Broadening Access to Intraarterial Chemotherapy Treatment of Retinoblastoma

Awareness, communication and collaboration make efficient and effective health care delivery available more widely than ever.

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Although retinoblastoma treatment has evolved over the past century to the point that the cure rate exceeds 95% in the United States, the fact remains that it is fatal in more than half of documented cases worldwide.1

Success in the United States, starting with early diagnosis and prompt treatment by world-leading practitioners who work collaboratively for the good of these pediatric patients and their families, is generally attributable to innovation and excellence in health care. Successes in collaboration, we believe, can be a model not only for improved treatment nationally, but also for improved care and cure rates internationally.

Memorial Sloan-Kettering Cancer Center in New York, which in 2014 marks the centennial of its treatment of this disease, developed and today offers what experts worldwide believe to be the world-leading treatment protocol: intraarterial chemotherapy (IAC).2 Physicians polled at the biennial meeting of the International Society of Ocular Oncology last fall in Cleveland overwhelmingly selected IAC as the first choice of treatment for retinoblastoma (D. Abramson, personal communication, 2012).

Lauded for its minimal long-term effect on patients when compared with other treatment methods, IAC nevertheless is a challenge to deliver efficiently and effectively on a national and worldwide basis.

These requirements are neither simple nor inexpensive to provide on a widespread basis.

The relative rarity of the disease challenges the ability to deliver IAC in an affordable, prompt, and convenient manner. Although IAC is available in 32 countries as well as at Memorial Sloan-Kettering and other locations in the United States, not every community can afford to provide this treatment modality when few cases may present.

The genetic disease presents in infants whose rapid growth in the first year of life also exacerbates tumor growth, suggesting a need to treat retinoblastoma quickly upon diagnosis. Treatment delays may cause the disease to worsen or create other challenges that ultimately affect treatment success.

Our experience in the case of a 10-month-old patient, described below, presents a program that can be a model to broaden treatment and potentially reduce international mortality rates. We found that physician communication, collaboration, and coordination...
accelerate effectiveness when treating a relatively rare disease with a new or rare medical procedure.

**RETINOBlastoma Frequency**

Retinoblastoma is the most common type of eye cancer in children, occurring both unilaterally (75%) and bilaterally (25%) in approximately equal numbers between boys and girls, most often before age 5.3 There are approximately 200 to 300 new diagnosed cases per year in the United States, making it the seventh-most-common pediatric cancer. To give 1 example of how this plays out on a local basis, 4 cases of retinoblastoma were reported in 2012 in the Kansas City metropolitan area, which has a population of approximately 1.8 million.

Still, survival in the United States exceeds 95%. More than 90% of patients retain at least 1 eye, and more than 90% of children treated for the disease retain 20/20 vision.4 Worldwide, the story is very different. Approximately 8000 cases occur globally, but the survival rate is below 50%.3

**Treatment Options**

All treatments for cancer have undesired consequences, and retinoblastoma treatment is no exception. Enucleation, or removal of the eye, was the only treatment in the late 1800s and early 1900s. It remains an option today, but the obvious disadvantage of loss of vision at a very young age makes it the least desirable option. Heat (thermotherapy), cold (cryotherapy) and laser (photocoagulation) also may be used to treat retinoblastoma. However, the effectiveness of these treatments depends on the size and location of the tumors.5

Systemic chemotherapy has been widely used for the treatment of retinoblastoma since the 1990s. It is often successful in reducing the size of the tumor so that local treatments such as laser or cryotherapy can kill the remaining cancer cells. However, systemic chemotherapy is less effective with large or extensive tumors, or if subretinal or vitreous seeds are present. Systemic chemotherapy also causes systemic toxicities for the patient, such as hearing loss, and might also increase the rate of subsequent leukemia or infertility. Other treatment options, such as radiation, dramatically increase the risk of patients developing other second cancers in the radiation field in patients with the inherited form of the disease.6

IAC, conducted on an outpatient basis with the child under general anesthesia, involves insertion of a catheter into the femoral artery. The catheter is passed through the abdominal and thoracic aorta into the internal carotid artery and then directly up to the orifice of the ophthalmic artery that supplies blood to the eye. A chemotherapeutic agent or agents are infused over a 30-minute period. The patient is discharged directly from the recovery room. No postoperative medication is prescribed.

