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Introduction

It is with great pleasure that I invite readers to browse through the first issue of our journal "Medicine and Public Health".

It is not surprising that as the articles in this issue were submitted not long after the most intense period of the pandemic, we notice a significant number of articles dealing with different aspects of the COVID pandemic. It heavily influenced virtually all aspects of healthcare, hence articles about its impact on areas such as cancer screening and emergency surgery are included.

There are also several interesting case reports ranging from an atypical presentation of gallbladder cancer, an atypical Amyand hernia, to the rare congenital malformation situs inversus. In addition, the reader will have the opportunity to consider the difficulties that accompany the differential diagnosis of a kidney mass and iliac crest mass in the section concerning images in clinical medicine.

All in all, I sincerely believe that the mix of articles prepared for this issue will meet the high expectations of our readership. And if this is so, I can assure you that we are already working on the next, and hopefully even more interesting issue of our journal.

Andrzej L. Komorowski
Deputy Editor

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ORIGINAL ARTICLES

The impact of the SARS-CoV-2 pandemic on screening tests rates in breast and cervical cancer

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

The global SARS-CoV-2 pandemic had a significant impact on the availability of screening for breast and cervical cancer. In Poland, two pandemic waves were observed in 2020, characterized by an increase in the number of confirmed cases and deaths caused by the SARS-CoV-2 infection. This situation has reduced the number of patients registering for mammography and cytological tests. The aim of this study is to describe the problem using the available numerical data obtained from the database of the regional branch of the National Health Fund regarding the significant decrease in the number of screening tests for breast and cervical cancer in the Podkarpackie Voivodeship during the SARS-CoV-2 pandemic.

Keywords: SARS-CoV-2 pandemic, breast cancer profilaxy, cervical cancer profilaxy, public health

Introduction

The SARS-CoV-2 pandemic had a significant impact on behavior associated with a healthy lifestyle in many societies in the world. It started with "patient zero", a case reported in Wuhan in China on December 1, 2019 [1]. By the end of 2019, there were 41 cases of pneumonia of unknown etiology [2]. After several months of observation of the spread of coronavirus to all continents and most countries of the world, taking into account that sanitary and medical services were inadequately prepared, at the beginning of March 2020 WHO decided to declare a state of global pandemic. During the first months, the countries with the largest increases in the number of cases were China, Italy and Spain. In Poland, the first confirmed case was recorded on March 4, 2020 in a patient who had come from Germany [3]. After that, two peaks in the number of cases were observed, with the

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highest daily survival rate of 27,875 cases [4]. Throughout 2020, 1,305,744 infections were recorded in Poland, of which 28,956 cases were fatal [5]. The introduction of drastic restrictions by individual countries has contributed to a gradual reduction in the number of cases and deaths due to pneumonia caused by SARS-CoV-2. During the lockdown period, only urgent medical services were guaranteed. All non-urgent services such as cervical screening and breast cancer screening were temporarily suspended. The SARS-CoV-2 pandemic caused a delay in or cancelation of screening tests, which resulted in a diagnosis being made at a later stage with a worse prognosis. Difficulties in access to healthcare and patients' fear of potential infection in health facilities delayed the diagnosis and adequate treatment of cancer patients. It is estimated that in the UK alone, around 3 million people left cancer screening during the five-month follow-up period, which resulted in around 350,000 fewer diagnoses [6]. Pandemic development indicators in relation to the number of new cases and deaths daily are presented in Figures 1 and 2.

