

Repair of Defect in Thoracic Wall Associated with Neoplasms —Literature Review

Josiane Morais Pazzini¹, Rafael Ricardo Huppes², Jorge Luiz Costa Castro³, Pedro Carvalho Cassino¹,
Stella Habib Moreira¹, Jorge Luis Gomez Alvaréz¹, Cláudia Sampaio Fonseca Repetti⁴,
Thayana Neiva de Lima Queiroz³ & Andriago Barboza De Nardi¹

¹ Universidade Estadual Paulista, Jaboticabal, SP, Brazil

² Centro Universitário de Maringá, Maringá, PR, Brazil

³ Pontifical Catholic University, Curitiba, PR, Brazil

⁴ Universidade de Marília, Marília, SP, Brazil

Correspondence: Josiane Morais Pazzini, Faculdade de Ciências Agrárias e Veterinárias, Universidade Estadual Paulista “Júlio de Mesquita Filho”, Jaboticabal, Rodovia de Acesso Paulo Castelane, São Paulo, Brazil. Tel: 55-169-9151-5157. E-mail: josipazzini@hotmail.com

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Abstract

The major malignant tumors found on the chest wall are sarcomas, including osteosarcomas, chondrosarcomas, fibrosarcomas, and hemangiosarcomas. Treatment of cancer, as well as chronic chest wall conditions, require radical surgical excision of the involved tissues. In addition to surgery, chemotherapy plays a role as adjuvant treatment in tumors affecting the chest wall, reducing chances of metastasis and prolonging the disease. The restoration of the chest wall has the main objective to restore the respiratory function, for this, a procedure is necessary that keeps the chest closed and stable. There are many materials used for chest repair, such as autogenous, synthetic, homologous and heterologous tissues. The main objective of this literature review is to address the main malignancies that affect the chest wall, as well as the resources most used to repair the damage caused by aggressive surgery in an attempt to promote greater safety margins.

Keywords: chest, reconstruction, surgery

1. Introduction

The treatment of neoplasms and chronic infections of the thoracic wall requires radical surgical excision of the involved tissues (Brasmer, 1971). The malignant tumors found in the thoracic wall are the sarcomas (Rivoire et al., 1994), among them the osteosarcomas, chondrosarcomas, fibrosarcomas and hemangiosarcomas (Orton, 1998). According to Doige and Weisbrode (1998), and Fossum (2008), the osteosarcoma is the neoplasm that most affects the thoracic wall, but the chondrosarcoma constitutes the most common primary neoplasm affecting the ribs of dogs (Daleck, Fonseca, & Canola, 2002). Daleck et al. (2002) affirmed that, in general, these tumors develop next to the costochondral junction and occur more intrathoracically than extrathoracically.

The tumor staging plays an important role in determining the patients prognosis as well as in defining their therapeutic possibilities. In determining the extent of the disease, the chance of success is better (Dobson, 2011). Thus, it is necessary to investigate the possibility of metastases as part of the initial evaluation of oncologic patients (Morris & Dobson, 2007).

An objective approach by means of physical, hematological, imaging exams and cytological and histopathological evaluation enables assessing primary tumors, local lymph nodes and distant metastases (Morris & Dobson, 2007). Radiographic exams are the most common technique used in veterinary oncology, thus the main indication for research on lung and bone neoplasm, since they help to determine the staging of the oncologic patient as well as to evaluate the therapy (Rodaski & Pierkarz, 2009; Lattimer & Haub, 2010).

The knowledge of the principles of oncologic surgery is fundamental. It is known that some care should be taken, such as wide and adequate surgical incision, tumor isolation with compresses, careful handling of the affected area, special care not to incise the tumor tissue, withdrawal of tumor with margin of safety, removal of adjacent

lymph nodes, and the marking of surgical margins in order to determine the operative site for adjuvant radiotherapy if necessary (Vieira, Lustosa, Barbosa, Teixeira, Brito, Soares, & Ferreira, 2012).

