Forensic Aspects in Polonium-210 Poisoning

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The human body is exposed to radiation resulting from the presence and degradation in the environment of natural radionuclides like uranium and thorium. In laboratories, several radioactive isotopes are being used: uranium-235, iodine-131, cobalt-60, and carbon-14. These radioactive isotopes are useful in scientific (dating human skeletal remains) and medical purposes (radiotherapy/radiodiagnosis), but they are also used in criminal context. Polonium 210 (Po-210) is a natural radioisotope occurring in the natural environment as consequence of uraniu-238 decay chain. The current paper presents a less known subject of lethal poisoning with Po-210 radioisotope, in order to underline the methods used for Po-210 identification in forensic samples. The authors performed a literature review of the scientific researchers published in the last years concerning polonium sources and its use as a poison. Polonium's effectiveness as a poison relies on its chemical characteristics only to the extent that they determine the isotope's distribution and retention in organs and tissues; the alpha particles are responsible for the lethal effect. Po-210 poisoning is particular, as it doesn't leave traces, it can be easily transported, and is not detected by airport scanners. Identifying this compound during a medico-legal autopsy is very difficult, as the post-mortem examination will not yield characteristic aspects, the forensic pathologist being forced to consider this as a potential cause of a rapid death, with significant visceral damage.

Keywords: polonium, poisoning, lethal, alpha particles, forensic pathologist

Current medical activity uses a variety of radioactive sources that are introduced into the human body intentionally, for medical research, diagnosis or treatment, and accidentally by faulty manipulation of radioactive substances. Intoxication defines the pathological condition caused by ingestion of one or more xenobiotic substances. *Toxic* (from the Greek term *toxicon*) refers to any chemical substance that can induce functional or structural damages in biological structures [1].

Two classifications of 210 polonium radioisotope (Po-210) have been mentioned in the literature:

a. according to the clinical-progressive criterion: acute and chronic poisoning;

b. according to the socio-legally criterion: voluntary poisoning (crimes, suicides, doping) and accidental poisoning (professional, therapeutic, household) [2].

Radioactive isotopes are part of a group of potentially harmful or lethal substances for the human body, little-discussed in the literature. For a long period of time, the only known radioactive isotopes were radium, thorium and uranium in their natural state. Researchers have also discovered and obtained artificial isotopes [1]. Po-210 is extremely lethal to the human body but the incidence of Po-210 poisoning is low, and difficult to prove in both clinical and forensic settings [2]. Presently, there are many radioactive polluted areas as a result of mining exploitation activities, which are now totally or partially de-allocated. The population living in the proximity of these areas is exposed to radiological risk due to the radioactive pollution existing in those areas [3].

The authors aimed to perform a meta-analysis of the current stage of research concerning Po-210 poisoning at the national and international level. The study underlines the major sources of natural polonium, clinical signs and symptoms in case of Po 210 exposure, methods of diagnosis of Po-210 poisoning, and identification of the lethal mechanism.

Experimental part

Materials and methods

At the Institute of Legal Medicine Iasi, an important part of the Toxicological Department's activity is represented by acute poisoning with different lethal substances. The research activity is focused on highlighting new methods for identifying lethal substances that are rarely used (methanol, ricin, pesticides, polonium, plumb etc.) [4-7].

This activity is multidisciplinary, aiming to establish the effects of substances at the cellular level, as for instance the destructions caused by lethal substances, explaining the lethal potential of acute poisoning [6, 7].

Based on critical analysis of 210-Po poisoning studies [8-17], the authors identify the principal source and ways of isotope use as part of international criminal activities, respectively the levels of intoxication up to the lethal stage (mode of manifestation), highlighted on the basis of the correlation between the forensic protocol and the results of this action.

