Malignant Hemangiopericytoma: A Clinical Overview and Case Study

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Hemangiopericytoma (HPC) is considered an unusual perivascular tumor. It is believed to originate from the cells that surround endothelial tissue, which are known as pericytes of Zimmerman (Marcus, Post, & Mancuso, 1994). Therefore, HPC can occur wherever endothelial tissue exists and develops primarily in the musculoskeletal system or skin. The function of pericytes is uncertain, but they are believed to provide mechanical support to enable the capillaries to have contractile power (Perez & Chao, 1998). HPC occurs in both sexes with equal frequency and is found primarily in adults and rarely in children (Perez & Chao). Congenital or infantile HPC usually behaves as a benign tumor despite histologic evidence of mitosis and increased cellularity (Brock, Morgan, & Anderson, 1995). Cases of spontaneous regression in congenital HPC have been reported (Brock, Morgan, & Anderson; Chen, Kassel, & Medrano, 1986). However, this phenomenon is rare when present in the adult population. The etiology of this disease is uncertain, and no strong clinical data exist to indicate a convincing link to specific causative agents. Some reports indicate a relationship between HPC and occupational vinyl chloride exposure (Hozo et al., 2000), as well as herbicidal exposure (Vietnam Veterans of America, 2002).

A comprehensive literature review revealed many cases of HPC in numerous parts of the body. The most common sites were the head and neck, followed by the lower extremities and retroperitoneum (Weiss & Goldblum, 2001). Most arise from soft tissue (Daugaard, Hurltberg, Hou-Jensen, & Mouridsen, 1988), which usually causes them to be classified as sarcomas. In about three-fourths of cases, the tumors are well circumscribed or encapsulated (Rosai, 1996). They grow relatively slowly and are considered malignant when the mitotic rate exceeds four per high power-field, they have a foci of necrosis, and they have increased cellularity (Perez & Chao, 1998).

The diagnosis of HPC is somewhat controversial and often is a diagnosis of exclusion. HPC has a highly vascular pattern, usually highlighted by a reticulin stain (Saldanha & Pia, 2001). This, however, can be present in other forms of connective tissue tumors. Pathologically, HPC also must stain negatively for muscle, nerve sheath, and epithelial markers (Brooks, 1994). Malignant HPC cases represent less than 1% of all vascular tumors and about 5% of all sarcomatous tumors (Kiefer, Wertz, Freudenberg, & Hasse, 1997). Because malignant HPC is a rare and often incurable disease, not much advancement has been made in the way of treatment and cure. Much of what has been published about the disease is from the 1970s and 1980s, with recent journal publications limited mostly to specific case studies. Many cases of HPC have an indolent behavior, although some, like the one outlined in this article, behave like high-grade sarcomas (Enzinger & Smith, 1976). The literature reports only one family in which three members were diagnosed with HPC, suggesting no evidence of an overall increased familial incidence (Plukker et al., 1988).

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Presentation

The clinical presentation and duration of HPC vary. Most cases of HPC are present for several months to years prior to removal (Weiss & Goldblum, 2001). Tenderness and pain are not often associated with HPC. Skin overlying the mass does not have any discoloration or redness to indicate its vascular origin (Gudrun, 1979) (see Figure 1). This is because the surrounding capillaries are emptied of blood by compression of the massive numbers of pericytes surrounding the tumor (Gudrun).

HPC in the lung, pelvis, and retroperitoneum generally is discovered when a tumor has grown to a size that causes symptoms. For example, HPC in the lung usually is discovered when a patient has chest discomfort or dyspnea with or without a cough that is caused by bronchial compression or irritation. HPC in the pelvis or retroperitoneum may cause urinary retention, hydroureter, or hydronephrosis; rare cases of constipation, abdominal distention, or vomiting have been reported (Weiss & Goldblum, 2001). Hypoglycemia has been associated with HPC in the pelvis and retroperitoneum (Pavelic et al., 1999; Rose, Tallini, Pollak, & Murren, 1999). HPC can produce insulin-like growth factors (Pavelic et al.). In patients with clinical hypoglycemia, symptoms abate with tumor removal (Weiss & Goldblum).

