years of over 90% have been claimed for this technique. The downside is that the horses require several treatments under general anaesthetic, usually two to three treatments at two-week intervals, and that the expense of the equipment necessary to carry out the procedure inevitably impacts on cost.

4. BRACHYTHERAPY WITH RADIATION

In the past, sarcoids in positions that make them very difficult to treat with other methods, particularly around the eyelids, have been treated by radiotherapy. The most effective radiotherapy technique was the insertion of iridium wires directly into the tumour. These were left 'in situ' for several days and then removed. Iridium is a radioactive metal, and during the period the wires were in place the radiation would exert its lethal effect on the rapidly dividing tumour cells.

The problem with the insertion of iridium wires is that someone has to

Figure 4 A horse undergoing laser resection of the small sarcoid gripped by the forceps at Rossdales Equine Hospital in Newmarket. Note the wide zone of surrounding skin that has also been removed (Courtesy Richard Payne, Rossdales Equine Hospital)

physically insert them, and in doing so inevitably exposes themselves to radiation. There is no safe level of radiation. Any radiation dose increases subsequent risk, so clinical workers' dose limits are controlled by law. This means that once a person has treated only a small number of horses they will have received such a significant dose of radiation that they could not treat any further ones for some time.

This problem has been circumvented by the development of an extremely clever machine now in use at the Animal Health Trust in Newmarket, overseen by Anna Hollis (*see Fig 5a*). Here the iridium wire is welded on to the end of a long wire. This is retracted into a radiation proof lead-lined chamber, therefore presenting no radiation risk to attendant staff. To administer radiation it is passed in turn down treatment catheters (*Fig 5a*). The sarcoid is first mapped in detail using sophisticated imaging software, so that the placement of the catheters can be carried out under imaging guidance, ensuring that all portions receive an effective radiation dose. Because the iridium source is completely contained within a safe chamber, the radiation dose it is capable of emitting can be far higher than the iridium wires previously used.

Once the treatment catheters are in place, the staff retire from the room (*Fig 5b*), and the machine feeds the iridium source down each guide catheter, until it arrives within the sarcoid. Because the iridium source can now be safely highly radioactive, the dose can be given over a far shorter time – a few minutes instead of a few days.

The machine then subsequently retracts the wire, along with its iridium source, back into the safety of the lead chamber. The horse has no residual radioactivity and can be treated normally after treatment.

Hollis has published preliminary results for this technique on 77 cases, with a success rate of 88%. The technique is not cheap, costing approximately £4,000 per horse, but is suitable for the treatment of peri-ocular sarcoid for which really no other effective treatment is possible, with very dramatic results (*see Fig 6*).

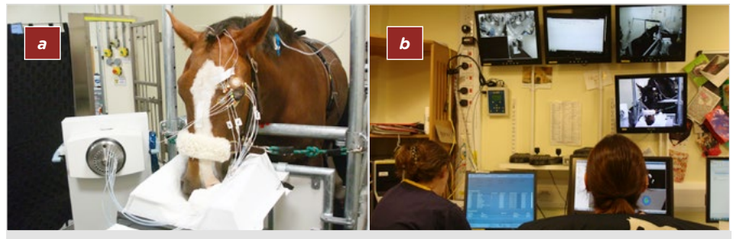

Figure 5 A horse undergoing radiation brachytherapy (figure 5a) at the Animal Health Trust, in Newmarket. This ingenious machine allows the staff to be out of the room and therefore not exposed to radiation during treatment (figure 5b) (Courtesy Anna Hollis, Animal Health Trust)

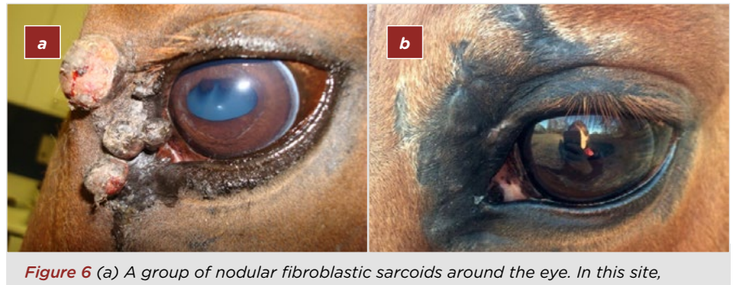

Figure 6 (a) A group of nodular fibroblastic sarcoids around the eye. In this site, treatment with almost any other means would be very difficult. (b)Three months following treatment, a very acceptable cosmetic result (Courtesy Anna Hollis, Animal Health Trust)

The future

Sarcoid is the only known example of the same virus producing two different diseases in separate species of animal, warts in cattle, and sarcoids in the horse. Our main problem with equine sarcoid form of disease is almost certainly the result of imperfect immunity in certain horses. Most horses when infected with BPV just shrug it off. A similar situation occurs in women, where over 90% are exposed to the human wart (papilloma) virus during life, but only a very small percentage go on to develop its linked disease, cervical cancer. This has led to the routine vaccination of all girls against the human papilloma virus, to boost natural immunity, and it's a logical research aim to investigate whether it would ever be possible to vaccinate the horse in the same way. In the meantime, it behoves us to take this damaging and potentially life-shortening disease very seriously indeed, and treat it hard whenever we see it.

Five important points about sarcoids

1. Small sarcoids only ever become bigger sarcoids. The rate of spontaneous resolution is so low it has to be considered negligible. We wouldn't dream of going to the local pharmacy for some herbal remedy or over-the-counter cream if we had aggressive skin cancer, so why do we do it for our horses?
2. The sarcoid itself is not the whole problem; there is always also an area of transformed 'sarcoid infected' skin around the obvious lesion, which must also be removed.
3. The most effective and clinical proven treatment should be used in the first instance. The prognosis for resolution decreases by almost half for any sarcoid which has undergone previous intervention. Use the best available treatment, and use it first.
4. A sarcoid on your horse is a fly magnet, and can act as a source of sarcoid-producing infective agent to other horses, or even to small wounds on the same horse. Speedy and effective removal sorts this.
5. The only truly predictable thing about the disease of sarcoid is its total unpredictability; these lesions are always potentially highly invasive and dangerous, and need to be taken seriously.