The authors identified eight studies (Health risk evaluations for ingestion exposure of humans to Po-210; Po-210 a poisoning; Po-210 in marine biota and the effective dose from seafood; The risk of natural radioactivity in tobacco and cigarettes smoke: Thermochromatography study of volatile polonium species in various gas atmospheres: A review of radiochemical analysis and estimation of Po-210 in soil matrices: Hair as an indicator of the body content of polonium in humans: preliminary study from study of five male volunteers: Po-210 poisoning a possible cause of death: forensic investigation and

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toxicological analysis of the remains of Yasser Arafat) after interrogating the PubMed and Research Gate databases using the keywords *polonium, radiation, death and forensic.*

Results and discussions

Following our literature review, the mentioned studies have identified aspects regarding the Po-210 isotope. In this sense, the authors reported: lethal doses of Po-210 may produce severe damage (bone marrow, spleen, liver, kidney, skin, lymph nodes); survivors of acute radiation syndrome are at high risk of cancer occurrence; an ingested dose of Po-210≥ 0.1-0.3 GBq determined organic failure within one month; the average annual effective Po-210 dose per average Korean adult, who consumes 42.8 kg of seafood a year was estimated to be 94μSv y-1, with 42–71% of this attributed to shellfish; the radon and HPGe revealed highest concentrations of radon and uranium in miami cigarettes, tobacco type sample and Macbith type cigarettes in America and Brazil; to determine Po-210 in tobacco by alpha spectrometry technique; under inert and reducing conditions in the absence of moisture, elemental polonium is formed, volatility of polonium oxides increases with increasing oxidation state; spontaneous deposition of polonium followed by alpha counting in a ZnS(Ag) detector provides a cheaper alternative to alpha spectrometry. However, for isotopic measurement alpha spectrometry is necessary; hair can be used to detect not only the amount of ingested polonium but also whether the intake was protracted or acute; analytical results that support the hypothesis of Po-210 poisoning essentially on the basis of unexplained Po-210 activities found in Yasser Arafat's belongings worn shortly before his death and on unexplained 210-Pb and 210-Pb activities found in his remains.

Radioactive isotopes can be found in natural form or can be artificially produced. Artificial Po-210 is obtained by dissolution of uranium and thorium, but the necessary techniques are extremely laborious and they offer minimal quantities with increased concentrations of impurities [8, 9].

The literature mentions a world-wide monthly production of about 100 g of Po-210, out of which about 8 g of Po are transported from Russia to USA.

Pharmacokinetics

Acid-soluble Po-210 can be administered as metal or oxide, most easily in citrate or nitrate solution via enteral, respiratory or cutaneous routes (fig. 1).

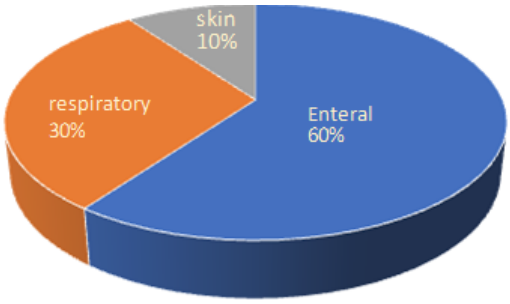

Fig.1. Administration route of Po-210

Enteral route

The enteral route is the easiest way of administration because it does not stain the beverage, and it does not change the taste or smell of ingested foods. Administered in citrate or nitrate solution, after ingestion, it passes into the bloodstream, and an amount of 10% to 50% is circulated and fixed in the target organs: liver, kidney, spleen, bone marrow, lymph nodes, skin (hair follicles) [9].

A study conducted in Canada on 14 volunteers, determined the factors favouring gastrointestinal absorption and the body retention time of polonium with harmful potential. Each volunteer consumed about 2 kg of reindeer meat containing polonium in its natural state. Urine and faeces samples were collected and analysed for 65 days after consumption. The mean polonium gastrointestinal absorption was of 56%. The effect of these findings increases the estimated dose for Po-210 ingestion in foods with an absorption factor of 1.5–3.5 [9].

The dose of irradiation of internal organs depends on Po-210 absorption; due to the morphological properties of the gastrointestinal barrier (mural diminishing, increase of vascularization at villous level, increased muco-ciliary absorption surface), the proximal segment of the small intestine has the highest Po-210 absorption rate. The efficiency of Po-210 assimilation depends on its physical and chemical characteristics with the ability to form colloidal substances. After gastrointestinal absorption, Po-210 passes into the blood and causes changes in the target cells: fibroblast and endothelial cells [10].

Respiratory route

Alpha radiations are associated with a helium particle having a large mass and a small radius of dispersion (a few centimetres in the air) which results in 100% immediate and integrated respiratory absorption. Inhalation of aerosols or particles containing Po-210 leads to deposition on the alveolar capillary membrane, with irradiation of the lung epithelium. From this level, the radiation can follow two pathways: inhaled ionic compounds or Po-210 soluble compounds can be absorbed into the bloodstream, and insoluble particles are eliminated through the tracheobronchial tree within a period of 18 to 35 days [10].

