

PANOSTEITIS

BY Fred Lanting

DESCRIPTION

One of the main reasons for a young dog to be "pulled" from a show, or excused from the ring, is the sudden lameness of a condition known as panosteitis, familiarly labelled "pano" by many breeders. Of some 130+ breeds recognized by the American Kennel Club and hundreds more by some other registries, a dozen or so have been reported to be affected. This mysterious disease causes sudden lameness in many younger dogs, but its greatest potential may be in false diagnosis. The disease has been given various names: hematogenic chronic osteomyelitis, enostosis, long-bone disease, panosteitis, and eosinophilic panosteitis. It was first described by Gratzl, and by Baumann and Pommer in 1951 in Vienna. Since then it has been reported in Sweden, Germany, Hungary, what was then Yugoslavia, and the United States, yet there is not as much information on this subject in the early scientific literature; there was no reference in several texts on orthopedic diseases, and Smith's otherwise comprehensive text on Veterinary Pathology had but a brief note on enostosis as "a German Shepherd Dog disease", "analogous to eosinophilic panosteitis". An obscure Yugoslavian doctoral thesis dated 1961 led to a couple of references, and a dogged search (pardon the pun) of the international orthopedic literature finally turned up a 1970 study published in the AVMA Journal. Personal contact with orthopedic and radiology specialists brought the search to some work at Purdue.

SYMPTOMS AND DIAGNOSIS

Clinical signs are those that are obvious or apparent upon gross examination of the entire dog, as opposed to microscopic or other types of study. Symptoms are determined by means which may include gait and motion analysis, and comparison with other limbs by manipulation and palpation. In humans such a case history would include a verbal report by the patient of his complaint. Radiologic study involves the use of X-rays, and histologic determination usually requires euthanasia and dissection of the tissues involved (long bones). A similar term, pathologic, also refers to laboratory findings of functional and structural aspects of the disease. Fortunately, a knowledgeable breeder can probably diagnose pano faster and cheaper than can a vet, merely by knowing the breed and pinching in the right places.

Panosteitis is probably a disease of the osteoblasts which, you will remember, are those bone cells that produce the organic osteoid and matrix vesicles needed for ossification. It involves a necrosis of fat cells in the marrow of long bones. It is a generalized (pan-) inflammation (-itis) of certain bones (os-). Specifically, it occurs in five of the long bones of the appendicular skeleton: the humerus, radius, and ulna of

the foreleg, and the femur and tibia of the hind limb. It has not been reported in the long but narrow fibula of the lower rear leg. More often than not, the first sign is a sudden lameness in one foreleg. Exhibitors have claimed it always occurs between the closing date for entries and the day of the show, after all arrangements and plans have been made, but this is something that has not been substantiated by unbiased scientific studies.

Intensity of discomfort varies not only with the progression of the lesion in the individual, but also with the difference in pain threshold between one dog and another. It may be so minor that one has to press and probe to elicit pain response, or it may be so bad that the dog will whimper and refuse to put any weight on the limb. The degree of pain is not closely correlated with the stage as seen on the radiographs. While lameness may sometimes be observed in only one limb, the disease has been radiographically discovered in at least two bones simultaneously in some 96% of affected dogs. Further, the typical lameness-recovery cycle of one or two weeks will shift from one leg to another, although there may actually be as many as seven bones involved at any one time. Usually, an upper arm will be affected first, followed by a femur or ulna, and often the problem will appear in another bone in the original limb or its partner. There may be a lapse of several weeks between episodes, and more than one phase may be present in the individual at any one time.

Partly because of the nature of the disease and the fact that the owner is not likely to do any damage to his dog by withholding treatment if it is indeed pano, this may be the easiest to diagnose at home with fair reliability. If the dog is of the typical age, and if you can elicit a definite pain response by pinching the suspected affected bone in the middle of the shaft, it is most likely panosteitis. If the pain is at the distal end of the long bone, it could instead be HOD, in which case a trip to the vet is certainly in order. Computing this simple test with the breed predilection and perhaps previous experience, the owner may save himself some expense. If you have any doubt, though, be sure to ask the doctor for a series of radiographs.