The margins of safety during the surgical procedure influence the prognosis and the period free of recidivation (Feeney et al., 1982; Sweet & Waters, 1991; Aronsohn, 1996; Bright, 1996; Kuntz, 1998; Hosgood, 1999). Large chest defects associated with trauma or aggressive oncologic surgery including three or more ribs may trigger thoracic instability (Fossum, 2008). The reconstruction of the thoracic wall should be rigid to avoid paradoxical movement in breathing (Ruiz, Gómez, Alfaro, Granel, & García, 1997) and should also be hermetically sealed to avoid pneumothorax (Orton, 1998). The main objective of thoracic stability is to allow for suitable ventilation in the postoperative period as soon as possible (Aguiar, 2001).

2. Literature Review

2.1 Osteosarcoma

The osteosarcoma (OSA) or osteogenic sarcoma is the most frequently diagnosed bone neoplasm in dogs, accounting for more than 85% of neoplasms with skeletal origin. It is characterized by the proliferation of malignant primitive mesenchymal cells with osteoblastic differentiation that produce osteoid or immature bone, with bone matrix of a non-reactive and non-metaplastic character (Daleck et al., 2016)

The osteosarcomas commonly affect the metaphyses of long bones, but have also been described in ribs, vertebrae and skull bones (Brandão et al., 2009). Daleck et al. (2016) state that osteosarcoma is a locally invasive and highly metastatic tumor. Approximately 98% of patients treated presented micro metastases at the time of diagnosis, although only 5% of them presented radiographic evidence of pulmonary metastasis at consultation.

2.2 Chondrosarcoma

Chondrosarcoma is a malignant neoplasm in which cartilaginous tumor cells produce a variable quantity of neoplastic fibrillar matrix (Hawkins, 2006), and may develop primarily in skeletal sites such as limbs and vertebral column (Thompson, Lester, Gannon, & Francis, 2002), and rarely in extra-skeletal ones such as soft tissues (Miller, Walshaw, & Bourque, 2005).

Chondrosarcoma is the second most common primary bone tumor, accounting for approximately 5% of cases, with predilection for the German Shepherd, Boxer and Golden Retriever races (Kleiner & Silva, 2003). In dogs, more than 60% of chondrosarcomas have been identified in flat bones like ribs and pelvis (Popovitch, Weinstein, Goldsmidt, & Shofer, 1994; Bohman, Koch, Bailey, Basanta, & Lee, 2014). It usually presents slow clinical evolution with a late metastatic process.

According to Thompson, Lester, Gannon, and Francis (2002), the tumor can be classified, as to location, as central (when arising from the bone) or peripheral (when arising from the periosteum). The secondary chondrosarcoma arises from the malignant transformation of a previous bone lesion (Thompson, Lester, Gannon, & Francis, 2002). In radiographic findings the lesion presents osteolysis and periosteal reaction, and may contain points of calcification and intralesional ossification with cortical thickening (Kealy, McAllister, & Graham, 2005).

2.3 Fibrosarcoma

Soft tissue sarcomas are relatively common neoplasms in dogs, accounting for 15 to 20% of all cutaneous and subcutaneous tumors (Priester, 1973). The sarcomas associated with the application of vaccines are most commonly found in cats; they are mostly fibrosarcomas, but other types of tumors have already been reported (Montanha & Corrêa, 2013). Fibrosarcoma is a malignant neoplasm of mesenchymal tissue (fibroblasts) that originates in soft tissue structures, especially in adult or elderly animals (Pulley & Stannard, 1990).

There are three variants of this type of tumor: the solitary form, the multicentric one and that associated with the application of vaccines and other injecting drugs (Ogilvie & Moore, 2001). New studies suggest that although the anti-rabies and feline leukemia virus vaccines are the most involved procedure in the onset of tumor, there are also cases associated with subcutaneous and intramuscular administration of the feline triple vaccine (Tannure & Santos, 2013). Solitary fibrosarcomas are usually firm, slow-growing, and may occur anywhere on the body (Chalita & Reche, 2003). The solitary form more often reaches older cats (more than 12 years) and is not associated with the feline sarcoma virus. Younger felines (less than 5 years) are more frequently affected by the multicentric form, that is compulsorily associated with the feline leukemia virus, and is more anaplastic and invasive than the solitary form (Meneses, 2012).

