IMPLANTATION OF NEOPLASTIC CELLS AFTER FINE NEEDLE ASPIRATION BIOPSY OF URINARY BLADDER AND LUNG CARCINOMA

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NEEDLE TRACT IMPLANTATION AFTER FINE NEEDLE ASPIRATION BIOPSY (FNAB) OF TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER AND ADENOCARCINOMA OF THE LUNG (3 CASES).

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Key words: tumoral seeding; dog; cat; carcinoma; fine needle aspiration biopsy.
SUMMARY

This paper reports three clinical cases of needle tract implantation of neoplastic cells on the abdominal and thoracic wall after ultrasound (US) fine needle aspiration biopsy (FNAB). Primary tumours were two transitional cell carcinomas of the urinary bladder (2 dogs) and one pulmonary adenocarcinoma (1 cat). All three masses growth up along the needle tract. To our knowledge, the seeding of pulmonary adenocarcinoma cells after FNAB on the thoracic wall has never been reported in veterinary medicine.

INTRODUCTION

The hypothesis of possible spreading of neoplastic lesions during surgical procedures was first suggested by human surgeons (Gerster and others 1885). Abdominal wall metastasis after resection of a gastric carcinoma were reported by Mayo in 1913.

In the following years, many authors stated that biopsy procedures of neoplastic lesions could be a cause of local recurrence because of malignant cells dissemination by the needle into the surrounding tissue (Ochsner 1947, Crile 1956).

In human medicine, dissemination of neoplastic cells after ultrasound-guided fine needle aspiration biopsy (FNAB) has been referred following percutaneous aspiration of different lesion of the head, neck, thorax and abdomen. Reports of single cases include diseases of the brain (Kim 2003, Aichholzer 2001), thyroid (Hales 1990) and parathyrnoïds (Åkerström 1988), pleura and lung (Seifer 1989, Paik 1994, Sacchini 1989, Takahashi 1992, Kim 2003), mediastinum (Oiwa 1985), thymus (Fujiwara 2003, Nagasaka 1993), liver (Hamazaki 1995, Chapoutot 1999, Takahashi 2004, Ishii 1998, Kim 2000, Sakurai 1983, Takamori 2000), pancreas (Kosugi 2004), kidney (Lee 1995, Gibbons 1997, Slywotzky 1994) and colon (Abdelli 1994). Carcinomas of the lung, liver, pancreas and prostate are over represented (Chapoutot 1999, Kosugi 2004, Paik 1994, Smith 1981). The incidence of this complication seems to be low. For hepatic carcinomas, needle tract implantation has been reported to occur in 1,1% of the cases (Ishi 1998) or 1,6% (Kosugi 2004); similar values
(1.4 %) were related to pancreatic carcinomas (Kosugi 2000). In a study including 4365 FNAB of lung lesions, dissemination of neoplastic cell was considered a extremely rare event (Kim 2003).

In veterinary medicine, post-surgical recurrence at the abdominal wall of a transitional cell carcinoma of the urinary bladder was described by Anderson in 1989.

In small animals, only three cases of needle tract implantation after FNAB has been published (Nyland 2002). All three cases were carcinomas, respectively of the urinary bladder, urethra and prostate.

This paper reports three cases (two dogs and one cat) of neoplastic cells spreading to the abdominal and thoracic wall after us-guided FNAB of two transitional cell carcinoma of the urinary bladder and one adenocarcinoma of the lung.

