

Principles of Surgical Oncology

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Introduction

Tumors in pets are often best approached with a multimodal approach, considering options in medical, surgical and radiation oncology. Surgery, however, is often a critical part of achieving a diagnosis and is often necessary in treatment. Surgery is also one method that is available that can cure some forms of cancer in animals and people. When thinking through cancer diagnosis and treatment, it is very important to manage the work up in a logical, stepwise fashion to achieve the optimal treatment pathway. When faced with a patient with a tumor, the clinician should ask themselves three questions and work through answering these questions in order. These questions are:

1. What is it?
2. Where is it?
3. How bad is it?

What is it?

This question refers to the tumor type. It is essential that this question is answered before any treatment is initiated. Removal of a neoplastic mass without knowing the tissue type will rarely give rise to a favorable result. This question can be answered by several different methods, including cytology, biopsy for histopathology and a presumptive diagnosis based on classic patterns of disease.

Cytology is generally achieved by performing a fine needle aspirate. The advantages of this test are that it is quick, easy, inexpensive and can often direct us towards a diagnosis. It is a very good first step towards achieving a diagnosis. It can often diagnose lymphoma and mast cell tumors and it can help to differentiate between an inflammatory and a neoplastic process. The disadvantages are that it may be nondiagnostic in some circumstances, it can also give us a vague diagnosis or even an incorrect one. For dogs that present every year with a large number of masses, it is recommended that their skin masses are mapped. This can be done using a standard histopathology submission form dog map and enlarging two of these pictures on one page. This sheet should be incorporated into the patient's record and should include patient information and a place to write information about each mass that corresponds to a number and location of the mass on the picture. The information about the mass should include the location (if there is any potential confusion based on the chart), size of the mass, mobility, firmness and whether the mass is in the skin, SQ tissue or deeper. It should also include the cytologic description of the mass and whether cytology was performed in-house or by a pathologist. Starting early with mapping masses will save a lot of time in the future and will allow you to keep track of your patient's masses so that new masses can be addressed and masses that were diagnosed as being benign (eg lipoma) can be monitored for growth. This method is

very important in multi-doctor practices where different doctors may see a patient for their annual physical examinations, but is also important for single doctor practices because it is impossible to remember the exact character of a dog's masses over the years. If the mass is neoplastic, there are three possibilities for the types of cells present. Round cells, spindle cells and epithelial cells. With practice, you may become very adept at categorizing these cells and recognizing characteristics of malignancy, such as multiple nuclei or nucleoli, anisokaryosis, aniscocytosis and mitotic figures.

If the cytology or the clinical impression of the mass is suspicious for a malignant process, a biopsy for histopathology is recommended. There are several different ways to achieve a histologic diagnosis and the method for achieving a biopsy should always be chosen with the eventual definitive resection in mind. Options for a biopsy include an incisional biopsy or an excisional biopsy.

An incisional biopsy can be achieved by taking a sample of the mass without disrupting the architecture of the mass. For subcutaneous masses, care must be taken to go deep enough into the mass so that the biopsy does not include only skin, SQ and muscle, but actually contains a portion of the neoplastic tissue. A result of normal muscle or fat is likely an indication that the biopsy technique did not go deep enough, rather than that the mass is a benign process. An incisional biopsy can be achieved using a skin punch, taking care to penetrate deep enough into the mass. A wedge of the tissue can also be taken. If the mass is completely SQ, you can make a small incision in the skin directly over the mass and then take a wedge or punch of the mass underneath. A Tru-cut biopsy can also be used very effectively to obtain a representative sample of the mass. Keep in mind that the centre of a large mass may be necrotic due to the lack of a blood supply and biopsies in this area may not be diagnostic. It is also important to keep in mind that if the tissue is a malignant process, the biopsy tract must be resected with the definitive resection, so the biopsy should be in a location that will be easily removed with the definitive resection. As well, the biopsy tract should be small (2cm maximum) and should be in one location only. For example, multiple incisions taken from multiple locations around the mass could result in multiple areas needing to be resected in a definitive surgery and this may compromise the ability to achieve clear margins of resection. The sutures used to take a biopsy should be left in place until definitive surgery so that the biopsy tract can be removed. Another area to keep this principle in mind is oral tumors. A mass arising from the maxilla may appear to be most easily biopsied by going through the upper lip. This will, however, result in the need to resect the lip when, in most cases, this is not necessary for oral masses of the maxilla. The need to remove a portion of the upper lip would lead to a less cosmetic end result for the patient. Osteosarcoma is another tumor type where the biopsy location may be important if a limb spare procedure is the owner's choice for a definitive tumor resection. If you are unsure of the best method of biopsy for one of your cases that you think will eventually require a major resection, contact your friendly neighborhood surgical oncologist to discuss the case and biopsy techniques before you biopsy.