Whether it is very common for the same bone to be the site of recurrence is not a matter of total agreement, although too many owners report it to be so, to ignore that strong anecdotal evidence. One study of 100 consecutive cases at New York's Animal Medical Center concluded that "after a bone has passed through all phases of the disease, it is unlikely that it will be affected again", and reported only one incidence of return to a previously affected bone. Another study released 5 years later held that "recurrence in the same bone was most frequently found in the radius, followed by the ulna...", but mentioned a 6-month or more interval between episodes in individual long bones. Symptoms of panosteitis may be confused, by the novice or the vet with limited experience, with OCD of the shoulder or one of the elbow dysplasias; if in the rear limb, it could make someone think the dog has

HD or cruciate ligament injury. A case history plus information on the breed, family, and diet can give some diagnostic clues. UAP, for example, if not already diagnosed on radiography, is often brought to light via trauma such as jumping off a ledge, but pano shows up regardless of traumatic occurrences. The most reliable and definitive diagnosis might possibly be by a series of radiographs which can show the early, middle, and late phases of the disease, but even then radiographic signs can be so minimal that they can be missed, even if the animal exhibits clinical signs and a number of films are correctly exposed. Radiographs in both major studies were taken every month from 5 to 30 months of age. This type of approach is not feasible for the typical dog owner, nor is it necessary or best in most cases, if experience is sufficient.

I find my own diagnostic method to be at least as reliable as a series of radiographs: first, I take into account the breed, and the second thing is to watch the dog walk, as other problems can give subtle differences in gait. Since I have long bred GSDs, and the disorder was once known as "that German Shepherd Dog disease", I have had much opportunity to witness its appearance in dogs of my colleagues. As soon as my first article on pano and my 1981 HD book were printed, in which I had said that I had never had a dog with pano, I found the worst case I had ever encountered, in one of my own dogs! By then, I had already plenty of practice in palpation (feeling) diagnosis as a part-time professional handler and consultant to other breeders. The third and most reliable physical test is to pinch the dog in the middle of the shaft of each of those ten bones (all the long leg bones except the fibula) and compare its reaction, bone to bone. Almost always, the dog will yelp with pain if you pinch the affected bone in the limb it has been favoring. Try to squeeze where there is very little muscle covering the bone, but only in the middle, not at the ends. Pain upon pinching near the joints can possibly lead you to suspect HOD or joint disorders, but possibly other than bone cancer, there is nothing that gives the same response to pinching the middle of the diaphysis (shaft) as pano does.

Three Phases

The first stage, the one most associated with acute pain, exhibits the least evidence of the lesion's presence in radiographs. There is some blurring, and an accentuation of the pattern of fibrous bands extending from the cortex (the hard, denser portion of the bone) inward toward the center of the medullary canal, where the marrow is located. Film contrast between the canal and cortex is diminished, and the radiodensities of the medulla and its lining are slightly greater. The fatty connective tissue takes on an appearance similar to eosinophilic granulomas (hence one of the early names for the disease) and bone is added to those fibrous bands, called trabeculae. The great deal of congestion in the medullary canal is almost undoubtedly the main reason for so much pain; if the poor dog could reason, he might imagine

his bones were about to burst from the increased pressure! If a hole is drilled (a punch biopsy) for the purpose of testing some of the marrow, pain is abruptly diminished.

The second phase is easily diagnosed in the clinic by the appearance of radiodense, mottled medullary tissue, beginning in the vicinity of the nutrient foramen, that hole in the side of the bone where blood vessels enter and leave. In pano's second phase, the borders of this hole are characteristically accentuated, the cortex appears less dense, and its inner lining becomes less roughened. In cases where the medullae are greatly affected, a remodeling (new bone cell formation) takes place as a secondary response on the cortex's outer layer, the periosteum, and it grows to several millimeters thick. This is the swelling or inflammation of bone that gives panosteitis its name. In 6 to 8 weeks these characteristics gradually merge into the third phase.

During the approach of the third phase, the fibrous bone that formed in the medulla is resorbed, giving the radiologist a more normal picture again, and production of blood by the marrow resumes a more normal procedure. It may take several months for the bone to regain normal shape and appearance, especially if pano had struck in the more mature youngster, but it generally does heal satisfactorily. Only a radiology specialist or a general practitioner especially well trained in this field will be able to tell later on if a particular patient had had pano.