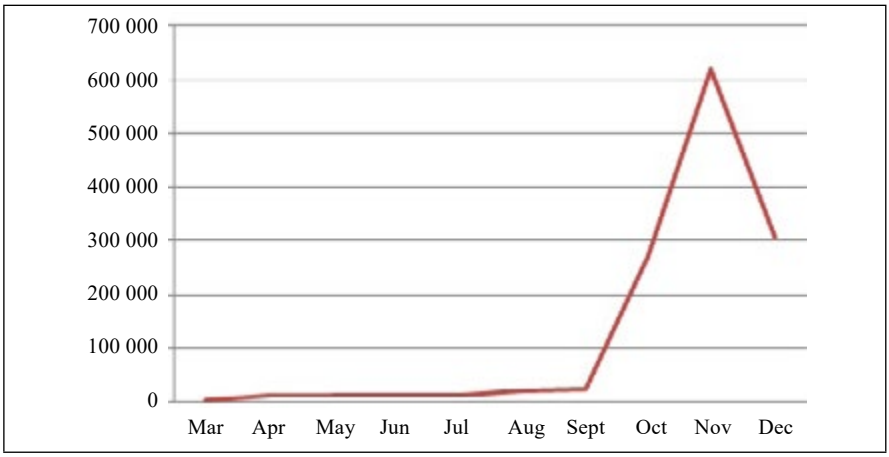


Figure1. Number of new SARS-CoV-2 cases reported in Poland in 2020

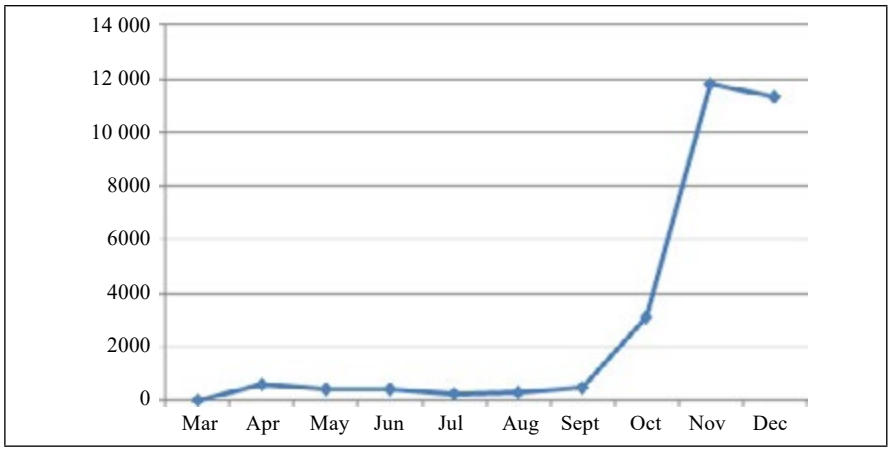


Figure 2. Number of deaths due to SARS-CoV-2 reported in Poland in 2020

Objectives

The objectives of our study are to compare the reporting of patients and the number of prophylactic procedures performed on the reproductive organs and breasts in the Podkarpackie Province in Poland during the SARS-CoV-2 pandemic.

Methods

The comparative data used in this study were provided by the provincial branch of the National Health Fund. The number of patients reporting for prophylactic examinations in the field of cervical and breast cancer in the years 2019–2020 was compared and contrasted.

Results

The purpose of secondary prevention of neoplastic diseases is to reduce morbidity and mortality. The aim of the cervical and breast cancer screening program is to achieve this goal. A measurable result of screening tests is achievable if 70% of cases are reported. In Poland, in accordance with the National Health Program 2016–2020, several types of screening test are carried out, including mammography in the prevention of breast cancer and cytological examination in the prevention of cervical cancer. At the time of the SARS-CoV-2 pandemic, a significant reduction in the number of cases reported to health services was noted, including among people covered by preventive programs.

Prophylaxis of breast cancer

The breast cancer prevention program which focuses on screening mammography is aimed at women aged 50–69 who have not had a mammogram in the last two years or annually for women at risk [7]. Between 2018 and 2020, 5,353,470 women were deemed eligible to take part in the breast cancer prevention program. 1,848,381 mammography tests were performed, which meant that 34.53% of those eligible were screened.

The percentage of studies carried out changed significantly after the outbreak of the global SARS-CoV-2 pandemic. In 2019, 49,955 mammography tests were performed in the Podkarpackie Voivodeship, and 32,510 mammography tests in 2020. The largest drops in the number of tests performed were recorded during the first wave of SARS-CoV-2 in April and May 2020; by 51.93%, 96.27% and 90.48%, respectively (by a total of 77.37%). However, during the second wave of SARS-CoV-2, the largest decrease in the number of mammograms performed was recorded in November – 46.04%. The number of mammographic tests is presented in Figures 3 and 4.