When found in the head and neck area, HPCs generally are smaller because of anatomic location and often are low grade (el-Naggar, Batsakis, Garcia, Luna, & Goepfert, 1992), which is indicated by a less aggressive or benign tumor with a low cellular mitotic rate. These usually are associated with nasal or sinus congestion, epistaxis, or proptosis, depending on the specific site of origin (Croxatto & Font, 1982; Setzkorn, Lee, Iliff, & Green, 1987; Weber, Henkes, Metz, Berg-Dammer, & Kuhne, 2001). HPC of the nasal passages and paranasal sinuses appears to be an entirely different histologic entity from HPC of the soft tissue (Batsakis, Jacobs, & Templeton, 1983; Compagno, 1978; Eneroth, Soderberg, & Anggard, 1970). For this reason, these tumors may be referred to as HPC-like tumors of the nasal passages (Weiss & Goldblum, 2001). HPC also can occur in the brain. It usually arises from the meninges and can resemble a meningioma (Jaaskelainen, Servo, Haltia, Wahlstrom, & Valtonen, 1985). Like other brain tumors, HPCs may present with peripheral neuropathy or signs of increased intracranial pressure, such as headache, vertigo, nausea and vomiting, and visual disturbances.

Radiographically, whether by magnetic resonance imaging, computerized tomography (CT), or plain x-ray films, HPCs are not specific and usually appear as well-encapsulated soft tissue masses (see Figure 2). Often, masses eventually grow to the point of displacement of adjacent structures, thus producing symptomatology. An angiogram may show evidence of rapid circulation, indicated by a richly vascular mass with dilation of the arteries and a diffuse capillary blush or opacification in the arterial phase, a dense uniform tumor, and dilation of the draining vessels in the vicinity of the tumor in the venous stage (Weiss & Goldblum, 2001).

Treatment

In general, management of benign HPC includes preoperative embolization followed by complete surgical resection (Walike & Bailey, 1971). Embolization is a method of stopping blood flow to a tumor. This can be done mechanically or through the use of chemicals that cause blood vessels to close. If cytotoxic agents are used, this method is referred to as chemoembolization. In addition to closing vessels, chemoembolization allows delivery of highly concentrated chemotherapy doses directly to the tumor by way of the arterial blood supply. Chemoembolization can be used to treat malignant HPC; however, malignant HPC also requires a more extensive and radical surgical approach (Perez & Chao, 1998). For incomplete resections or recurrence of malignant HPC, the addition of radiation therapy (RT) or chemotherapy may be indicated. Unfortunately, the role of chemotherapy in malignant HPC has not been widely studied because HPC occurs so rarely (Perez & Chao). Doxorubicin alone or used in combination with other chemotherapeutic agents has been shown to be the most effective for metastatic HPC, producing complete or partial remissions in 50% of cases (Durr, Nerlich, Lienemann, Muller, & Refior, 2000; Wong & Yagoda, 1978). However, other multiagent combinations, including cisplatin, ifosfamide, and gemcitabine, have shown some success in reducing HPC of the lung with mediastinal lymphadenopathy (Fujita, Minase, Takabatake,
Cyclophosphamide, methotrexate, and dacarbazine have been used to treat HPC with varying degrees of success (Wong & Yagoda). Positive outcomes using interferon alfa have been reported in two advanced cases of malignant HPC (Kim & Kramer, 1996).