Interestingly, no fractures accompanying or following panosteitis that could be considered related have been reported, despite temporary changes in the porosity and density of these organs as found in histopathologic examinations of euthanized dogs. Perhaps this is due to the dog's extreme reluctance to put weight on the afflicted limb during the first two phases. Nor was there any evidence of acute infection or chronic (lasting) inflammation. The disease and recovery reach a point of cessation, with some evidence of its having been there observable upon dissection and microscopic examination of the tissues. A little of the marrow typically seems to be permanently replaced by fibrous connective

tissue rather than bone, and the thickening of the outer surface gradually returns to normal.

SIMILAR DISORDERS AND SYMPTOMS

You have seen that the differential diagnosis which the owner can make with fairly good accuracy (pinching the bone) will distinguish panosteitis from HOD and other disorders; the vet can confirm it with radiographs and examination. Another disorder which can give x-ray pictures very similar to the "milky" or "cloudy" appearance of panosteitis is erythrocyte pyruvate kinase (PK) deficiency. Some years ago, a screening program to eliminate this hereditary enzyme metabolism disorder in Basenjis was thought to have been successful, but around 1990, a few more were diagnosed. The osteosclerosis, an abnormal increased density of bone, is apparently a pleiotropic effect of the

homozygous presence of the deficiency gene. Pleiotropy means one gene (or identical gene pair, if recessive) gives rise to more than one disease or characteristic; Alaskan Malamute dwarfism/anemic blood disorder is another example. In the Basenji disorder, the bone density that could take as much as two years to develop might be one of the evidences of the genetic problem, but only if accompanied by other tests. Even then, it might be missed, as some affected dogs will show normally high erythrocyte PK activity at the time of the tests. But if some of the other symptoms are looked for, the diagnosis is easier. Affected dogs often have heart murmurs, atrophied muscles, progressive anemia, stunted growth, rapid heartbeats, and swollen livers, hearts, and spleens.

HEMOPHILIA WITH SIGNS OF PANOSTEITIS

Some dogs have shown such frank signs of panosteitis that a tentative but fairly strong diagnosis of pano has been made, and then upon further tests run because of additional symptoms, they were found to have Hemophilia A. Of course, it is possible that some dogs can have both disorders at once, but based on the incidences of the two, the coincidental appearance might be hard to imagine except in certain isolated GSD families. Dr. Jean Dodd, a noted blood specialist, has seen some notable connection between pano and von Willebrand's Disease (vWD), a different type of hemophilia. I think that probably the signs of pano or the actual development of enostosis, as some prefer to call it, in the hemophiliac dog, come about via bleeding in the marrow with osteoblast (bone depositing cells) activity.

CAUSE OF PANOSTEITIS

The cause or etiology is unknown, but fortunately the disease is self-limiting: it follows a progressive pattern and generally the animal recovers with or without treatment to a normal state or one so close that you might not be able to tell it had occurred without cutting the bones for microscopic examination. In worse cases, some permanent scarring can be identified by those especially adept at reading the radiographs for this lesion. Since panosteitis is a disease of the fatty bone marrow in the long leg bones of the adolescent or young adult dog, it may be that research on bone marrow will lead to an understanding of the etiology and hence the best treatments, cure, and prevention of the disease.

Panosteitis was originally designated as hematogenic chronic osteomyelitis associated with fever and infection. Later work indicated these conditions, when present, were coincidental rather than causative. As mentioned earlier, infection is generally not associated, and malignancy is likewise absent. Only one of the 100 dogs in the Animal Medical Center study had tonsillitis (the tonsils are "traps" for infectious agents circulating throughout the body). Whenever vaccines, flea powders, worm medicine, diet, and other environmental factors have

been implicated, rechecking has found that the only common denominator was physiological stress. Bacteriologic cultures of marrow, and the histologic examinations, rule out bacterial agents. White blood cell and eosinophil counts were within normal in nearly all cases, the rare exceptions being no doubt a result of some co-existing but unrelated problem. An eosinophil, by the way, is a type of cell of the peripheral blood or bone marrow, and a high level is an indication of some sort of infection or attack by parasites.

