Practical Radiation Oncology (2012) 2, 233–236

practical radiation oncology
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Teaching Case

Intact performance of a cochlear implant following radiotherapy in a child with acute lymphoblastic leukemia

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Received 1 June 2011; revised 17 June 2011; accepted 20 June 2011

Cochlear implants, via direct electrical stimulation of the auditory nerve, allow the restoration of hearing and speech recognition in both adults and children having sensorineural deafness. These devices typically contain both external components (speech processor, microphone, transmitter) and internal components (including the cochlear stimulator and electrode array), which are surgically placed under the skin behind the ear and in the cochlea. According to the National Institute on Deafness and other Communications Disorders, by June 2010, over 188,000 individuals worldwide had received cochlear implants, including approximately 41,500 adults and 25,500 children in the US.[1] Given the important role of radiotherapy (RT) in the multidisciplinary management of various malignancies, the tolerance of cochlear implants to therapeutic doses of radiation is an important consideration. In this work, we present a case of a pediatric patient with leukemia found to have sensorineural deafness, who then received a cochlear implant and subsequently received RT to the whole brain. Literature regarding RT in the setting of a cochlear implant and the importance of early childhood implantation for language-speech development is reviewed.

Introduction

Cochlear implants, via direct electrical stimulation of the auditory nerve, allow the restoration of hearing and speech recognition in both adults and children having sensorineural deafness. These devices typically contain both external components (speech processor, microphone, transmitter) and internal components (including the cochlear stimulator and electrode array), which are surgically placed under the skin behind the ear and in the cochlea. According to the National Institute on Deafness and other Communications Disorders, by June 2010, over 188,000 individuals worldwide had received cochlear implants, including approximately 41,500 adults and 25,500 children in the US.[1] Given the important role of radiotherapy (RT) in the multidisciplinary management of various malignancies, the tolerance of cochlear implants to therapeutic doses of radiation is an important consideration. In this work, we present a case of a pediatric patient with leukemia found to have sensorineural deafness, who then received a cochlear implant and subsequently received RT to the whole brain. Literature regarding RT in the setting of a cochlear implant and the importance of early childhood implantation for language-speech development is reviewed.

Case description

This review was prompted by the case of a 4-year-old girl with relapsed acute lymphoblastic leukemia (ALL) seen by the authors in Colorado. She was initially diagnosed at age 2, and received systemic therapy as specified by the Children's Cancer Group 1991 protocol "Phase III randomized study of escalating dose intravenous methotrexate (MTX) without leucovorin rescue vs oral MTX and single vs double delayed intensification in children with ALL," leading to early disease remission. During maintenance therapy, at age 4, a routine lumbar puncture revealed an isolated central nervous system relapse, and she initiated systemic treatment as specified by the Children's Oncology Group AALL02P2 protocol "Treatment of late isolated extramedullary relapse from ALL." That treatment regimen is composed primarily of chemotherapy, but also includes planned cranial radiation therapy at the end of Intensification II to reduce the risk of future central nervous system relapse.

Conflicts of interest: None.

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1879-8500/$ – see front matter
doi:10.1016/j.prro.2011.06.015

During treatment, she was found to have hearing loss and speech delay. Audiologic testing was performed, confirming the presence of bilateral sensorineural hearing loss. She initially tried bilateral hearing aids, but did not develop speech. The recommended management of her hearing loss was placement of cochlear implants. However, as radiation therapy to the brain would be required in the future, we discussed the potential risks of radiation to the cochlear implant. The manufacturer recommends against placing the implant directly within a radiation field. However, after review of the literature, we deemed that the dose of radiation required would be unlikely to adversely affect the cochlear implant and that early implantation would improve development of speech. Given the possibility of malfunction, we chose to implant a single cochlear device first. She underwent placement of a Cochlear (Sydney, Australia) Nucleus CI512 on the right side, with the surgery performed during a period of sufficient hematologic recovery. One year after placement of the cochlear implant, she received whole brain RT to a total dose of 12 Gy in 8 fractions using 6 MV X-rays. Opposed lateral beams were utilized, with the resulting dose distribution approved to the 100% isodose line. As the dose planned for whole brain RT was felt to be unlikely to cause implant dysfunction, and was also well below the consensus dose constraint for the cochlea,[2] no special techniques were utilized to minimize dose to either of these structures. No hotspots within the cochlea-cochlear implant were allowed. The digitally reconstructed radiograph is shown in Figure 1, with the cochlear implant noted with an arrow. She tolerated radiation therapy well. One month after RT, the cochlear implant was queried and observed to be operating with no errors. She continues with her chemotherapy and is tolerating treatment well.