HPCs, like most sarcomas, are considered to be relatively resistant to RT, thus requiring high doses. For unresectable sarcomas found in the extremities, doses of up to 7,500 cGy are used, although the area that receives more than 6,000 cGy is limited to the tumor plus a minimal margin (McGinn & Lawrence, 1998). HPCs in extremities are treated with RT in a similar fashion. RT for HPC in other parts of the body usually is dictated by specific organ and tissue site tolerance. Because HPC in the brain tends to recur, postoperative RT appears to have a definite role for primary HPC following resection (Perez & Chao, 1998). RT also should be considered for postoperative malignant HPC, as well as for palliative or salvage treatment with or without chemotherapy.

Case Study

Mr. D, a 58-year-old man, presented to his primary care physician for an annual physical examination in February 1999. He had a routine chest x-ray that revealed a 3.5 cm ovoid soft tissue opacity at the right middle to lower lobe of his lung (see Figure 3). It appeared to be fluid within the minor fissure, and the physician recommended that he return in six months for a follow-up chest film. By October, he began to develop some firmness of his right chest wall with rib tenderness, as well as very mild edema and discomfort in his upper left arm. His chest film at that time displayed a pleural-based soft tissue opacity of the right lateral hemi-thorax measuring 14 cm by 6 cm and an additional 1.5 cm opacity in the left lower lobe (see Figure 4). At that point, CT scans of the chest and upper left extremity were done. They confirmed a large mass in the right chest invading through the rib cage, as well as multiple pulmonary nodules throughout both lung fields (see Figure 5). In addition, the upper left extremity had an abnormal 3.5 cm by 4 cm by 7 cm mass within the soft tissue of the humerus (see Figure 2). At the time of the CT scans, the healthcare team believed that this represented a sarcoma-like tumor.

A general surgeon was consulted and, because of what appeared to be multifocal disease, surgical excision was ruled out. However, a biopsy was obtained from his right lateral chest wall mass in November 1999. Malignant HPC was diagnosed and later confirmed by an outside pathologic consultation. A primary site of origin never was determined. The healthcare team presumed that it was in either the right thorax or upper left extremity. The patient was referred to a medical oncologist, who recommended that he receive a chemotherapy regimen consisting of doxorubicin, ifosfamide, and mesna for a total of six cycles. The patient’s workup prior to chemotherapy was essentially negative, with the exception of some destruction on the right fifth and sixth ribs found on bone scan. This clinically correlated with Mr. D’s chest wall discomfort. Until that point, Mr. D’s workup had been performed on an outpatient basis, but because of the complexity of the proposed chemotherapy regimen, the healthcare team decided to administer each cycle of his chemotherapy on an inpatient basis. After reaching the nadir after his first cycle of chemotherapy, the patient required an additional hospitalization for neutropenic fever. This prompted administration of filgrastim after subsequent cycles of chemotherapy. After his second cycle in late January 2000, a restaging CT scan was performed, which showed slight tumor regression in the chest and upper left arm. After the fourth cycle, repeat CT scans appeared essentially unchanged, and Mr. D was considered to have stable disease. Cycles five and six were administered, and one-month follow-up CT scans performed in mid-May 2000 showed further regression within the chest and upper left arm. The chest lesion measured 9 cm by 7 cm, and the left arm mass measured 5 cm by 5.5 cm.

After completion of the sixth cycle of chemotherapy, Mr. D consulted a second major cancer center for an additional opinion regarding further management. The healthcare team at the second center believed that he would benefit from further high-dose ifosfamide and mesna. The chemotherapy was administered from June–August 2000. Despite the continued therapy, Mr. D’s upper left arm mass continued to grow and he had a chemoembolization procedure in an attempt to slow the growth of his disease. This was performed in December 2000 using mitomycin, doxorubicin, and cisplatin. An observable decrease in the size of the left arm mass occurred. However, the arm mass again began to grow rapidly, and he developed skin ulceration distal to the axillae on the medial side of his left humerus. A second chemoembolization of the left arm and also of the right chest wall mass was performed in March 2001 using the same drugs and resulted in only slight, temporary radiographic and visual regression of his disease in both the chest and left arm. Mr. D had a brief break from chemotherapy, during which CT scans showed continued growth in all locations of his tumor. In addition, he began to develop
palpable soft tissue masses over his posterior rib cage and in his right forearm (see Figure 1). These masses were not painful for Mr. D, with the exception of growing discomfort in his upper left arm.