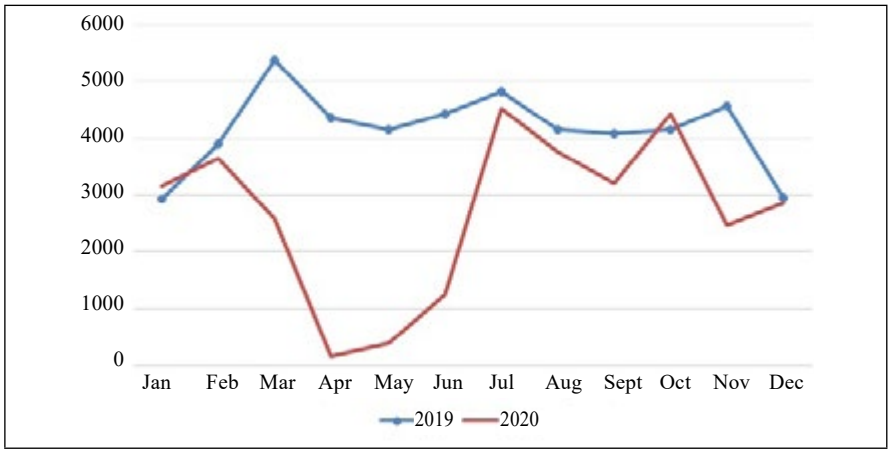
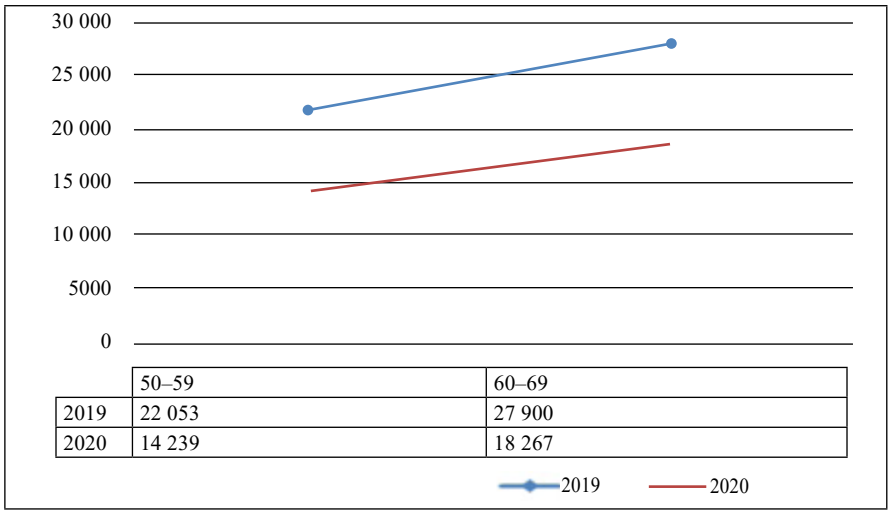


Figure 3. Amount of mammography tests performed in the Podkarpacie Province in 2019–2020



	50–59	60–69
2019	22 053	27 900
2020	14 239	18 267

Figure 4. Amount of mammography tests performed in the Podkarpacie Province in 2019–2020 divided into age groups

Cervical cancer prevention

The cervical cancer prevention program carried out by screening smears is aimed at women aged 25–59 who have not had a Pap smear test in the last three years, who have risk factors or have completed oncological treatment for cervical cancer. Between 2018 and 2020, a total of 9,977,646 women were deemed eligible for the cervical cancer prevention program. 1,380,428 cytological tests were performed, which meant that 13.84% of those eligible were screened.

In the case of cervical cancer screening, the SARS-CoV-2 pandemic resulted in significantly lower patient reporting. In the Podkarpackie Voivodeship, 22,694 were registered in 2019, and 13,833 pap smears were performed in 2020, which is a decrease of 39.05% compared to the previous year. The largest decrease in the number of cytologies performed was recorded during the first wave of SARS-CoV-2, in March, April and May, of 66.05%, 94.97% and 72.24% respectively (total 77.04%) compared to the number of tests performed in those months a year earlier. During the second wave of SARS-CoV-2, in October and November 2020, there was a decrease in the number of tests performed of 40.76% and 35.9% compared to the previous year (38.5% in total). The number of cytological tests carried out is presented in Figures 5 and 6.