**CASES REPORT**

**Case 1**

A 10 year old, male, crossbreed dog was presented because of macrohematuria. Blood work and standard radiographs of the chest were normal. Ultrasound examination of the abdomen showed an irregular, inhomogeneous thickening of the urinary bladder wall, in the area of the trigone, with loss of normal wall layering. A free-hand FNAB was performed using a 22G hypodermic needle connected to a 5 ml syringe. Cytological analysis revealed a transitional cell carcinoma of the bladder. The owner of the dog decided for a palliative chemotherapy protocol (meloxicam 0,1 mg/kg/s.i.d. (Metacam, Boeringher Ingelheim). After 10 months, the dog was represented because of a large ulcerated para-penile mass. This lesion was about 6 cm in diameter and involved the subcutaneous tissue of the abdominal wall, in the same area where the FNAB needle was performed (Fig. 1). A second ultrasound examination showed a diffuse, hyperechoic thickening of the urinary bladder wall up to 1 cm of thickness. There was complete loss of normal wall layering and irregular mucosal surface (Fig. 2a). In the bladder lumen, some hyperechoic structures were visible and
referred to blood clots. In the area of the subcutaneous mass, the abdominal wall appeared thickened up to 3 cm with a complex mass appearance (Fig. 2b). A Tru-cut biopsy sample from the abdominal wall lesion was taken for histopathology and examined with Hematoxylin-Eosin and immunohistochemistry CKpool technique. In the peritoneal serosa, proliferations of anomalous transitional epithelial cells of the urinary bladder were visible, organized in a tubular and papillotubular, well differentiated pattern. The cells had irregular margins, large nuclei, with evident nucleoli, and eosinophilic cytoplasm. Moderate fibroplasia of the serosa was present without lesion suggesting neoplastic thromboembolism (Fig. 3).

Spreading of the carcinomatous cells to the abdominal wall was confirmed. Due to a poor prognosis, the owner requested euthanasia.

Case 2

A 12 year old, castrated male, crossbreed dog underwent cystotomy to remove bladder stones. Forty days after surgery, the dog was presented because of pollakiuria and hematuria and abdominal ultrasound was performed. The ultrasound examination showed multiple hyperechoic area in the wall of the urinary bladder and a hyperechoic, irregular, broad-basis mass protruding into the lumen from the ventral wall of the bladder neck. An us-guided FNAB of the urinary bladder mass was performed using a 22G needle connected to a 5 ml syringe. Cytology confirmed the diagnosis a transitional cell carcinoma of the bladder.

The dog was treated with piroxicam (Feldene, Pfizer, 1 mg/kg sid per os) and cimetidina (Zytac, Intervet, 5 mg/kg bid per os).

After three months, an irregular, ulcerated, 5 cm large mass was present in the abdominal along the tract where the FNAB was taken, on opposing side to the surgical scar. Because of worsening of the clinical condition of the dog, the owner elected euthanasia. A post-mortem FNAB of the ulcerated mass was taken and the spreading of the tumoral cells was confirmed.
Case 3

A 12 year old, Persian female cat, was presented because of lameness of the right forelimb. The cat was in good body condition; both forelimbs were radiographically normal but lung abnormalities were detected, therefore a complete x-ray examination of the thorax was performed. Two round, well defined lung nodules, about 2 cm large, were visible in the right middle and left caudal lung lobes. (Fig. 4). It was possible to visualize one of the lung nodules with ultrasound because it was adjacent to the thoracic wall. It appeared as a well defined, hypoechoic homogeneous round lesion surrounded by normal air-containing lung. From this lesion, an US-guided FNAB was performed with a 22G needle connected to a 5 ml syringe. Cytological diagnosis was lung adenocarcinoma. Two weeks later, a one cm large lesion was present on the thoracic wall, in the same area of the us-guided aspiration. Cytology of the mass confirmed needle tract implantation of the lung adenocarcinoma to the thoracic wall (Fig. 5).

After ten days, the clinical condition of the cat worsened because of hemesis and anorexia, and the owner elected euthanasia.

DISCUSSION

FNAB is a commonly used procedure both in human and veterinary medicine to characterize organ lesions, since it allows to obtain sample for cytological or bacteriological examination. This technique is easy to perform, quick and inexpensive. Because of small size of the needle, complications related to organ damage or post-procedures haemorrhage are rare (Leveille 1993), therefore this technique can be considered sure. However, needle tract implantation of neoplastic cells has been rarely reported in human medicine, and first cases in dogs are described (Nyland 2002).