An excisional biopsy may be performed in certain instances. It is, however, very important that a curative intent resection is not compromised by this technique.

Examples of excisional biopsy that are appropriate include:

1. A 2mm mass on the lateral aspect of the digit in a large dog. The mass is removed as a marginal excision. If the mass is benign, there will be no further treatment. If the mass is malignant, a digit amputation will be necessary and the biopsy tract will not affect this definitive surgery.
2. A 1cm mass over the flank of a dog. Cytology was nondiagnostic. Options would include an incisional biopsy or an excisional biopsy. The owner just wants the mass removed. You explain to the owner that you will remove the mass with large margins (2-3cm laterally and one fascial plane deep to the mass). If the mass is malignant, it has been removed appropriately. If the mass is benign, you have given a larger dose of surgery than necessary, but the mass is gone.
3. In cases of a presumptive diagnosis, such as hemangiosarcoma of the spleen or osteosarcoma, the tumor is often excised (eg splenectomy or amputation) without a definitive histopathologic diagnosis. This is appropriate in cases where the histopathologic diagnosis will not change the treatment of the patient and the pattern of disease is extremely suggestive of a common form of neoplasia.

An example of when an excisional biopsy is not appropriate for the patient is removal of a mass with moderate margins with no knowledge of the tissue type. If this mass is then diagnosed as a malignant process, the definitive resection has been compromised. A very dangerous logic is "removing as much as you can", without knowing what the mass is. If you do not know what the mass is, remove as little as you can and do not disrupt the tissues around the mass. This is because the tissue surrounding the mass contains tumor cells and the excision will disrupt the tissue architecture and the fascial planes, making it more difficult to determine and achieve clean margins of resection. The resection also becomes much larger than it would have been prior to mass removal because the entire scar must be removed using 3cm and a fascial plane deep. If the fascial plane below the mass was already disrupted, you must go another fascial plane deep to achieve clean margins. This next fascial plane could be the body wall. It is also possible that a patient who would not have required radiation may need radiation to clean up the field. The potential consequences of a dirty resection of an unknown tumor include: a significant increase in morbidity to the patient, a significant increase in cost to the client, and the potential to lose the ability to cure the patient. The logic of "just removing the mass and then finding out what it is" is very dangerous and can have serious consequences. Do not be surprised by your results. The pitfalls of this approach are not always apparent to the doctor who has made this error because the problem is then referred on. It is also very important not to be completely guided by the client by the decision to just remove a mass. Most clients "just want the mass removed". They do not like looking at it, it bothers the dog and they do not want to think that their dog might have cancer. However, when clients are educated about the reasoning behind a logical, step-wise approach to tumor diagnosis and treatment, most of them are relieved to have this knowledge and will pursue more diagnostics, even if this is more costly up front. It is almost never more costly overall to take this approach.

It is important to remember that when multiple masses are biopsied, the surgeon must change gloves and instruments to prevent seeding tumor cells to multiple sites. As well, it is critical to keep a very good record of where each biopsy came from, the use of a tumor map can be very helpful in these cases. **

A presumptive diagnosis is sometimes made in cases where the pattern of disease points very strongly to the diagnosis and/or the mass is in an area that is difficult or impossible to biopsy. As mentioned earlier, this type of diagnosis is also made in cases where the treatment will not change based on the type of tumor. Examples of this include a primary bone tumor. If the radiographic diagnosis is consistent with a primary bone tumor and the signalment of the patient is also consistent with the diagnosis, bone biopsy is considered unnecessary by some surgical oncologists. If, however, there is a bone lesion in a location or patient that is not consistent with a primary bone tumor, a biopsy is recommended. A bleeding splenic mass will need to be removed regardless of whether it is hematoma or hemangiosarcoma. A lung mass will need to be removed regardless of whether it is an abscess, granuloma or tumor. The advent of advanced imaging can help us to characterize these tissue types better in a noninvasive manner, but will only allow us to reach a more educated presumptive diagnosis.

Where is it?

Once the question of what is it? Has been answered, the next question is where is it? This refers to staging of the disease. Staging of the tumor determines where exactly the tumor is locally and also if the tumor has metastasized to other sites. Local extent of tumor can be determined by palpation and ultrasound. Generally speaking, this question is most commonly answered by three-dimensional imaging such as CT scan or MRI prior to a large definitive surgery.