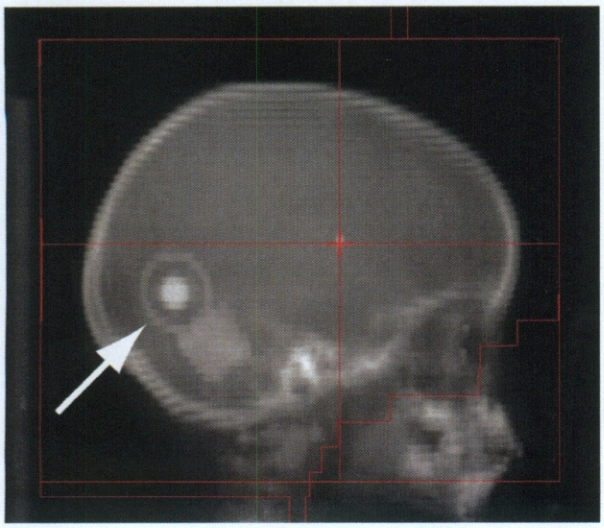

Figure 1

Discussion

Importance of early childhood implantation for speech-language development

Evaluation of deaf children receiving cochlear implants has demonstrated the critical role of these devices in providing the peripheral auditory input necessary for proper development of language and speech skills. Such studies have pointed out the age-related plasticity of the auditory system and underscored the importance of implanting children during a key early period of heightened sensitivity.[3] Svirsky et al followed the language development of 70 children receiving cochlear implants, with assessments made 4 months prior to implantation, as well as 6, 12, 18, 24, and 30 months afterward.[4] Implanted children demonstrated greater gains in expressive language than those predicted for unimplanted deaf children. The cumulative gains achieved by children with cochlear implants up to 2.5 years post-implant were about the same as those expected from children with normal hearing. The authors found that cochlear implant users already possessed a language delay with respect to normal-hearing children at the time of implantation. Earlier implantation was felt to keep this delay from increasing further.

Harrison et al performed similar work elucidating the importance of the timing of cochlear implantation.[5] Eighty-two children with severe to profound hearing loss from birth attending the Cochlear Implant Program at the Hospital for Sick Children in Toronto were grouped into subsets by age at implant, and followed up to 8 years post-implant. Outcome measures, including tests of auditory comprehension and speech perception, were prospectively obtained. After 60 months post-implant, children implanted at $\leq$5 years of age scored higher than those who were older at the time of implant. In phoneme and word speech perception tasks, those implanted at 2 years of age outperformed all other age groups. Importantly, the authors felt that older children may not achieve levels obtained by those implanted at an early age, even with long periods of implant use. The existence of a sensitive period for central auditory development may stem from the reorganization of the auditory cortex, which occurs following a period of auditory stimulus deprivation in deaf children. Electroencephalogram studies of children during passive listening have shown a pattern of cortical activation in early-implanted children; specifically, along the superior temporal sulcus and inferior temporal gyrus, which is similar to that observed in normal-hearing children, and in sharp contrast to that found in late-implanted children.[6] Sharma et al have similarly demonstrated that cortical auditory evoked potential morphology and cortical response latency differed between children implanted before age 3.5 years or after age 7 years.[7] Given that auditory stimulation does not lead to normal activation of cortical auditory association areas in late-implanted children, it has been suggested that the late introduction of new sensory input via cochlear implant

Table 1 Summary of studies assessing tolerance of cochlear implants to radiotherapy