The neoplasm is characterized by nodular, pseudoencapsulated and locally invasive mass (Perrone, Botelho, Amaral, Menezes, & Andrade, 2004). Surgery is the treatment of choice, for which it is essential to obtain a wide

surgical margin (Heller, Martha, Stebbins, Reynolds, & Hauck, 2005). Chemotherapy and radiotherapy may be used as a supportive treatment, both in the pre and postoperative periods, in cases in which the surgery is not effective or possible, and also in cases of recidivation and metastasis. The prognosis is from reserved to poor, varying according to factors such as location, recidivation and metastasis, and tumor size (Tannure & Santos, 2013).

2.4 Hemangiosarcoma

Hemangiosarcoma is a mesenchymal tumor that originates in the endothelial cells of the vessels; therefore it can initiate in any tissue that contains blood vessels (Hammer, 2004). It is a malignant neoplasm that primarily affects the spleen, liver and right atrium (Brown, Patnaik, & Macewen, 1985; Lorimier & Kitchell, 2002; Smith, 2003).

When superficial, the hemangiosarcomas are masses located in the epidermis, dermis or subcutis, with an apparent predilection for the ventral abdominal skin. They can be classified according to the depth of invasion within the cutaneous structures. Stage I includes tumors limited to the epidermis or dermis; Stage II tumors are located in the hypodermis, with or without epidermal involvement; and Stage III tumors invade the underlying musculature (Page & Thrall, 2004).

It has a high degree of invasiveness, rapid and common growth causing metastases; and the spleen, heart, skin and liver are the most frequently affected sites (Graham & O'keefe, 2003; Page & Thrall, 2004).

The treatment is based on aggressive surgery, associated or not with chemotherapy, and several chemotherapeutic protocols are involved (Macewen, 2001). Chemotherapy is of utmost importance for treatment, fighting the high-grade metastatic character of the neoplasm. Doxorubicin-based protocols, solely or in combination with other drugs such as prednisone, cyclophosphamide, vincristine, and methotrexate lie among the most commonly employed ones. The prophylactic antibiotic therapy is indicated using sulfamethoxazole/trimethoprim (10 to 20 mg/kg OV, every 12 hours) and should be administered from the first to the eighth day of protocol (Macewen, 2001; Rodaski & De Nardi, 2004).

Although the use of biological therapy such as immunotherapy with liposome has not yet been thoroughly studied, it presented a four-month increase in the survival rate of patients that used it in an adjunctive way associated with surgical resection and chemotherapy. Palliative radiotherapy is rarely used in cases of canine hemangiosarcoma because of the location and the high rate of metastasis, in spite of the decrease in cutaneous masses without interfering with the patient's survival time (Macewen, 2001).

However the life expectancy is short: less than 10% of animals can reach 12-month survival (Brown et al., 1985; Smith, 2003).

3. Treatment

The primary goal of the thoracic wall restoration is to reestablish the respiratory function as quickly as possible. This requires a procedure that keeps the chest closed and stable (Bright, 1996).

Costal wall trauma with large tissue losses and costal neoplasms require surgical resection at full thickness of the involved tissues. According to Freitas et al. (2004), for a successful treatment, several materials are available to be used for chest repair, such as synthetic and homologous and heterologous organic tissues.

Repairs for chest wall defects have been performed after the resection of malignant diseases (Ohno, Kuwata, Yamasaki, Akizuki, & Satoh, 1998). According to Bjorab (1996), the most used techniques are the chest wall reconstruction with skin flaps, muscle, fascia lata, metal meshes; polypropylene meshes (Marlex), resin acrylic molds and synthetic materials.

According to Feeney et al. (1982), primary and secondary tumors of the thoracic wall have been observed to most frequently involve from the 5th to 9th rib region in dogs. The site of injury is important to determine the type of repair needed for the thoracic reconstruction (Aronsohn, 1984). In human patients, the anterior wall of thorax can be reconstituted by three main muscles: the pectoralis and the rectus abdominis for small defects, and the great dorsal for large defects (Ruiz et al., 1997).

3.1 Materials Applied in Thoracic Reconstruction

3.1.1 Bone Allografts

Cortical bone allografts are biodegradable and commonly used in the treatment of fractures in mammals. The grafts can be conserved resulting in cell death, and operate primarily as occupants of space and support for the growth of the host's new bone. The various means and methods of preserving cortical bones are intended to

decrease the antigenicity of the donor cells to be implanted in the host, as well as to maintain an accessible stock of available bone (Stevenson, 1998).