Dissemination of neoplasia by us-guided aspiration can occur because during movements of the needle tumoral cells are spread in the surrounding tissue and/or vessels. However, tumor
autotransplantation studies indicate that at least one million cells are necessary for successful implantation (Southam, 1961, Vaitkevicius, 1964). It is known that only few cell can survive because local protective mechanisms and the host immune response are able to destroy abnormal cells (Smith 1981). Moreover, Weiss (1988) estimated that only one of 100,000-1,000,000 neoplastic cells entering the circulation eventually can produce metastasis. It has been stated that during FNAB the number of disseminated tumour cells are normally less than that required for successful implantation (Glasgow 1988), and this explain why needle tract implantation is rarely observed (Ishi 1998, Kosugi 2004).

Factors which can influence implantation of neoplastic cells include specific features of the tumour and technical aspects of the procedures.

Cells implantation is related to tumor aggressiveness (Sacchini 1989): in human medicine, pancreatic cancer and mesothelioma are reported to have a propensity to spread along needle tracts (Boutin 1983; Fornari 1989; Smith 1981; Warshaw, 1991). Moreover, the number of tumour cells which may spread along the needle tract is proportional to the tumor redifferentiation (Ferrucci 1979).

In veterinary medicine, transitional cell carcinoma of the urinary tract (bladder or urethra) was reported by Nyland in two of three cases (Nyland 2002) and in two of three cases of this report. Therefore, it seems to be over represented. However, it must be considered that this is a common neoplasia in small animals and that aspiration procedures from the urinary bladder like cystocentesis and FNAB are routinely performed. If this neoplasia really had high propensity to spread, we probably would expect higher incidence of this complications.

One of the two dogs with transitional cell carcinoma of the urinary bladder (case 2) underwent cystotomy forty days before FNAB: it is not completely excluded that tumour spread occurred during surgery. However, the abdominal mass was located on the opposite side to the surgical scar and this suggests that the FNAB was the cause of the seeding.
To our knowledge, the Persian cat of this report (case 3) is the first published case of implantation of a lung adenocarcinoma following FNAB in veterinary medicine. Unfortunately, no data are available about biological behaviour of lung adenocarcinoma in small animal. Lung biopsies are not routinely performed in clinical practice because pulmonary lesions are often difficult to reach. If the lesion has contact with the thoracic wall, US-guided aspiration or biopsy can be performed. Otherwise, only fluoroscopy or CT-guided procedures are possible. It could be hypothesized that lung adenocarcinoma in cats may have high propensity to spread to the thoracic wall after FNAB. However, in a recent study including 39 cases of CT–guided FNAB of the lung (30 dogs and 9 cats), this complication was not reported (Vignoli 2004).

In this cat, the time between the aspiration procedure and the development of the chest wall mass was very short (only two weeks) if compared with recently published data in humans (Kim 2003), where reported recurrence time is between 2 and 16 months. This could confirm a possible high aggressiveness of lung adenocarcinoma in cats.

In humans, it has been assessed that the risk of tumour seeding increases with the size of the needle and the number of passes (Ferrucci 1979). To reduce this complication, small diameter needles (22 G or smaller) are suggested (De May 2000). Injection of foreign material into the lesion, like ethanol, saline solution, contrast medium or local anaesthetics, can promote dissemination of cells because it increases pressure inside the mass (Roussel 1989, Zerbey, 1994, De May 2000). To reduce the risk of dissemination of neoplastic cells during FNAB, some guidelines are suggested in human medicine (Kosugi 2004):

- If surgery follows, the route of the needle tract can be removed with the primary tumour
- Piston-like motion of the needle into the tumour should be avoided, because it could break malignant tissue into smaller pieces.
- To avoid cells falling when a needle is released from a tumor, physicians must constantly absorb debris using negative pressure.
The best way to avoid the risk of needle tract implantation is to change technique, if possible. If a malignant neoplasia of the urinary tract and prostate is suspected, cytological sample can be obtained by traumatic urethral catheterisation. This procedure consist of an external manipulation of the bladder and urethra during suction by an urethral catheter. In 1996 Lamb described a similar ultrasound–guided procedure, which offers the advantages to guide the tip of the catheter in contact with the lesion. With this technique, the probability to obtain a diagnostic result is higher and the captured sample can be larger enough to permit histological examination.

In conclusion, even if needle tract implantation after FNAB is a rare event in small animals, this should be considered when FNAB is performed. Urinary tract carcinomas in dogs and lung adenocarcinoma in cats seems to have higher risk of neoplastic dissemination.