Clinically, secondary to repeated irradiation, the triad composed of bronchial epithelial hyperplasia, destruction of alveolar elastic structures, and formation of intra-alveolar hyaline membranes is described.

Skin route

The skin pathway has a lower incidence compared to other Po-210 penetration pathways in the body, because helium particles associated with alpha radiation emitted by polonium cannot overcome epidermal barriers. In case of a skin injury and contact with a soluble form, Po-210 has the potential for transdermal indirect toxicity [10].

In a study examining the direct dermal absorption of polonium chloride, absorption was found to be at least 2% per day. These results indicate that a lethal amount of Po-210 could be introduced through the skin, passing into the blood and remaining for a prolonged period of time, causing chronic intoxication [11].

Mechanism of action

The mechanism by which radioactive isotopes produce cellular lesions is the basis of their cytotoxic properties. The mechanism of the biological action of ionizing radiation is based on *target theory* and *chemical theory.*

By direct effect, ionization releases an amount of energy sufficient to transform, denature or inactivate a series of biologically active molecules in a small region around an action point called target.

By indirect action, alpha radiation does not act on biologically active molecules, but absorbs energy and dissociates, producing free radicals, resulting from the radiolysis of water which constitutes the cellular environment. The action of the two mechanisms, directly and indirectly, cannot be clearly delimited in the human

body, as, in relation to the damaged structure or function, one of the mechanisms is predominant [12].

Alpha particles emitted from polonium disintegration are absorbed into the human body, causing the entire symptomatic arsenal. Death can occur within days or weeks from the time of irradiation with Po-210 [13].

In the human body, Po-210 causes two major effects: somatic, which can be early and late (depending on the absorbed dose and time of exposure), and genetic.

Somatic effects are similar to irradiation disease and are expressed through asthenia, alopecia, lymphopenia; haematopoietic syndrome with thrombocytopenia, myelosuppression and gastrointestinal nausea, vomiting, abdominal pain, diarrhoea. The poisoning symptoms of Po-210 are similar to the final stage of neoplasia. Liver and kidney have major lesions, nausea, vomiting, massive dehydration, diarrhoea, hair loss.

Clinical picture

The clinical effects of Po-210 irradiation can be classified as acute and chronic exposure effects (fig. 2).

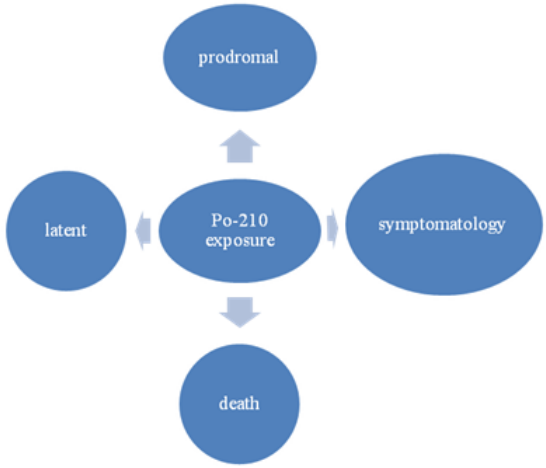

Fig. 2. Clinical stages of Po-210 exposure

- the prodromal stage begins in the first hour after exposure, lasting up to 2 days, and includes anorexia, nausea and vomiting that can mimic any abdominal pain syndrome;

- the latent stage lasts between 1–6 weeks, and manifests by good general condition; haematologically, the patient presents stem cells that fall into apoptosis;

- the debut stage manifested by anorexia, fever, altered general condition, fast numeric drop of hematopoietic cells; death may occur through infection or haemorrhage within a few months;

- the healing stage appears in case of interrupted Po-210 exposure at the beginning of the treatment; the medullary cells begin to repopulate crosslinked connective tissues with rapid profiling within a few weeks to 2 years. Otherwise, death by multi-organ dysfunction syndrome (MODS) occurs at a dose ≥ 1.2 Gy.

The response to ionizing radiation exposure varies with cell type and is characterized by an increased rate of mitotic replication. Spermatogonia, ovogonia, gastrointestinal tract cells as well as hematopoietic cells (lymphocytes and erythroblasts) are the most sensitive to irradiation, while collagen-producing cells (muscle and bone) are least affected by exposure to radioactive substances [13,14].