According to Oliveira et al. (1999), the materials used as bone graft can have three action mechanisms: osteogeny, osteoinduction and osteoconduction. The grafts do not contribute to osteogeny, but are capable of promoting osteoinduction and providing a supporting structure and osteoconduction. The most important point is the contact between the graft and the receptor's bone, and the rigid fixation. The graft rejection is the result of antigen receptor sensitization (Brown & Cruess, 1982).

Each individual presents a pair of alleles, from each locus, responsible for the encoding of antigens on the surface of cells, of codominant expression. In other words, a particular person expresses in the cells 2 antigens HLA-A, 2 HLA-B, 2 HLA-C, 2 HLA-DQ, 2 HLA-DP and 2 HLA-DR. Thus, the possibility that a transplant can be successful is largely due to the degree of compatibility between donor and recipient (Brown & Cruess, 1982). In clinical transplantations, there are three types of rejection: hyperacute, acute, and chronic. The clinical signs related to rejection include fever, hypertension, edemas, sudden weight gain, shortness of breath and increased pain sensitivity at the site of transplant. Hyperacute rejection occurs minutes after transplant and is due to the reaction of IgG antibodies against HLA class I in the transplanted organ. Acute rejection is the most common one and occurs within the first six months post-transplant. It is mediated by T lymphocytes, that infiltrate the allograft, undergo clonal expansion and cause destruction of tissues. Moreover, the chronic rejection occurs when the allograft function slowly deteriorates with histological evidence of hypertrophy and fibrosis (Brown & Cruess, 1982).

The search for new tissue preservation methods has been increasing with the use of bone implants, so the pure glycerin was the method chosen by Costa (1996). This method has been shown to preserve the osteoconductive and osteoinductive functions of implants, and stands for a good conservative method as it reduces antigenicity because of a low cost and an easy mode of preparation and storage (Leite, Marques, Gomes, & Pigossi, 1979; Costa, 1997). However, the resistance of these fragments was observed to decrease considerably (Costa, 1996). The use of polymers in the medullary canal of the bone implants was indicated with the purpose of increasing their resistance (O'Brien, Straw, & Withrow, 1993; Straw & Withrow, 1995). The polyurethane resin, developed by Chierici and Miller (1984), was used in dogs by Ignácio in 1999 and by Maria (2001), showing to be biocompatible and biotolerant without presenting osseointegration.

3.1.2 Polypropylene Meshes

Chest defects that involve three or more ribs may be reconstituted by prosthetic meshes, such as polypropylene meshes (Brasmer, 1971), it was used to reconstruct the thorax after the removal of the portions of the 10th, 11th and 12th rib. The synthetic material (Marlex) is resistant to infections, non-reactive, can be autoclaved and highly resistant to traction (Figure 1) (Bjorab, 1996).

In accordance with Fossum (2008), on performing the resection of three or more ribs because of thoracic wall neoplasms, surgical reconstruction is necessary to restore the continuity of the chest wall. The use of a polypropylene mesh is recommended with the free margin facing the outer side of defect to prevent irritation and adhesion, and the borders should be folded to increase their strength, and fixed internally to the ribs with polypropylene thread (1-0 or 2-0). A single mesh is usually enough for the defect correction (Bjorab, 1996).

The use of a polypropylene mesh associated with the mobilization of the dorsal large muscle was the method adopted by Matthiesen, Clark, and Orsher (1992) successful in restoring the chest wall after block resection of 40 neoplasm-affected dogs.



Figure 1. Photographic image of polypropylene membrane. Reconstruction of chest wall in dog

3.1.3 Cartilage

The cartilage is considered a good material for the production of autogenous and even xenogeneic bioprotheses because of its low metabolic activity in avascular environment, leaving the host protected against its antigens (Belanger, 1981). The characterization of the cartilaginous tissue as immunologically privileged, when concluding that its easy acceptance by the receptor is due to the weak antigenicity of the tissue and to the fact that the chondrocytes are protected by its matrix (Figure 2) (Ferri, Calich, & Vaz, 1977).

The high plasticity and modeling ability of the cartilage associated with its firm consistency enables obtaining varied forms, easily adapting to the recipient bed. It also allows the bonding of fragments by suture and can be adapted in its dimensions and geometric conformations. In addition to these peculiarities, it requires no blood supply and may be considered an excellent bone substitute (Bruschini et al., 1992).