Author	Implant	Dose-fractionation scheme	Setup	Findings
Ralston et al[10]	CI22M and CI24M	Initial dose of 50 Gy in 25 daily fractions, followed by an additional 50 Gy in 5 10-Gy fractions, followed by a final additional single dose of 50 Gy (total dose of 150 Gy)	Implants placed between 2 water equivalent plastic blocks measuring 30 × 30 × 5 cm, which were separated by 1-cm thick perspex blocks to maintain geometry and provide side scattering; RT delivered using 2 parallel opposed 4-MV beams	Following initial 50 Gy, the only detectable abnormality was compression of the CI22M unit stimulus current curves (which would manifest clinically as a perceived change in sound quality and loudness). The CI24M unit's stimulus current curve was changed by ≤5% to 50 Gy. Both models demonstrated a change in stimulus current amplitude above 50 Gy. A clinically insignificant decrease in RF link range was found in the CI22M unit at 150 Gy.
Klenzner et al[11]	Nucleus CI24 M or CI24R(CS)	RT was initially delivered to either 100 Gy in 2-Gy fractions or 96 Gy in 1.6-Gy twice-daily fractions. Following completion of either schedule, devices received an additional 5 Gy × 4 fractions, up to a total dose of 120 Gy or 116 Gy, respectively.	Implants embedded in a solid-water phantom; RT delivered using 6-MV beams at a source-implant distance of 100 cm	No dysfunction or implant failure was observed up to 100 Gy. In the CI24R (CS) model receiving hyperfractionated RT, a significant drop in output amplitude was seen at 106 Gy, with a failure in impedance measurement at 111 Gy.
Baumann et al[12]	CLARION 1.2	Varying schemes: 1) 69 Gy over 9 functions with single doses varying between 0.1-30 Gy; 2) 90 Gy in 3 functions delivered a few days apart; 3) 58-68 Gy over 29-34 fractions of 2 Gy each	Implants placed on a 10-cm thick synthetic block, covered by a 0.5-cm thick plexiglass to avoid dose buildup; RT delivered using ^{60}Co, with approximately 1.2-MV gamma rays and a source-implant distance of 54-192 cm	Temporary difficulties were noted in obtaining an RF lock after single doses of 20 Gy and 30 Gy; function was found to be normal upon retesting 1 minute (20 Gy) and 12 hours (30 Gy) later. 30 Gy × 2 caused transient inability to obtain an RF lock; a third fraction of 30 Gy (up to 90 Gy) rendered the implant dysfunctional. At 2-Gy fractionation, 58 Gy led to an inability to obtain an RF lock; 68 Gy rendered the implant dysfunctional, with analysis revealing a breakdown in the main integrated circuit.
Klenzner et al[13]	Nucleus 24k	Single implant given single fractions of 16.3 Gy, 6.2 Gy, and 20 Gy	Implanted subcutaneously behind the L ear and into the cochlea of a fixed cadaver head (position confirmed by X-rays); immobilization using a plastic mask; 3 consecutive fractions of 16.3, 6.2, and 20 Gy delivered within a 2-hour interval with 6-MV photons	No significant changes were observed in impedance or current output of the implant up to a total dose of 42.5 Gy.

RF, radiofrequency; RT, radiotherapy.

placement in these children may result in abnormal sensory perception and atypical responses.[6]

Hearing loss associated with treatment of pediatric malignancies

In the case described here, sensorineural hearing loss was presumed to be due to methotrexate (MTX)-induced ototoxicity. The incidence of auditory impairment as a late neurologic sequelae experienced in adult survivors of childhood ALL was recently reported by Goldsby et al.[8] The incidence of any hearing impairment was 1.4%; the adjusted relative risk (RR) of any hearing impairment for ALL survivors, compared with siblings, was 1.9 (P = nonsignificant). On multivariate analysis, intravenous high-dose MTX was associated with a RR of 1.5 for development of auditory-vestibular-visual sensory deficits ($P = .12$). In a broader context, Whelan et al recently reported auditory complications among patients included in the Childhood Cancer Survivor Study.[9] The Childhood Cancer Survivor Study is a retrospective initiative assessing health outcomes of survivors of pediatric malignancies diagnosed and treated between 1970 and 1986, based on questionnaires completed by over 14,000 patients. Compared with siblings, survivors at 5+ years post diagnosis displayed an increased risk of problems hearing sounds (RR = 2.3), hearing loss requiring an aid (RR = 4.4), and hearing loss in one or both ears not corrected by an aid (RR = 5.2).

Tolerance of cochlear implants to RT

A few studies have assessed the functional capacity of specific types of cochlear implants following varying RT dose-fractionation schemes. Results from these prior studies are summarized in Table 1. When exposed to conventional or hyperfractionated RT regimens, cochlear implants appear to tolerate doses up to 100 Gy, with low risk of permanent dysfunction.

RT tolerance differences exist between specific cochlear implant models. Ralston et al reported alteration in the CI22M implant stimulus current curve following 50 Gy in 25 fractions. They noted that this change in stimulus current could be compensated for by reprogramming the speech processor at the completion of radiation, which could be performed by an audiologist in approximately 1 hour.[10] Cochlear Nucleus 24 models tolerated total doses up to 100 Gy without dysfunction or permanent failure, while a CLARION (C/O: Advanced Bionics, Valencia, CA) 1.2 device has been shown to experience permanent dysfunction at 68 Gy from low energy photon irradiation.[11,12] Specific implant models also appear to retain functional ability following exposure to single large RT doses, such as those utilized in radiosurgery.[13]

Conclusions

Our case report offers further support for the expected tolerance of cochlear implants to RT in most clinical situations, as evidenced by the available literature. Close communication between radiation oncology, medical oncology, otolaryngology, and audiology is necessary for the optimal management of children requiring radiation therapy to a cochlear implant. Assessment of device performance should be obtained prior to and after the planned RT course. In children, cochlear implantation should be performed as soon after the discovery of sensorineural deafness as feasible to optimize development of speech, comprehension, and language skills. Given the increasing use of cochlear implants and the important role of RT in the treatment of many cancer patients, national guidelines on the management of these patients' implants should be developed.

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