Transmission

In an experiment to discover possible genetic, infectious, or contagious modes of transmittal, German Shepherd Dogs with a history of panosteitis were crossed with Pointers from a family in which it had not been observed. Also, purebred Pointers and German Shepherd Dogs were kennelled side-by-side separated only by a wire fence, and pups of both breeds were raised together in the same pen. Regardless of contact, the Pointers remained free of the disease while the Shepherds routinely developed it. The crossbreeding results were inconclusive, even though only one incident of panosteitis showed up as late as the fourth generation of back-crossing the female crossbreds to male German Shepherd Dogs.

Panosteitis does not appear to be related in any way to other radiographically similar diseases. It has no bearing on, nor is it affected by, other bone or joint diseases such as hip dysplasia or the various manifestations of osteochondrosis. Although radiographically panosteitis resembles some human bone conditions, there is no real counterpart in man.

It has previously been thought that nutrition might not have anything to do with the lesion, despite it occurring mostly in large, fast-growing breeds. Calcium intake did not seem to have any bearing on it, as evidenced in bone healing studies. However, more testimonial evidence has since been mounting among "breeders and feeders" that diet can indeed make it much worse or more likely to appear in families predisposed to it. When I was preparing the older article on panosteitis for the AKC Gazette, I undertook a review of my first 140 German Shepherd Dogs, and until my 1981 book was in publication, I had encountered only one case of panosteitis in the bloodlines I was using and developing. It happened seven months after the dog was sold to a home where his diet was considerably "richer" than the balanced commercial dry dog food he was used to. Clinical symptoms ended about ten days after onset, and we really don't know if the administration of prednisone had anything to do with alleviating it (cause and effect relationship with this corticosteroid on pano not established), but no further episodes occurred. It was some time later that one of my pups at home developed the worst case I have personally encountered, and I did not record what diet we had been using about that time, but he was produced by a different sire than any

of my other dogs.

A question of nutritional impact on the disease can be raised when comparing the dog's change in diet with the predominant diet of those in the 100-dog study: raw or cooked beef, eggs, cereal, and milk. Perhaps most of those 100 patients were from "pet homes" where a dog is more likely to have been "overnourished". There are other questions which can only be answered through research, but there is no current active project regarding the cause and environmental control of panosteitis. From personal experience as well as speaking with scores of breeders, I am almost totally convinced that those dogs with breed and/or family susceptibility for pano, who are fed very "rich" diets (high protein, especially) are the ones most likely to come up limping with the disorder. One after another, people have told me that by going to a lower-protein but still highly digestible food, and not feeding very liberally, they have stopped the course of pano in their kennels. An informal survey by the GSD Club of America later apparently confirmed this connection between pano and high-protein rations.

BREED, AGE, AND SEX CORRELATION

When first described, one of the names given the disease was "chronic osteomyelitis of young German Shepherd Dogs", but as it was studied in subsequent years, other breeds were found to be affected, including the Rottweiler, Airedale, Irish Setter, German Shorthaired Pointer, Doberman Pinscher, Great Dane, Basset Hound, and Saint Bernard. One observer has seen panosteitis in all of the better-known large and giant breeds, but it has also been found in the Miniature Schnauzer, the Scottish Terrier, and the Beagle.

The apparent prevalence in the German Shepherd Dog may partly be due to the large population of this breed (worldwide, it is number one), though we cannot overlook the very strong genetic aspect. Clinics such as the one in which the data on 100 consecutive cases were collected have a preponderance of GSDs as patients. Body size is correlated with the number of cases seen in a veterinary hospital or educational institution. Growth rate is a possible factor, as it seems to be with HD. Most of the large and giant breeds have a rapid early growth pattern, though the commonalities of growth rate and large size with panosteitis may not be as closely related as they are with HD. If breeds such as the Dobe and Collie, with their relatively flatter growth rate curve continue to have low incidence of pano in relation to their populations, it still might not be conclusive evidence of cause-and-effect, but may point to a connection. Some believe that pano may be an indication of an immune system insufficiency, as are such disorders as DM, pannus, susceptibility to Demodex, and many other disorders; interestingly, the GSD leads the parade in incidence in many of these disorders.

If one subtracts the extremes of a very few diagnosed after full maturity, the curve of ages at time of episodes rises from about 5 months to a peak around 10 months, and rapidly diminishes, with very

few cases after 18 months of age. In the one study mentioned earlier the extraordinary number (10) found at age 24 months may not be representative. The first German Shepherd Dog to win Best In Show at Westminster, Covy-Tucker Hill's Manhattan, reportedly had at least one episode of pano at 4 years of age, but this was not documented, at least not with any vet's findings given to me.

