

Anesthesia for Patients with Oncological Diseases Treated with Chemotherapy: A Retrospective View

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1. Introduction

In principle, a patient with a malignant tumor and a candidate for a surgical intervention is not different from any other patient of the same age and with the same comorbidity. The difference starts at the moment the malignant disease influences the patient's clinical condition, due to such factors as malnutrition and infection. Thus, for many years, the influence of malignancy on anesthetic procedures was not a subject of specific clinical studies. However, one particular situation, that of the oncologic patient treated with cytostatic drugs and needing anesthesia for a surgical procedure, created a new domain of clinical interest.

The first report on cytostatic toxicity was published in the middle of the last century [1]. Clinicians have since known that administration of chemotherapy produces adverse drug reactions, including hematological hazards, by affecting bone marrow functionality and producing anemia, leukopenia-neutropenia and thrombocytopenia. The hematological changes induced by chemotherapy lead to fatigue, and high risks of infections and bleeding, which clearly impact anesthesia in patients who undergo surgical interventions.

The first papers that dealt with the anesthetic problems caused by chemotherapy were published in 1963 [2] and 1968 [3]. However, they described patients with oncological diseases who received moderate dosages of cytostatic agents.

The Department of Anesthesia at the National Institute for Oncology, Bucharest, Romania, was established in the year 1960. In 1963, this department was recognized as a clinical and research center, and started seeking topics that could be investigated in relation to oncological diseases. The result was the publication, during 1965-

1972, of ten papers, all involving problems related to anesthesia for patients with oncological diseases who were treated with cytostatics.

This paper offers historical insight into the anesthetic and critical care aspects relevant to patients with oncological diseases more than one half century ago.

2. The First Problem: The So-Called “Cytostatic Disease”

The aim of the usual cytostatic treatment at that time was the disappearance, or at least the significant reduction, in tumor size. Consequently, large doses of cytostatic agents were used. Patients often received chemotherapy, almost concomitantly, through a number of routes: intravenous, intraarterial and intraperitoneal; sometimes at very short intervals. The result was the appearance of a complex of clinical syndromes, the first of which was severe pancytopenia, defined as a leucocyte number close to 300-500/mcL, and a thrombocyte count of about 15,000/mcL. Other vital systems are also affected, leading to hepatic failure [4], inhibition of adrenal function [5], polyneuropathy, aggravation of diabetes mellitus [6] and hydro-electrolyte imbalance due to vomiting and diarrhea. All these side effects were included in what was then referred to as “cytostatic disease”. This term was first used in the Romanian literature [7] and much later in Russian literature [8].

During the period discussed, the literature was very scarce regarding the effect of cytostatic drugs on anesthesia for patients with cancer, and nothing was known about so-called “cytostatic disease” and its impact on anesthesia technique. Our first paper on the subject [9] described the pre-, intra- and postoperative problems

of patients treated preoperatively with large, single or fractional doses of cytostatic drugs. Among other measures, we proposed the use of corticosteroids for treating the adrenal insufficiency, and intra- and postoperative preventive use of antibiotics. The next paper described problems related to anesthesia techniques in oncologic patients who were preoperatively treated with cytostatic drugs [10]. This was followed by a study on the respiratory effects of intraperitoneal cytostatic administration during surgery [11]. These papers presented the main anesthetic concerns regarding oncologic patients treated with cytostatic drugs, especially accurate preoperative preparation of the patients. This includes management of the hematological effects of cytostatic treatment, such as blood transfusion, reinfusion of autogenous bone marrow, and the administration of corticosteroids and of metoclopramide for nausea treatment.