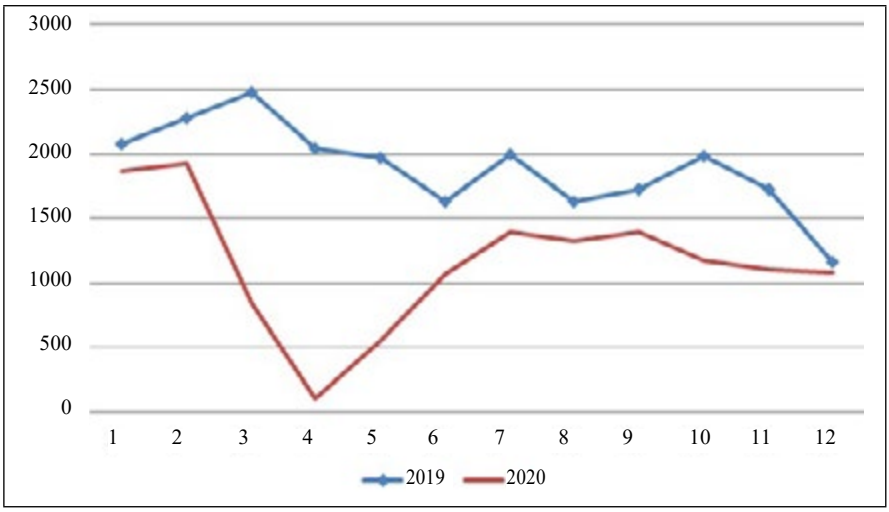


Figure 5. Amount of cytological tests performed in the Podkarpacie Province in 2019–2020

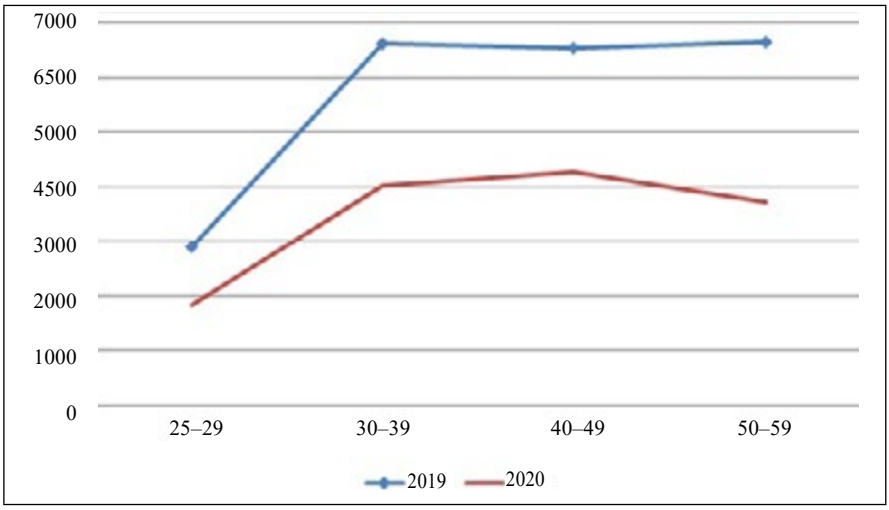


Figure 6. Amount of cytological tests performed in the Podkarpacie Province in 2019–2020 divided into age groups

Discussion

The available literature lacks statistical analyses and publications on the impact of the SARS-CoV-2 pandemic on the number of preventive examinations carried out in countries that have breast and cervical cancer screening programs.

Sprague et al. present an analysis of statistical data concerning prophylactic mammography from many centers in the period of the first wave of cases in the USA. Between January and July 2020, 66.2% of the number of prophylactic mammograms were performed compared to the same period a year earlier. The study also noted a gradual increase in the number of mammograms performed during the period of falling SARS-CoV-2 cases in the USA in May and June 2020 [8].