The methods for staging for metastatic disease will depend largely on the tumor type. For a benign mass, such as an epulis, no staging is required. For other masses, the staging tests performed will depend on the biologic behavior of the tumor type. In general, carcinomas tend to metastasize to lymph nodes and sarcomas tend to metastasize to lungs, however, this just a generalization and the reverse can be true in some cases. Three-view thoracic radiographs are always a good first step in staging. It is inexpensive and it is a very common site for metastasis. Although it does sound academic, three-views of the thorax are necessary to avoid missing a metastatic nodule. The upper lung field will be more aerated and therefore a nodule will be more apparent due to the contrast with the air in the lung. A nodule in the upper lung will also be more apparent due to magnification because of an increased distance from the plate. Multiple views will also allow the visualization of a nodule that was hidden by other thoracic structures. CT is becoming a tool that is much more sensitive for the assessment of pulmonary metastatic disease. However, thoracic radiographs should be performed as the initial screening test.

Staging can also be performed by evaluating regional lymph nodes. The local lymph nodes should be palpated in all cases and should be aspirated in cases that have a tendency to metastasize to lymph nodes. Any questionable lymph nodes should be

biopsied (incisional or excisional biopsy). For some masses, the abdominal lymph nodes may need to be assessed using ultrasound or CT. An example of this is anal sac adenocarcinoma, which has a very high rate of metastasis to the sublumbar lymph nodes.

Abdominal ultrasound may also be appropriate in some cases, or as a method of evaluating older patients for overall health status prior to a major surgical intervention. Bone scan or long bone survey radiography should be performed in cases of osteosarcoma and should be considered in cases that have a tendency to metastasize to bone (for example TCC and other carcinomas).

For cancers that have a tendency to metastasize early in the course of disease, such as hemangiosarcoma or osteosarcoma, it is very important to explain the significance of the staging tests to clients. Most clients have a hard time understanding that if their pet is deemed clear of gross metastasis, they still have a high risk of microscopic disease. Spending time explaining this to clients early on will save a lot of confusion for them later in the course of disease. It is the reason why chemotherapy is recommended in these cases and why it extends their lifespan, but, unfortunately, does not cure their disease.

How bad is it?

This question refers to both the stage of the disease and the grade. Grade refers to the histologic grade of the tumor. This is often designated as grade I, II or III, with I having the least aggressive biological behavior and III having the most aggressive biological behavior. The grading system is particular to each tumor type and every pathologist may have a slightly different approach to tumor grading. It is important to keep in mind that although the grading system helps us to predict the biological behavior of the tumor, each tumor type has a continuum of histological appearance and they are being categorized somewhat arbitrarily. It is also possible that the grade may shift from the incisional biopsy to the definitive resection because the pathologist will have more tissue to work with.

Information regarding the tissue type, stage of disease and histologic grade can now be assessed to give the owner a prediction of prognosis and a plan for treatment.

Treatment Plan

The treatment plan will be based on the information from asking the three questions: What is it? Where is it? And How bad is it? From this point, recommendations and options can be presented to the owner. These plans will vary in aggressiveness of treatment and in cost and all options should be discussed with the owner. In general, the goals of therapy may be curative intent, palliative, or the owner may not wish to pursue further treatment and may elect for euthanasia when the patient's quality of life declines.

Surgical Principles

Based on the correlation of the information regarding the disease and the owner's wishes for treatment, a dose of surgery can be determined. There are four doses of surgery that can be administered to a tumor:

1. Intralesional – This involves removal of the mass leaving microscopic or gross disease behind. Examples of when this would be considered an appropriate treatment would be a benign lipoma, where the mass is shelled out. Another example would be a low grade sarcoma in a very geriatric patient. In some cases the mass is extremely large and over the body wall. If the owners goal is palliative, it may be appropriate to cytoreduce the mass to reduce discomfort in the patient. This will not cure the patient and the mass will certainly recur.
2. Marginal resection – The mass is removed with minimal margins. This therapy may be considered appropriate in a location where a wide resection is not possible. Example of this would include removal of a brain tumor or removal of a large anal sac adenocarcinoma. Another example of this would be a malignant mass (eg. Soft tissue sarcoma or mast cell tumor) that is removed from the distal extremity with minimal margins, with a plan to treat with full course radiation post operatively.
3. Wide resection – Removal of a mass with curative intent. Although recommendations may vary with tumor type, this generally involves the removal of the mass with 2-3cm margins laterally and a fascial plane deep to the mass. The mass is removed en bloc and the tumor capsule is not invaded or handled at the time of surgery.
4. Radical resection – Removal of an anatomic segment with curative intent. The best example of this is an amputation for osteosarcoma. Other examples may include thoracic wall resection and hemimandibulectomy.

