Herpesvirus type 2 in biopsy of a cow with possible pseudo-lumpy-skin disease

J. Brenner, B. Sharir, H. Yadin, S. Perl, Y. Stram

IN May 2008, examination of a primiparous Israeli Friesian-Holstein dairy cow, exhibiting lumps on and around the perianal region, and the underside of the tail (Fig 1), revealed additional variant skin lesions. These were presented as scattered circular multifocal skin lesions, approximately 2 cm in diameter. Some had lost hair and resembled ringworm lesions, and were scattered among the lumps on the caudal and dorsal regions between the neck and the hips (Fig 2). These were interspersed with a few well circumscribed hairless lesions (Fig 3).

General examination of the herd revealed additional cows with similar lesions, but whereas the original cow exhibited about 30 lesions, the others showed between one and three. The general condition of the cow presented was poor and it deteriorated, developing hindquarter lameness due to sole ulcers and pyogenic arthritis. The cow was also seropositive for bovine leukaemia virus according to agar gel immunodiffusion tests. The productivity of the other affected cows was not reduced.

In the light of previous outbreaks caused by lumpy-skin disease virus (LSDV) infection in 1989 (Yeruham and others 1995), 2006 (Brenner and others 2006) and 2007 (Brenner and others 2009), it was important to diagnose this episode and identify the causal agent, especially as the affected cow belonged to a farm approximately 250 km from the previous foci of LSDV (Yeruham and others 1995, Brenner and others 2006, 2009).

Bacteriological, mycological and parasitological tests on hair and skin samples all yielded negative results. Skin samples were fixed in 10 per cent neutral buffered formalin for 48 hours, embedded in paraffin wax, sectioned and routinely stained with haematoxylin and eosin. Microscopic examination of the stained sections revealed moderate to severe orthokeratotic hyperkeratosis. The superficial dermis was diffusely infiltrated by lymphocytes and some macrophages. The infiltrate involved the adnexa of the skin; some hair follicles were keratinised and serous glands were mildly dilated. There were also multifocal perivascular lymphocytic infiltrates in the deeper dermis. The histological lesions supported a viral aetiology and the absence of deep ulcerations and sequestra indicated possible pseudo-lumpy-skin disease (PLSD).

Because of serious statutory implications, LSD was excluded first. A PCR (Stram and others 2008) applied within 24 hours of the biopsies arriving at the Kimron Veterinary Institute laboratories was negative for LSDV. It was also applied to determine the presence of bovine herpesvirus type 2 (BHV-2) DNA in the skin lesions (d’Offay and others 2003), using the primers BHV-2F CGACGGCAAGGT GATAACCA at positions 1526-1542 of the BHV-2 glycoprotein B gene and BHV-2R AACGTGCTGACTGCGGTAA at positions 2044-2063 of the BHV-2 glycoprotein B gene.

It is assumed that detection of BHV-2 may help to determine whether skin lumps are caused by this viral infection. However, the presence of BHV-2 is not sufficient to determine PLSD, because BHV-2 can be involved in two additional distinct clinical conditions: bovine
ulcerative herpes mammillitis (BUHM) (Gibbs and Rweyemamu 1977, Gibbs 2004), and infection with PLSD. The latter occurred during the 2007 LSD outbreak in Israel (Brenner and others 2009) and is yet to be explained in the published literature. A serological survey of cattle in Minnesota revealed approximately 30 per cent of cattle in herds both with and without a history of skin conditions to be BHV-2 seropositive (Dardiri and Stone 1972), suggesting that the virus is widely distributed. Therefore, serodiagnosis is not a good predictor for BHV-2 PLSD in the absence of clinical manifestation.

BHV-2 belongs to the Alpha-herpesviridae subfamily, which can produce mild to moderate disease in ruminants, although BHV type 1 (BHV-1) can cause serious problems and mortality in dairy herds. However, BHV-2 is it probably transmitted mechanically whereas the other BHVs are transmitted mainly via respiration. Generally these herpesviruses cause localised diseases, with barely detectable levels of viraemia. Systemic diseases are of minor concern, as with PLSD (Pate and Didlick 2008).

Cattle infected with BHV-2 might exhibit lesions of BUHM or PLSD (Gibbs 2004), two clinically distinct diseases that have never been seen in the same infected cow. BUHM has been associated with a painful localised ulcerative udder, whereas PLSD appears as a superficial generalised cutaneous condition.

PLSD, also known as Allerton virus infection, and generalised infection of cattle with BHV-2, occurs primarily in southern Africa (Gibbs 2004). However, it has been reported three times outside Africa: in Australia (St George and others 1980), the UK (Woods and others 1996) and the USA (d’Offay and others 2003) in 1979, 1994 and 2003, respectively. To the authors’ knowledge, the episode reported here is the fourth recorded case of PLSD outside Africa.

PLSD might be confused with other bovine skin conditions: the lesion most closely resembling PLSD is primarily LSD sensu stricto. In Australia, ringworm (Tricophyton verrucosum) was suspected to be the cause of infection in cattle, which delayed the true diagnosis of PLSD (St George and others 1980). In particular, lesions showing hair thinning are sometimes erroneously believed to be caused by T verrucosum infection.

Often it is impossible to isolate BHV-2, probably because of the interference of specific antibodies generated during convalescence (Dardiri and Stone 1972). A positive PCR remains the sole laboratory procedure that can provide conclusive confirmation. However, this necessitates demonstrating BHV-2 DNA in the skin biopsy samples. Kemp and others (2008) succeeded in isolating BHV-2 from only one animal, although they described a vast outbreak of BHV-2 infection manifested as BUHM in adult cows, and as circular lesions on suckling calves’ muzzles.

The natural transmission mode of BHV-2 is not clear. It is thought to be spread by inoculation into the dermis by biting flies (Gibbs and Rweyemamu 1977, Letchworth and others 1982), since it has been isolated from biting flies fed on PLSD-infected cattle (Weaver and others 1972).

PLSD, the generalised cutaneous form of BHV-2 infection, does not seem a serious disease in itself, but it raises concern during differential diagnosis to discriminate between PLSD and LSD (Yeruham and others 1993, Brenner and others 2006) and similar skin lesions, such as ringworm (St George and others 1980) and Dermatophilus congolensis infection (d’Offay and others 2003). Recently a calf, secondarily infected with BHV-2, probably via its dam during an outbreak of BUHM in the UK, showed a circular lesion (Kemp and others 2008) resembling the circular lesions in Fig 2. This resemblance needs further epidemiological investigation since it could contradict the axiom that clinical aspects of PLSD and BUHM are never found in the same cow.

References