Naidich et al. report a 58.42% decrease in the percentage of mammographic tests performed in several dozen centers included in the study in the state of New York (USA) between March and April 2020 [9]. Similar observations were made in the same period in the work of Yin et al., where the decrease in the number of mammograms performed was on average 72.1%, and the largest weekly decrease was observed at the beginning of April 2020, when only 5.4% of the tests were performed compared to the period before the pandemic [10]. Miller et al. compared the number of Pap smear test in the period before the lockdown was announced in the US, lasting from mid-March to mid-June, as well as during and after the lockdown. These figures were compared to the number of tests performed in 2019 in the relevant time periods. During social isolation, a decrease of 78–82% in the number of tests performed was observed, and a decrease of 24 to 29% in the few months of follow-up after the lockdown ended [11].

The studies by Burger et al. present mathematical models illustrating the possible health risks caused by inhibition of the Pap smear test as part of cervical cancer prophylaxis. It has been estimated that in 2027 the incidence of this disease will increase by 5–7 / million of women surveyed if the number of screening tests carried out during the pandemic, which lasted six months, is reduced. In the event of a 24-month deadlock in which smear tests are abandoned, the incidence could increase by 38–45 / million women tested [12].

In response to the limitations related to the global SARS-CoV-2 pandemic regarding the prevention of breast and cervical cancer, many learned societies have decided to issue new recommendations or proposals for procedures as far as screening these cancers is concerned. An example is the position of the American Society of Cervical Colposcopy and Pathology (ASCCP), which issued recommendations initiating a temporary suspension of planned procedures. Only in field cases was it recommended to limit the number of cytological examinations. There are also recommendations regarding the performance of a follow-up colposcopy on the basis of the Pap smear result [13,14]. Recommendations are issued by learned societies in order to unify the treatment of patients during the SARS-CoV-2 pandemic, while maintaining the priorities of screening and sanitary safety [15–17].

The authors of this study also point out the great importance of conducting further research, which will certainly have an impact on understanding of the impact of the SARS-CoV-2 pandemic on women's health [18].

Conclusions

The increased effort of sanitary services and the adaptation of health care systems should contribute to the development of safe management standards and broaden patients' access to oncological prophylaxis and treatment. This will enable the improvement of the public health situation across the globe at the time of the SARS-CoV-2 pandemic.

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Atomic-level cancer studies – a new challenge to distal interdisciplinary science

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

Background: Nowadays, the amount of cross disciplinary research in many branches of science is growing dynamically. Multidisciplinary, interdisciplinary and transdisciplinary evaluations are being carried out. Scientific progress, in combination with the development of knowledge and new technical discoveries, allows the most complex problems to be considered in an innovative way, which results in original solutions, not present in the previous, more traditional understanding.
Materials and methods: We reviewed the current data on the evaluation of pathological tissues using current mass spectrometry methods, including advanced isotope ratio mass spectrometry in the first known atomic level cancer studies.
Results: The first attempts to estimate the stable isotope ratio in pathological tissues appeared as a potentially new method of understanding the biology of cancer. The changes in stable isotope concentration showed the relationship with the fundamentals of cancer – its promotion stage, and the mechanisms of its progression as well as its relationship to the standard prognostic biomarkers. The advanced multidisciplinary analysis of the results of isotope ratio assessment in cancer studies culminated in the creation of 'The Revolve(r) Heavy Nitrogen Theory of Death', which explains the phenomena of the proliferation force of cancer cells.
Conclusions: Stable isotope profiling performed using the highly advanced and creditable isotope ratio mass spectrometry approach reveals the previously unknown area of pathological tissue biology. Overcoming interdisciplinary barriers opens a new branch of medical studies with a potential clinical application. The intriguing results of the first attempts and potential clinical implications should form the basis of the next atomic-level cancer studies projects.
Keywords: cancer, biomarkers, stable isotopes

Introduction

Advanced interdisciplinary approaches are located at the crossroads of the traditional methods of evaluation, and their rapid development is currently being observed [1]. These tools are also highly valued due to their extreme reliability, which fulfils even the highest demands; this has been proved in forensic medicine investigations [2]. The same reliability allows

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interdisciplinary projects in medicine with a potential clinical application to be conducted, which is especially necessary in cancer studies for the purposes of routine oncology.