There is a nearly 4:1 ratio of males to females affected by panosteitis; the clinical signs are more severe and the disease more nearly chronic in males. This echoes a pattern seen elsewhere. Early in the U.S. space program it was discovered that women could withstand the stress of G-forces (acceleration) better than men. The U.S. Army determined that female dogs can run 26% longer and swim 46% longer than males. Bitches lead many racing teams of sled dogs because they can run smoother and calmer, some racing enthusiasts claim. And females are much less prone to non-specific lameness (presumably this included pano) according to the records of Zero Kennel (racing specialists). It appears the stress of estrus (bitch's season is her highest stress period) or pregnancy contributes somewhat to susceptibility.

TREATMENT

A great number of treatments have been proposed and tried, but all have had very limited or extremely questionable success, and then only as partial palliatives; nothing has been conclusively shown to have a cause-and-effect relationship. Since the cause is unknown, treatment is indicated and routinely prescribed only for the symptoms. Aspirin, sulfa compounds, other antibiotics, vitamin C, Prednisolone or similar steroids, and calcium supplements have been most commonly attempted. Of the analgesics and other medications tried, buffered aspirin (less irritating to the canine digestive tract) probably has the greatest effect and widest application in relieving some pain in some dogs. It and the corticosteroids have the largest number of proponents, but it has been my observation that most dogs with panosteitis do not respond to these anymore than they do to anything else. Corticosteroids do have an anti-inflammatory action and can give remarkable relief in many ailments (and by some reports do a little good in alleviating some pain in pano), but as in the case of all drugs and foreign substances, there are cautions. Prolonged or excessive use of aspirin can cause stomach bleeding in dogs; steroids can bring on cardiovascular problems including ruptured capillaries, and can damage the immune system at least temporarily. If you decide to try a pain reliever in spite of my advice, if there is overwhelming compunction to do something, make sure you discuss with your veterinarian the possible side effects and contraindications. For every "cure" or "successful" treatment, you can find a score or more cases in which it did not work at all.

One orthopedist said to me, "It's sort of like treating a cold in a human patient where, if you give medicine it takes about seven days to get over it, and if you do nothing it takes about a week." In the case of this

disease, however, it may take anywhere from 2 days to 7 weeks for the pain to leave one site with 1 to 2 weeks quite common. Radiologically and histologically, it can be 2 months between onset and the beginning of the late phase, and then several more months before cortex and endosteum (inner lining of the marrow cavity) regain normal appearance. It may take considerably longer for the disease to run its course in all the bones that may become affected. I have observed that most cases are outgrown by age 18 months to 2 years, with most initial episodes coming around 8 to 10 months of age; in many dogs the disease will strike at a much later age than in others. It is rarely a chronic situation in regard to pain; in most cases symptoms appear only intermittently in many bones, and many dogs will have but one episode in one bone.

Many of us experienced breeders believe that nothing you do will likely make a fig's worth of difference in either pain relief or remission. One private practitioner with much experience in orthopedic disorders claimed that Zylprime relieved clinical and radiographic symptoms within 5 days, but we know that many cases self-resolve in that period of time anyway, and the experiments were not duplicated elsewhere. It appears that nothing gives completely satisfactory results, so the best course of action is no action at all; let the dog decide how much weight to put on the limb and just wait. Perhaps the best treatment regimen for dogs with pano is in the nursery rhyme, "Leave them alone, and they'll come home, wagging their tails behind them." It may be best to let the dog restrict his exercise by himself, give him emotional support so he doesn't go without food to the extent of exposing himself to diseases or stresses he can't handle, and simply wait it out.

CONCLUSIONS

In summary, panosteitis is a self-limiting disease affecting many of the long leg bones, predominately in large dogs between 5 and 18 months old. It is apparently unrelated to other lesions of the skeletal or blood systems, and occurs only in the canine, more in some breeds than others. Cause is unknown, but high-protein diets seem to make symptoms worse or longer lasting. Panosteitis is "self-limiting", i.e., it will "go away" whether one treats it or not. Since afflicted dogs "outgrow" the disease with little or no expense, it is unlikely much research funding will become available to study it. The dog owner should consult his veterinarian to rule out other problems that may be more serious.

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