Chapter 31
Research and Ethics in Pediatric Oncology

Case Presentation

An 11-year-old girl presents with a distal metaphyseal osteosarcoma of the left femur, and lung metastases. Chemotherapy allowed a complete response of lung metastases and a slight volume reduction of the tumor of the thigh. The surgeon proposed an amputation, which was denied by the teenager and her parents. After 3 months of treatment abandonment, she returned to the hospital because of pain. Chest X-rays showed lung metastases. Treatment with second-line chemotherapy and radiotherapy is proposed on an experimental basis.

1. Would it would be ethical to proceed with this program?
2. Should it be discussed with the parents, who are illiterate?
3. Should the patient be informed?

Research on diagnostic and therapeutic approaches has been the main tool to improve the quality of care of childhood cancer in developed countries. Besides diagnostic and therapeutic approaches, the research may also involve epidemiology, organization, funding, and organization of care or the sociocultural aspects of pediatric oncology. Even though this group of diseases is rarely encountered compared to adult cancer, appropriately organized international teams made a great impact. This is now considered as a model in medical practice. In well-organized pediatric oncology units, up to 70 % of patients are included in prospective research programs. Patients enrolled in international network programs have also show to have a better outcome. Hence, among the competences that a team should have to support children with cancer, the ability to conduct research and participate with other teams in national and international programs, is of great added value.

However, research must respect the principles of ethics. The team should respect the basic principles of human rights, and pay attention to possible exploitation of

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vulnerable patients and families for commercial purposes. In most countries, regulation to protect patients is implemented. One of the most effective ways of protection of persons is the use of a review by independent ethics committees.

Furthermore, the authors and editors of scientific publications have ethical obligations. For the publication of study results, investigators have to ensure the accuracy of their results. Negative as well as positive results should be published or made available. Funding, and any potential conflicts of interest must be clearly outlined in the publications.

In developing countries, searching for the best diagnostic and therapeutic approaches adapted to local settings is one of the best research fields. The rights of the child and their parents to get best possible care must always be respected.

Informed Consent

This is one of the fundamental ethical principles. Indeed, respect for the dignity and autonomy of subjects are at the basis of ethics. Children, their parents or their legal representatives must give their informed consent without any constraint or influence. Consent must be voluntary and reversible.

The information given to parents must enable them to understand the rationale for the study, the type of investigations, the expected results and potential risks (Table 31.1). They should also be informed of available alternatives and about the measures taken to protect confidentiality of their personal information. The process of consent must take into account the sociocultural context.

Information of Children and Relationship with Parents

The treatment of cancer in children requires a genuine alliance between the healthcare team and parents, and the relation should be established on the basis of mutual trust. The interests of the child must prevail in all cases. Parents must be convinced of the relevance of therapeutic choices. The use of traditional or alternative

Table 31.1 Rules of informed consent

• The information must be given in an understandable manner
• Explanations of the benefits and potential risks should be included
• The consent must be given prior to inclusion in the study
• The consent must be collected without any constraint or influence
• The consent must be well documented

Table 31.2 Ethical principles for conducting research in humans

• Protection of life, health, dignity, and privacy of the person
• This must be based on updated scientific literature and other relevant sources of information as well as appropriate experimentation carried out in laboratory and, where appropriate, on the animal
• Research topics should be aimed at improving the health, well-being, or human knowledge
• Research must be done by qualified persons and under the supervision of competent doctors
• The methodological choice must be adapted to the objective of the research and should answer the questions raised by the research
• The criteria for selection of the target population should be based on a scientific validity and not on economic vulnerability
• The risk must be reduced to the minimum, and in all cases be justified by a potential benefit to the patient or the community
• An assessment by a third party not involved in the study and in particular an Ethics Committee is recommended to avoid potential exploitation
• Duly obtained consent should be obtained after giving information to parents and possibly to the child
• Throughout the research, the investigator must ensure well-being of persons subjected to the research work, protect their personal data, give them an update of the study as needed and allow them to withdraw from the research if necessary

medicine can be a handicap to the treatment, but should not be systematically denied to the extent that there is no risk to the child.

Establishing a relationship of trust with the child is recommended. To do this, caregivers should avoid giving false information and take into account the cultural environment, the child's age and maturity for sensitive information.

In the relatively mature child and adolescent, his or her opinion should be taken into consideration. The help of a psychologist may be necessary.

The Fundamental Principles to Govern Medical Research

The Helsinki declaration, adopted by the World Medical Association in 1964, summarizes the basic principles to govern research involving human beings (Table 31.2).

The Ethics Committee

The Ethics Committee must be independent of the sponsor, investigator or any other form of undue influence. Membership must provide scientific resources, but also civil society, scholars, and theologians. This must ensure respect for the laws and regulations in place in the country, and should have the right to monitor the progress of ongoing studies. The investigator has the obligation to provide the Committee

with information on the progress of the study and on the occurrence of significant adverse events. The investigator should also communicate to the Committee information on financing potential conflicts of interest as well as the procedures of inclusion of participating patients in the research program.

Adapted Diagnostic and Therapeutic Approach

The issue of use of developed country's diagnostic and treatment approaches in settings where resources are very limited is frequently raised. The capacity of the family and the healthcare system should be properly evaluated before applying those approaches. Adaptation of these approaches should be carefully studied and may need approval of the Ethics Committee. These approaches should nevertheless be evaluated regularly.

Ethics and End-of-Life

The management of the end-of-life period is difficult and sometimes raises ethical issues. Therefore, it is important that clarity on the objectives of care is observed between the patient, the parents, and the medical team. Progress in medical resuscitation techniques to artificially maintain life sometimes poses an ethical problem regarding the suspension of these therapies when there is no more hope of cure. In developing countries, the problem is frequent, given the difficulties of access to care and cultural considerations. Many families prefer that patients die at home. In all cases, good palliative care and, particularly, pain should be provided.

In the event of conflict between the healthcare team and family concerning the continuation of care, the opinion of the Ethics Committee is required. "Futile" treatment may indeed be challenged according to the sociocultural context (Table 31.3).

Table 31.3 Practical recommendations

• Clinical research must be justified by the benefit for the patient or for new scientific knowledge
• An independent Ethics Committee must validate the relevance and the methodology of the research
• Informed consent is a major component in clinical research
• Adaptation of diagnostic and treatment approaches in resource-limited countries should also be closely monitored as clinical research projects
• End-of-life care can pose an ethical problem when they mobilize significant resources without anticipated benefit

Suggested Reading

Committee on Bioethics of the American Academy of Pediatrics (1995) Informed consent, parental permission, and assent in pediatric practice. Pediatrics 95:314–317

Emanuel EJ, Wendler D, Grady C (2000) What makes clinical research ethical? JAMA 283:2701–2711

Devine S, Dagher RN, Weiss KD, Santana VM (2008) Good clinical practice and the conduct of clinical studies in pediatric oncology. Pediatr Clin North Am 55:187–209

Joffe S, Fernández CV, Pentz RD et al (2006) Involving children with cancer in decision-making about research participation. J Pediatr 149:862–868

Varelas PN, Abdelhak T, Hacein-Bey L (2008) Withdrawal of life-sustaining therapies and brain death in the intensive care unit. Semin Neurol 28:726–735

Burns JP, Truog RD (2007) Futility: a concept in evolution. Chest 132:1987–1993