The literature indicates that success in interdisciplinary projects depends on many factors, namely the selection of research leaders and scientists, motivation, communication and external support, as well as the availability of financial sources for the working groups [3–5]. Nowadays, there are funding programs devoted to promoting interdisciplinary research. The problems with conducting these studies appear to be both of a cognitive and epistemic nature, and those that affect the effectiveness of multidisciplinary research must be better understood [6]. Despite the many advantages, some mistakes characteristic of interdisciplinary studies have been observed, such as inappropriate selection of disciplines, aims of the studies, members of research teams, methods or indicators of the expected solutions, as well as environmental sources of problems that are difficult to avoid, e.g. language barriers, lack of experience or insufficient funds, and the necessity to create new methodological modes [5,7].

The relationships between branches chosen for interdisciplinary studies have to be evaluated by the scientist who wants to carry out such demanding projects. It is pointed out in the literature that there are important differences between close and distal types of interdisciplinarity in scientific research. The first results in projects that are easy to carry out as well as numerous benefits, whereas the second – distal interdisciplinarity (if the projects successfully reach their aims) – only yields a limited number of solutions [3–5].

Interdisciplinarity in medicine shows has great potential and also appears to be a source of new clinical, diagnostic and therapeutic protocols, or leads to the implementation of more comprehensive patient care [1,8–10]. Interdisciplinary research proves that combining areas that by their nature have little in common with each other allows hitherto unknown aspects of the phenomena under investigation to be revealed, including disease processes, which, as emphasized, is of particular importance for the further development of medicine [1]. Distal interdisciplinary findings in medicine are resulting in a new generation of biomarkers with a potential clinical application.

Distal interdisciplinarity in mass spectrometry cancer biomarkers

The National Institutes of Health Biomarkers Definitions Working Group (1998) reports that a biomarker is a trait that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention. The

working definition of biomarkers is still evolving and new groups of these factors are being introduced and modified along with technical and scientific progress. At present, the most rapidly developing group appears to be molecular biomarkers – the genes themselves and their products, as well as changes at the mRNA level [11]. They are already being introduced into oncology and thanks to their documented clinical impact have made a real breakthrough in its routine procedures.

For the purposes of medicine, biomarkers, which can aid in clinical evaluation, are divided into two groups, namely prognostic and predictive parameters [11,12]. Optimal biomarkers are those that are highly specific and can be measured without difficulty in easily obtained materials, e.g. body fluids, such as saliva, blood serum and urine, or they are available with limited injury/complications, e.g. by fine needle aspiration biopsy. The prognostic factors emphasize the predicted natural course of the disease and the prognosis; they are also associated with overall survival (OS). Predictive parameters are related to the likelihood of a positive response to the treatment given. The search for new tumor biomarkers, as well as the achievement of optimal treatment results [12,13], remains the goal of creating new, effective therapeutic protocols.

Historically, the first breakthrough in prognostic parameters was made in immunohistochemistry. This traditional diagnostic method, used routinely in differential diagnosis, appeared to be of prognostic value; the relationship between expression levels was idenitifed and the prognostic parameters were documented [14]. Nowadays, the most numerous biomarkers are of a molecular nature, and they are widely identified via proteomic analysis. Thanks to the use of cancer biomarkers, many aspects related to cancer can be analyzed. The evaluation of these parameters allows one to predict the cancer growth (e.g. BRCA1 germline mutation in breast and ovarian cancer), conduct screening tests (e.g. PSA in prostate cancer), assess targeted therapy utility (e.g. KRAS and antibody anti-EGFR in colorectal cancer), and monitor the disease (recurrences by CEA estimation in colorectal cancer) [12,13,15].

The additional benefits of biomarker estimation is that they make it possible to shorten the treatment time and at the same time minimize both negative side effects and the costs of the therapy. Therefore, the main aim of many contemporary studies is to search for new ways to reveal new biomarkers, which are of special importance for cancer patients.