3. Specific Aspects of Anesthesia Techniques

During the years 1965-1972, the second field of clinical interest was the effect of chemotherapy in cancer on anesthesia techniques. Step-by-step, we developed a protocol that dealt with the prevention and management of complications as a result of pre- and intraoperative cytostatic use. The protocol included five main aspects. The first was prevention of nausea and vomiting, by using halothane as a main volatile agent, and administration of metoclopramide (for the first time used in this context) [12]. The second aspect was moderate hyperventilation and the use of hypothermia, as the effect of the cytostatic drug on the tumor was expectedly increased by alkalosis and low body temperature. The third aspect was intraperitoneal administration of procaine solution for preventing acute respiratory failure caused by the intraperitoneal administration of cytostatic drugs at the end of the surgical procedure. The fourth aspect was maintenance of the endotracheal tube in the immediate postoperative period and continuation of mechanical ventilation if airway edema presented due to surgery in the immediate vicinity. The last aspect was the treatment of prolonged apnea caused by pre- or intraoperative administration of cytostatic drugs.

A particular situation was represented by the pre-operative or intra-operative use of drugs such as AB 132 (ethyl-2.2 dimethylene imido phospho carbamate) [13], thiophosphoramidate or sarcolysin [14], which all reduced the efficiency of plasmatic cholinesterase in the process of succinylcholine hydrolysis. Sometimes, the administration of succinylcholine was followed by prolonged postoperative apnea, which necessitated continuation of mechanical ventilation.

In the year 1961, Duff et al [15]. proposed an original method for preventing negative effects of cytostatic drugs on the bone marrow, which consequently reduced the hematological problems created by this treatment. The method was used for treating tumors on the upper parts of the body. The first step was lumbar spinal anesthesia, which relaxed the muscular abdominal wall. This was followed by the application of a heavy sandbag on the abdomen, with

the aim of temporarily ceasing blood flow to the lower parts of the body, as was monitored by the disappearance of the femoral pulse for 10-20 minutes. Subsequently, the cytostatic drug was administered through an arm vein. Thus, the drug did not reach the bone marrow at the level of the pelvis and legs. The pathophysiological effects of this method disturbed the stability of the cardiovascular function, due to abrupt physiological changes such as pulmonary hypertension, increased vascular resistance in the upper parts of the body, and intracerebral hypertension.

We published the results of the described method in nine patients [10]. We found that, compared to general anesthesia, spinal anesthesia resulted in greater cardiovascular stability, as evident from better values of blood pressure and pulse, and lesser need of vasoconstrictor drugs after releasing the abdominal pressure. We advised against using this method in hypertensive or older patients.

4. Discussion

The period during which we were obliged to face the multitude of problems related to anesthesia for oncologic patients treated with cytostatic drugs was very demanding and entailed substantial clinical responsibilities. Then, cytostatic treatment for cancer was at its very beginning.

The Romanian School of Oncology established a series of protocols for cytostatic administration in huge doses, a regimen that is no longer acceptable. Eventually, the disastrous effect of cytostatic drugs on vital organ functionality, especially on the hematopoietic system, reduced in most instances the volume of the tumor. However, it created favorable conditions for the development of dangerous infections and sepsis, which negatively influenced patient outcomes.

Anesthesiologists of the described period were obliged to find solutions for reducing or even preventing negative effects of cytostatic drugs on routine anesthetic techniques, as these drugs became established in most operating rooms around the world. Thus, we had the opportunity to be the first in the world to describe the proper preoperative preparation of the cancer patient who was treated with massive doses of cytostatic drugs. We were also first to present a protocol for preventing or reducing the negative effects, such as nausea, vomiting and prolonged apnea, of cytostatic agents on anesthetic techniques. Moreover, we presented for the first time, a patient who had a hepatic coma after administration of methotrexate, which was then a very commonly used cytostatic drug [16].

5. Conclusions

We acknowledge that the majority of chemotherapy methods used about 60 years ago are no longer in use, and have been replaced by safer techniques and drugs. However, anesthesiologists, who represented a young medical specialty at that time, were expected to cooperate with surgeons and oncologists, and to assist them in curing a dreadful disease, or at least in postponing the final outcome.

Even today, anesthesiology is considered a service profession. However, in the past, like every situation since, we first served the patient.

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