In May 2001, the patient visited a third major cancer center for another opinion. The healthcare team there believed that Mr. D would benefit from enrollment in a phase II clinical trial using eteicinacside 743 (ET 743), which is believed to trigger apoptosis in soft tissue sarcomas. This investigational drug, administered via IV, is an alkaloid compound isolated from a sea squirt (PharmaMar, 2002), which is a small marine chordate animal. In June 2001, Mr. D received his first of four cycles of ET 743. CT scans after the fourth cycle showed further growth of the lesions in the chest and left arm, and he ceased to participate in the study. His left axillae and upper left arm were almost entirely replaced by tumor. He had developed multiple ulcerated areas on his upper left arm that were draining serous fluid (see Figure 6). In addition, the ulcerations and massive tumor burden had led to tissue necrosis in the upper left arm. The left arm had massive +4 pitting edema, and he had very limited range of motion in the shoulder and elbow joints. A surgeon was consulted again to see whether palliative debridement or limb removal would benefit Mr. D. However, he was a poor surgical risk because of his compromised pulmonary function. This was further reinforced by the risk of excessive bleeding because of the extensive vasculature of the tumor in his arm. Therefore, in November 2001, Mr. D was placed on thalidomide for symptom palliation. Because of the increase in the size of his arm mass and the resulting increase in pain, which could not be controlled by sustained release opioids, the healthcare team decided to consult a radiation oncologist while continuing the thalidomide in an attempt to palliate his disease.

Mr. D was prescribed and completed a course of RT to the upper left arm for metastatic HPC. He received a total dose of 7,200 cGy using a hyperfractionated (twice daily) technique delivering 120 cGy per treatment. The treatments were administered via linear accelerator using photons with 1 cm of bolus. Bolus, a tissue equivalent material that can be manufactured from paraffin, aqueous gelling agents, or tissue equivalent rubber (Hendee & Ibbott, 1996), is placed over the area to be treated, in this case the left humerus, and allows delivery of a higher dose of RT to the skin and superficial tissues. After RT, Mr. D was able to verbalize that he had less pain as demonstrated by a decrease in his pain scale rating from an eight at rest prior to RT to a three or four at rest after RT.

Throughout the course of radiation, Mr. D’s wound care provided an exceptional challenge to the nursing staff in the radiation oncology department. To control odor and help prevent infection, nurses dressed the necrotic ulcerated wounds of the upper arm with a compounded mixture of silver sulfadiazine cream and metronidazole. Metronidazole is useful especially for controlling malodor as anaerobic organisms colonize fungating lesions (Bird, 2000). The dressings consisted of highly absorbent gauze followed by 8 by 8 inches combine dressing pads wrapped with Kling conforming gauze bandages (Johnson & Johnson, Arlington, TX). In addition, activated charcoal, odor-absorbing pads were placed between the combine pads and under the Kling® bandages. Activated charcoal has been shown to be effective in absorbing odor (Bird; Thomas, Fisher, Fram, & Waring, 1998). Because of the copious amount of drainage and the fact that Mr. D was receiving twice-daily treatments, the dressings were changed a minimum of twice per day, more often if needed. The patient’s wife was a practicing RN and received a brief review of the dressing change procedure to ensure that the wounds were dressed consistently. As his RT progressed, Mr. D’s left arm became visibly smaller. He developed a brisk, grade III radiation dermatitis with moist desquamation in the treatment field of the entire upper left arm. This prompted the addition of 2% lidocaine jelly to the silver sulfadiazine and metronidazole compound that was applied to the open wounds and the affected desquamated area with each dressing change. During the RT course, the patient required multiple blood transfusions, prompting the addition of epoetin alfa to stimulate production of red blood cells. The healthcare team could not determine whether Mr. D’s anemia was the result of massive tumor burden, as HPCs often are highly vascularized (Morandi, Stefani, DeSantis, Paci, & Lodi, 2000), or if bone marrow involvement had become a factor.