Wide and radical resection are reserved for curative intent surgeries and generally are performed for patients that are negative for metastatic disease. These surgeries take a great deal of planning. Three-dimensional imaging (CT or MRI) is usually necessary to evaluate the extent of the neoplasm and plan the surgical resection. The use of three-dimensional imaging will greatly increase the chances of achieving a surgical cure. Tumor cells are able to take on characteristics of muscle cells, meaning that they have the ability to contract and move throughout the tissues. This is how tumor cells metastasize (by moving into blood and lymphatic vessels) and how they invade the surrounding tissues locally. The cells that are in the periphery are the most aggressive cells in the tumor cell population. If these cells are left behind, the tumor will regrow and will contain a more aggressive population of cells.

Prior to surgery, a general plan of how the defect that is created will be reconstructed should be made. A skin flap may be necessary to replace a defect in the skin. It is critical that the flap is planned for preoperatively and that this area is clipped, prepped and draped in the field at the time of surgery. At the time of surgery, the use of a sterile ruler and pen can be very helpful to trace out the mass, the proposed margins of resection and the planned flap. Mark your margins around the mass with 3cm margins

laterally and trace this around the mass. This will result in a circular or oval shaped incision. Do not create an ellipse at this time. This will create one of two problems: it will either compromise the margins by taking less tissue than is required, or it will commit you to reconstructing in one direction. The reconstruction and the removal of “dog ears” should be done once the mass is removed and the defect is being closed.

During resection, it is very important to continue with an en bloc resection that does not “cone down” to remove less of the deeper tissues. This can be prevented by suturing the skin to the deep fascia to prevent it from slipping and to maintain the appropriate orientation. The problem with coning down is that the deep tissues are critical to remove, as they may contain tumor cells. If this tissue is not removed then the difficult closer created by a large skin defect was created in vain because dirty margins are a very real possibility. The fascial plane refers to either a layer of muscle or the fascia around a muscle. This does not include a layer of fat or subcutaneous tissue, as tumor cells can readily penetrate these tissues. Tumor cells move via the path of least resistance, they can generally move laterally more easily (through fat and SQ) and will stop when they reach the fascia of a muscle. The decision to take the fascia around the muscle or the muscle itself depends on the regional anatomy. If it is possible to remove the fascia only, this is preferable, as it will result in less morbidity to the patient. However, it is not always possible and in most cases, our patients adjust well after removal of a single muscle. One notable example of an excellent fascial plane is the antebrachial fascia, which can be used as the deep layer when removing soft tissue sarcomas in this area.

Although the surgeon should have a reconstruction plan in mind preoperatively, it is important not to focus on how to close the defect during resection, as it may cause you to take less tissue than is necessary for a cure. It is possible that some resections will not be 100% reconstructed at the time of surgery and that some open wound management may be necessary. This possibility should be discussed with owners prior to surgery.

Whether or not to change the instruments and gloves after the mass has been removed is somewhat controversial. The reasoning behind this action is that there may be tumor cells on the surgeon’s gloves or instruments and that this may result in further tumor seeding. If surgical oncology principles are strictly adhered to, the surgeon should not come into contact with tumor cells during resection because the incisions are well outside the tumor capsule with a healthy margin of tissue around this tumor. That is to say, the surgeon should be working in normal tissue that is free of gross and microscopic tumor. If the surgeon has not followed these principles, or if the tumor cells exist outside of the proposed margin, then the surgery is compromised whether gloves and instruments are changed or not. There are two instances when I will change gloves and instruments:

1. The mass has been removed and I am going to elevate a skin flap. I will change the gloves in this case because if the margins do come back dirty and radiation or a recut is an option, it is possible that the field will not have been

contaminated. Having said this, when the histopathology comes back dirty, technically the entire scar should be considered dirty.

2. If the tumor capsule is inadvertently entered, the surgeon should close the area where the tumor capsule was breached with a simple continuous pattern. The area should be lavaged and gloves and instruments should be changed. The tumor resection should be continued to include a larger area of tissue (usually deeper). In this case a second change of instruments/gloves could be considered once the tumor has been removed. If the tumor capsule is inadvertently opened, the risk of recurrence increases.