Doherty et al. (1995) evaluated the application of bovine pericardium treated with glutaraldehyde in different concentrations in the thoracic wall, diaphragm, abdominal wall and sternum of dogs. Good results were obtained, both by the tissue acceptance in the recipient bed and the tensile strength of rupture. The bovine pericardium preserved in 0.5% glutaraldehyde was considered adequate for the reconstruction of defects of the thoracic-abdominal wall and the diaphragm because it is easy to acquire and manipulate surgically, in addition to being moldable, highly resistant and provoking no immunological reactions.

Shahar, Shamir, and Johnston (1997) reported that the reconstruction of the chest wall with the use of muscle and myocutaneous flaps, omentum transfer and the use of synthetic materials are complex techniques with a high probability of failure. Regarding the materials used as meshes, the authors observed that the implantation of this type of prosthesis requires strictly aseptic conditions of use, hardly found in cases of bite wounds.

According to Doherty et al. (1995), as the reconstruction of the chest wall using pedicled bioprotheses of muscles can cause another defect that also needs to be rebuilt, this type of restoration is not advisable when the area to be repaired is considerably large.



Figure 2. Photographic image of biological membrane of cartilage of swine. A) biological membrane preserved in liquid glycerin. B) Hydration of the biological membrane in physiological solution. C) Hydrated biological membrane ready to be used

3.2 Neoadjuvant Chemotherapy

Chemotherapy in thoracic neoplasms is used in a neoadjuvant way after the surgical resection of tumor or after the radiotherapy procedure, in an attempt to promote local and distance control. This therapy is instituted to control potential micrometastases in patients that present from moderate to severe risks of recidivation or metastases. The response will be evaluated over time by means of the observed recurrence rates and the increase in patient survival (Rodaski & De Nardi, 2004).

Combination chemotherapy is always advantageous because each chemotherapy medicine destroys a constant fraction of tumor cells, regardless of the total number of cells, and the fraction exterminated by one drug is independent of the fraction exterminated by another (Rosenthal & KianAng, 2004). In addition to potentiating the destruction of cancer cells, there is a reduction in the possibility of resistance and poisoning.

3.3 Radiotherapy

Radiotherapy can be used as therapeutic or palliative. The therapeutic form is generally reserved for patients that present locally aggressive and non-metastatic tumors. Soft tissue sarcomas are good examples of tumors that can be treated with radiotherapy. The mechanism of DNA damage is the primary cause of cell death after the exposure to ionizing radiation, and the cell division is most often required for radiation damage to manifest (Rosenthal & KianAng, 2004).

According to Macneil, Hasty, Evans, Redlich, and Berk (2009) of Michigan State University, there are three main methods of treatments. The teletherapy, also called external radiotherapy, is the most commonly used modality. It consists of using a machine that emits an external beam of radiation on the patient. The machines used include orthovoltage equipment, linear accelerators and cobalt pumps. The brachytherapy consists of the use of implants of radioactive materials to emit the radiation directly into the tumor. Finally, the nuclear medicine, that systemically administrate radioactive substances that aim the tumors.

The conventional fractionation in radiotherapy involves 1.8 to 2 Gy per day in three to five weeks; however is not always the best choice. The preservation of normal tissues is extremely important. There is a dose of tolerance for each organ. The aim of hypofractionation is to increase the dose per fraction by decreasing the number of fractions with the purpose of decreasing the amount of clonogenic tumor cells, inhibiting tumor cell repair between fractions, and overcoming resistance of hypoxic and S phase cells (S for synthesis in the cell

cycle, a less sensitive phase to radiation) (Macneil et al., 2009). Despite the great therapeutic importance in Brazil, the radiotherapy in animals is restricted to isolated research in some public universities.

4. Final Considerations

The surgical approach in the chest wall in cases of neoplasm should be very aggressive, thus, the use of materials that allow the reconstruction and stability of the thorax is of paramount importance for a suitable pulmonary ventilation. In addition, the knowledge of adequate techniques to restore the thoracic wall allows us to respect the necessary margin of safety, positively influencing the prognosis of the patient and reducing the risks of tumor recurrence.

It is also important to emphasize that the association of neoadjuvant chemotherapy is extremely necessary to reduce the chances of metastases and to extend the free-of-disease period in cancer patients.

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