The genetic effects secondary to the action of radiation on deoxyribonucleic acid (DNA) are major and concern the entire genome. Radioactive isotopes are genotoxic, causing breakdown of DNA structure, with chromosomal mutations and underlying carcinogenic effects.

Treatment of Po-210 poisoning involves the early administration of Dimercaprol, an agent used in mercury (Hg), gold (Au), bismuth (Bi), lead (Pb) poisoning.

Complementary examinations

Complementary examinations include the toxicological, nuclear physics and genetic examination. The toxicological examination allows for the analysis of biological samples (urine, faeces and hair) by gas chromatography coupled with mass spectrometry (CC-MS). The literature presents the importance of using CC-MS system, especially in an acute poisoning case with mixture substances [15]. Also, the literature show that the GC-MS method is very useful for certitude diagnosis for diverse substances and the GC-MS/MS technique significantly increase the signal-to noise ratio and is very sensitive method for the determination of some unknown chemical structures [16]. The lowest lethal dose of Po-210 is between 0.6 and 1.2 micrograms [17].

Nuclear physics examination determines Po-210 or its stable compound – lead (Pb), in bone tissue (iliac crest, femur, stem, ribs, hair). Studies show that hair is a perfect bioindicator for the presence of radioactive polonium even after a single dose; the longer the exposure time, the more accurate the results of the determination.

Histological examination is not an elective method, but it can highlight changes in lymph nodes, and the presence of medullary degenerative lesions.

Tanatogenesis

From a forensic point of view, Po-210 intoxication has an increased incidence in males in the second decade of life. Po-210 poisoning is, most frequent, accidental, professional or therapeutic, suicidal (exceptional), or homicide — polonium being a very strong poison (ten times stronger than cyanide) [18].

Human bodies become radioactive through external exposure and radioactive contamination, elements that need to be carefully assessed at the time of forensic autopsy.

In irradiation deaths, necropsy is performed under special conditions (specially arranged autopsy rooms), the personnel being protected against radiation and controlled according to the protection rules, the washing water removed as radioactive water, and the samples taken in special containers [19].

The autopsy does not reveal pathognomonic signs of Po-210 intoxication as with any radioactive substance; histopathological examination identifying visceral anaemia, intracerebral haemorrhage without any history of cranial trauma, liver cirrhosis, intestinal bleeding erosions, degenerative and necrotic lining of the mucosa [20, 21].

The death of Po-210 poisoning victims can occur due to bone marrow aplasia, MODS or any type of neoplasia.

Famous cases of Po intoxication

The most famous irradiation with Po-210 was in 1943–1947 as part of the Manhattan-University of Rochester project in which four volunteers where injected with Po-210 and one has ingested Po-210 to evaluate the dispersion rate of the substance in the body and its distribution. In 1946, the daughter of the Marie Curie, Irene Joliot-Curie, was accidentally exposed to polonium after the explosion of a polonium capsule. In 1956, ten years later, she died of leukaemia [13].

In 2004, Yasser Arafat dies in a French military hospital with the official diagnosis of multiple organ failure.

In 2006, Alexander Litvinenko, former officer of the Russian FSB secret service, died in a hospital in London

with a diagnosis of leukaemia. At the autopsy, chromatogram coupled with mass spectrometry is performed, which highlights a suspicious graphic route. Following multicentre research, the radioactive substance is found to be polonium [22-24].

In 2012, Yasser Arafat exhumation is carried out with three forensic expert teams; it is demonstrated the existence of a minimum amount of Po-210 and lead in the skeleton through multiple calculations and mathematical analyses. At the moment of speaking, the cause of death of Yasser Arafat has not been officialy confirmed as poisoning with Po-210, the amount of radioactive substance identified being very low; during eight years, radiation from the Yasser Arafat's body had time to be halved 23.8 times, meaning that it was reduced over 250,000 times [25].

Conclusions

Polonium intoxication is one of the most difficult diagnostics of exposure to radioactive materials, being easily confused with the symptoms of a gastrointestinal or abdominal pain syndrome.

Exposure to Po-210 does not present pathognomonic criteria for clinical or forensic diagnosis, necropsy being inconclusive, with non-specific macroscopic changes in the target organs.

Multicentre studies in the territory of former communist countries could open new diagnostic paths for patients or former patients suspected of being irradiated or exposed to consecutive doses of radioactive substances.

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