Part of the surgical planning should be based around decreasing patient morbidity. Because wide and radical resections are by nature, painful, it is critical that an appropriate analgesic plan is made for perioperative and post operative pain control. This may include a cox-2 sparing NSAID (such as Meloxicam) if it is not contraindicated; opioids, such as a fentanyl CRI for intraoperative and postoperative use; hydromorphone prn; and a ketamine CRI for perioperative use (to prevent wind up) and post operative use. Another very useful mode of pain control for major resections is a pain diffusion catheter. (Mila) These catheters come in various sizes and the size corresponds to the length of tubing that is to remain in the wound. The end of the catheter in the wound is closed ended, with multiple holes along the catheter. The dark line on the catheter delineates the end of this region of the catheter. The catheter is laid in the wound and bupivacaine is administered every 6-8 hours (1-2mg/kg) in a sterile fashion to give a local anesthetic to the wound bed. This company also makes a pump which will administer the bupivacaine as a CRI to the wound. Administer the first dose as the patient is recovering from surgery. Do not administer with bicarbonate, as this can clog the holes in the catheter.

It is also critical to plan for the potential for a large volume of rapid blood loss. The patient should be typed and a blood transfusion should be readily accessible. For high-risk cases, the blood should be in the OR and ready to administer when it is needed.

The use of drains is traditionally contraindicated in surgical oncology. This refers to Penrose drains. The reason that a Penrose drain should not be used is because it will need to exit ventrally and this will require tunneling the drain to a distant site. Theoretically, if the resection is not clear of tumor cells, these tumor cells may be transferred along the drain. If a further definitive resection or radiation is required, it will be necessary to resect or irradiate the drain tract, which may not be readily detectable and will increase morbidity. A closed suction drain, however, may be useful in large resection/reconstruction cases where there is a lot of dead space. This type of drain can exit just adjacent to the incision and does not create a new tunnel in the tissues, and should not therefore be a concern when placing a closed suction drain. The same logic should follow when a pain catheter is used.

Once the tumor has been removed, it should be inked for margin assessment. Although India ink and suture tags can be used, I would recommend the use of a commercial tissue inking system. Discuss the color that the pathologist prefers, generally black or

yellow is preferred and blue or red is discouraged, because it is difficult to see with H&E stain. The lateral margins and the deep margin should be marked. Blot the tissue so it is dry and paint a small amount of ink on the tissue using a Qtip. If too much ink is used, the ink may run into the lateral tissues and create an artifact that is difficult for the pathologist to interpret. Although tissue inking is very important and can give us important information regarding the presence or absence of tumor cells at the margin (clean or dirty margins), it is by no means perfect. It is not recommended to paint the entire mass with ink because it is not practical or possible for the pathologist to make slides of this entire region of tissue (it would likely amount to hundreds of slides). Ink a representative area (ie four quadrants of tissue laterally and the fascia deep to the tissue) unless there is an area that you are particularly concerned with, then focus on that area and mark it with a different color. It is absolutely critical that you communicate well with the pathologist regarding the location of the tumor, the type of resection and the way that the margins were inked. Once the mass is inked, breadloaf it to allow the formalin to fix the tissue. This involves slicing the mass partial thickness in 1cm slices to allow for complete fixation. Then place the mass into a large formalin jar. If the mass is sectioned into smaller pieces to allow placing it into smaller jars, the orientation of the mass will be lost and margin evaluation will be difficult, if not impossible. If the pathologist can see tumor cells extending to the inked area, it is likely that there are still tumor cells remaining in the tissue and a recut surgery or radiation may be necessary. It is important to interpret the results of the lateral and deep margins differently. If the pathologist sees tumor cells within 1-2mm of the lateral margins, then this is either a dirty margin or a clean but close margin. If the pathologist sees tumor cells within 1-2mm of the deep margin ink, but there is a fascial plane (layer of fascia) between the tumor cells and the ink, then it should be considered clean. If there are tumor cells within 2cm of the deep inked margin but there is no fascia removed deep to the tumor and this is 2cm of SQ fat, it is possible that this margin will be called "clean" could in fact be dirty.

By following the principles of surgical oncology, an optimal treatment pathway for every cancer patient can be reached. The decisions should be made in a logical, stepwise fashion, taking into account the characteristics of disease and the wishes of the pet owner. It is very important for general practitioners to work in concert with their pathologist and surgical oncologist to develop the best possible plan for each patient.