Because of the complex care required by Mr. D and his family, the behavioral and nutritional medicine teams were consulted to address the patient’s needs. Mr. D and his family were instructed in how to identify and avoid dehydration and electrolyte imbalance, for which he was at risk because of his open, draining wounds. In addition, he was instructed to increase his daily intake of proteins to assist in wound repair. Throughout RT, Mr. D did not initiate conversation very often. Much of the time, he came and went for his twice-daily RT as if nothing were happening to him. This method of distancing probably was a defense or coping strategy that assisted him in dealing with his disease. Denial also may have been used as a coping mechanism. The behavioral medicine team was asked to evaluate Mr. D and his family regarding their mood and coping strategies. The findings and recommenda-

Hemangiopericytoma tumor erosion through multiple areas of the skin surface with necrotic tissue. To the left is the patient’s axillae, and the practitioner’s hand is on his elbow. Note the massive surrounding edema in the humerus.

**Figure 6. Hemangiopericytoma Tumor Erosion**
tions made were confidential and, therefore, unknown by the author.

Mr. D’s RT was administered from December 20, 2001, through February 1, 2002. After completion, his left arm was visibly smaller with an edema level of +2 pitting. As stated previously, his pain also lessened, allowing a decrease in his daily dose of long-acting pain medication. Unfortunately, a one-month evaluation was not possible because Mr. D developed increased weakness, anorexia, and shortness of breath during his convalescence at home. A chest x-ray demonstrated widespread metastatic disease in both lung fields that contributed to his respiratory compromise (see Figure 7). During that time, he was willing to enroll in hospice care and died five weeks after the completion of RT.

Conclusion

Adult cases of HPC usually follow a benign course, but 20%–30% of cases do, as in Mr. D’s case, behave in a malignant fashion (Jalal & Jeyasingham, 1999). Diagnosis often is delayed if patients are asymptomatic or present with a number of vague complaints (Morandi et al., 2000). Unfortunately, the nursing literature contains minimal information about HPC. Nonetheless, oncology nurses play an important role in the care of patients with this and other unusual malignancies. In addition to physical care, education and emotional support are important aspects of care that should not be ignored. This is especially true when working with patients and their families at the end stage of disease. Oncology nurses should use all of their resources to meet the needs of patients diagnosed with rare cancers. Nurses should act as coordinators of the multidisciplinary team, responsible for integrating and advocating every aspect of oncology care.

For information about local or national support groups for sarcomas or HPC, contact the American Cancer Society at 800-ACS-2345 or visit www.cancer.org or the Sarcoma Alliance at 415-381-7326 or www.sarcomaalliance.com.

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References


This chest x-ray shows extensive bilateral thoracic disease. It was taken 28 months after the chest film seen in Figure 4 and two months prior to the patient’s death.

Figure 7. Extensive Bilateral Thoracic Disease
Rapid Recap

Malignant Hemangiopericytoma: A Clinical Overview and Case Study

- Hemangiopericytoma is an unusual tumor that can occur wherever endothelial tissue is found.
- The most common sites of presentation include head and neck, lower extremities, and retroperitoneum.
- Most are present months to years prior to removal and usually are discovered when symptoms occur.
- Adult cases usually follow a benign course, but 20%–30% behave in a malignant fashion.
- Treatment of choice always is surgery, perhaps with chemotherapy or radiation therapy, depending on tumor aggressiveness.
- Aggressive metastatic hemangiopericytoma can be quite a challenge for oncology nurses, requiring a multidisciplinary approach to holistic care.