The treatment kills the tumor and cures the cancer while avoiding major disadvantages of other methods: hospitalization; patient transfusions and associated ports susceptible to infections and other issues; and short- or long-term systemic effects of chemotherapy.4

IAC has completely changed the management of retinoblastoma worldwide and become a standard of care in the United States. It is universally accepted by insurance companies and has been widely described in medical journals and the general media, improving awareness.

**Challenges**

Although IAC is significantly less expensive for the patient in the long term, the relatively low frequency of retinoblastoma challenges IAC delivery. In the United States, most hospitals that manage more than 20 retinoblastoma cases annually offer the procedure. However, health care providers in smaller communities may have difficulty justifying addition of IAC, particularly in an era of health care transition spurred by federal legislation.

The best solution to these challenges includes improving communication and using current and increasingly affordable technology to consult, collaborate, and coordinate diagnosis, treatment, and follow-up care, thus delivering the most efficient and effective treatment possible.

**Case Experience**

In Kansas City, a girl presented at approximately 3 months of age with bilateral retinoblastoma. The patient’s father had a history of bilateral retinoblastoma with multiple surgeries, and the child’s own cancer was very aggressive. The patient was treated with systemic chemotherapy plus local laser at Children’s Mercy Hospital in Kansas City.

Although initial results were encouraging, a recurrence was referred to Memorial Sloan-Kettering Cancer Center for IAC. The only alternative to enucleation was intraarterial chemotherapy. Images and notes from examination were shared with Memorial Sloan-Kettering.

Treatment was scheduled promptly, and the patient and her parents traveled to New York for the procedure. The treatment team included an ophthalmic oncologist to examine the patient, confirm the diagnosis, and update the condition; an interventional neuroradiologist to perform the procedure; and an anesthesiologist and other surgical team members trained and experienced in the procedure.

Communication with the referring physician was constant. The procedure’s outcome was communicated to the
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local physician during the 1-hour procedure, even before the procedure was completed, and doctors were able to communicate with family members at the treatment site.

Postoperative examination is critical to ensure the tumor is responding, as well as to identify if additional therapy is required. Initially, the IAC team conducted follow-up exams; eventually, these exams were alternated with the local physician. Ultimately, the local physician performed all necessary follow-up exams. Communication continued throughout the follow-up regimen to monitor results for maximum patient benefit.

Of particular value throughout the IAC treatment protocol is complete and consistent support both locally and at the IAC treatment site. Patient and patient-family considerations include but are not limited to easing the emotional, financial, physical, and logistical strains of dealing with an infant or toddler whose eyesight is threatened.

When both the local doctor’s office and the remote IAC team communicate efficiently, and when details such as travel, lodging, and social services associated with long-distance outpatient care are consistently provided both locally and remotely, confidence is raised and the patient and the patient’s family are better able to contribute to a positive outcome.

LESSONS LEARNED

We were guided by 4 principles in this case, and we recommend these steps for all health care practitioners:

(1) Know what you can do and what others can do.
Health care is an ever-evolving profession and industry, meaning providers must be constant students, staying abreast of new procedures and developments. In this case, a visiting professorship provided insight to doctors in Kansas City, who then had other referral options for treatment of a condition that was rare in the community.

(2) Know whom to contact and when.
Doctors are best able to retain a patient’s trust, loyalty, and gratitude when the patient receives the best possible treatment, even if that means treatment provided by another doctor or health care provider.

(3) Communicate with other providers in a way that benefits patients.
Sharing appropriate information means the latest information and the best thinking from multiple sources are brought to bear for the benefit of the patient.

(4) Make sure there is 2-way communication for follow-up and support.
Keeping lines of communication open, even when distance separates the providers, ensures that new experience, knowledge, or training of any provider remains available to the patient.

SUMMARY

IAC to treat retinoblastoma is a new and highly effective surgical procedure with a 95% cure rate in the United States. Thus, ophthalmic oncologists prefer IAC, and it now is the most common initial management strategy in the United States, even though multiple treatment options are more widely available.

However, IAC requires specialized skills and equipment not easy to replicate on a widespread basis. The case described here shows that cooperation by treating physicians allows patients to receive the standard of care, even if the patient and the patient’s nearest ophthalmic oncologist are half a continent away.

The worldwide retinoblastoma cure rate is below 50%, even though IAC is available in 32 countries. To ensure that the standard of care becomes more widely available, collaborative partnerships similar to the model exercised in this case can be established with current and additional IAC treatment sites. Collaboration based on knowledge, communication, and 2-way collaboration can bring the most affordable, safest, and most effective retinoblastoma treatment to patients worldwide.

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