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**FIGURE 1. Case 1:** Mixed breed dog. 10 months after a FNAB the dog was affected by a large ulcerated mass lesion in the parapenile area.

**FIGURE 2. Case 1:** Mixed breed dog a) Ultrasonographic examination of the urinary bladder. There is a diffuse inhomogeneous thickening of the wall with complete loss of normal layering. The mucosal surface is irregular, some hyperechoic spots with acoustic shadowing are visible (areas of minaralization). b) Longitudinal sonogram of the caudal abdominal wall at the level of the ulcerated mass: an irregular, inhomogeneous mass with nodular appearance is visible in the subcutaneous tissue.

**FIGURE 3. Case 1:** Mixed breed dog. Microscopic sections of the subcutaneous mass, hematoxylin and eosin stained (a, b) and immunoistochemistry CKpool technique (c). In the peritoneal serosa, proliferations of anomalous transitional epithelial cells of the urinary bladder are visible, organized in a tubular and papillo-tubular, well differentiated pattern. The cells show irregular margins, large nuclei, with evident nucleoli, and eosinophilic cytoplasm. Moderate fibroplasia of the serosa is present without lesions suggesting neoplastic thromboembolism (a and c). Fig. b showes a moderately differentiated pseudoglandular structures covered by atipical transitional epithelial cells of the urinary bladder infiltrating the connective of the abdominal wall. Minimal linfoplasmacelluler infiltrate is present.

**FIGURE 4. Case 3:** Persian female cat. Right lateral (a) and ventrodorsal oblique (b) radiographic projections of the thorax. There are two lung nodules in the right middle and left caudal lung lobes.

**FIGURE 5. Case 3:** Persian female cat. Fine needle aspirate from one of the pulmonary nodules: a large, three-dimensional cluster is surrounded by pinkish necrotic debis. Note the stongly cohesive arrangement of pleomprhic epithelial cells having high nuclear-to-cytoplasmic ratios. (MGG-40x)

**FIGURE 6. Case 3:** Persian female cat. Fine needle aspirate from the subcutaneous nodular lesion grown in the site of previous pulmonary fine needle biopsy: the cells show cytomorphologic features similar to primary pulmonary carcinoma. (MGG-65x)
A large ulcerated mass lesion in the parapenile area is visible. In the same area a FNAB of a transitional cell carcinoma of the urinary bladder was taken ten months before.
Diffuse hyperechoic thickening of the wall of the urinary bladder, particularly near the trigone area. The border of the urinary bladder is very irregular. Within the bladder some echoic structures are visible and referred to blood clots (a). Heterogenic mass lesion in the subcutaneous tissue (b).
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Isthopathology of the abdominal mass with Hematoxilin-Eosin (a and c) and immunoistochemistry Ckpool technique (b). In the peritoneal sierosa were visible several proliferations of transitional epitelial cells of the urinary bladder with large nuclei, vescicolar with evident nucleolo, some cytoplasm, eosinophilic with irregular and softened borders. Those elements appear organized in a tubular and papillotubular well differentiated pattern. Moderate fibroplasia of the sierosa. No neoplastic thromboembolism were visible in the sample examined (a and b). Moderately differentiated pseudoglandular structures covered by atypical transitional epithelial cells of the urinary bladder wich infiltrate the connective of the abdominal wall was visible. Minimal linfoplasmacellular infiltrate was also present (c).
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Right lateral (a) and oblique ventrodorsal (b) views of the thorax. The images show two round consolidation areas in the right middle and left caudal lung lobes. Air bronchograms are well visible on lateral view in the right middle lung lobe. On the same view moderate ventral spondiloarthritis at the thoracic spine are present.
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Fine needle aspirate from pulmonary mass: a large, three-dimensional cluster is surrounded by pinkish necrotic debris. Note the strongly cohesive arrangement of pleomorphic epithelial cells having high nuclear-to-cytoplasmic ratios. (MGG 40x).
Fine needle aspirate from a skin nodular lesion grown in the site of previous pulmonary fine needle biopsy: the cells show cytomorphologic features similar to primary pulmonary carcinoma (MGG 65x).