The dynamic development of mass spectrometry, for which four Nobel Prizes have been awarded and which has already opened a new area of biomarkers, shows, especially in proteomics, new directions for studies with the use of high-resolution mass spectrometry. Proteomics is a new discipline

that aims to investigate the proteome – the protein component encoded by the genome (PROTEin complement of the genome). The creation of a separate research unit (Human Proteome Organization) is to lead to the classification of proteins, similar to the cataloging of genes in the Human Genom Project. Until the 1970s, protein masses were determined using methods such as electrophoresis, ultracentrifugation and chromatography, but the measurement error was 10% to 100%, which precluded clinical studies of human tissues. Only the introduction of mass spectrometry in the nineties of the last century made it possible to study proteins while maintaining high sensitivity of measurements. The usefulness of the mass spectrometry method for the search for new biomarkers in pathological conditions, especially cancer, is currently well documented [16].

Mass spectrometry methods

Mass spectrometry (MS) is an analytical technique based on measuring the mass-to-ion charge ratio (m/z) in the gas phase. Mass spectrometry substances to be studied with the use of the mass spectra of atoms and their molecules. The essence of the method lies in the fact that ionized atoms or molecules of substances are separated by the value of the m/z ratio and recorded separately using a mass spectrometer. From the mass spectrum obtained, the mass values and the relative content of individual components in the sample are determined. MS came to the fore at the turn of the 19th and 20th centuries thanks to the research work of Joseph John Thomson and Francis William Aston. Joseph John Thomson, the discoverer of the electron who researched electrical conductivity in gases, was awarded the Nobel Prize in Physics in 1906. The research carried out by him and his student, Francis William Aston, resulted in the construction of a mass spectrometer. For his invention and research on isotopes, in 1922, Aston also received the Nobel Prize – in chemistry. A breakthrough discovery in spectrometry was its coupling with gas chromatography in 1956 (GC-MS, English: Gas Chromatography – Mass Spectrometry), which made it possible to separate the mixture and perform a qualitative analysis of all its components. The development of the method of electrospray ionization (ESI) has led to the development of another combined technique – liquid chromatography-mass spectrometry (LC-MS). The invention of the ion trap – a new type of analyzer, resulted in 1989 in another, and not the last, Nobel Prize in the history of mass spectrometry – in Physics, for Wolfgang Paul and Hans Georg Dehmelt. The fourth Nobel Prize, in the field of chemistry, was awarded to John Fenn and Koichi Tanaka in 2002 for the use of electrospray ionization in the analysis of biopolymers and the

development of a new research method – Matrix-Assisted Laser Desorption Ionization (MALDI), and its use in conjunction with a Time of Flight (TOF) analyzer. Contemporary MS is a highly developed technique of mass measurement. The devices allow molecular weight to be determined with previously unattainable accuracy, especially with the use of nuclear cyclotron resonance with Fourier transformation [17,18]. MS definitely has a competitive edge in comparison to other analytical methods, mainly due to the possibility of identifying substances present in very low concentrations, as well as the analysis of complex mixtures. The most commonly used methods of ionization are solid matrix laser desorption and electrospray, and the most valuable for tissue estimation is MALDI due to the possibility of assessing molecules directly on tissue sections without the need to homogenize the material [19–21].

Currently, cells, tissues and body fluids (mainly plasma) are being tested, which is yielding reliable results from samples with a very low concentration of the proteins being searched for (less than 5 femtomoles) [22]. MS may also be combined with protein databases and programs for de novo sequencing. In proteomic research, biochemical, physicochemical and bioinformatic methods are used, which enables the simultaneous analysis of thousands of proteins. New branches of this method have appeared e.g. interactomics (interactive proteomics) that studies the interactions between proteins at the atomic, molecular and cellular level. Although primary, proteomics has found application mainly in non-clinical areas. Currently, the leading direction in the development of proteomics is diagnostics, which confirms the existence of pathological changes, their differentiation, and determines the boundaries of pathological lesions, as well as clinical proteomics. This focuses on disclosing the differences between the proteome of healthy and sick people, leading to the disclosure of biomarkers of pathological processes (alleles of genes, metabolites or proteins) and to the search for changes in protein profiles caused by the therapy implemented [23–26]. It is assumed that the assessment of multicomponent sets of proteins and peptides selected from the complex proteomic profiles of blood serum will have a clinical application [27].

Proteomics is attempting to conquer modern oncology, its achievements have revolutionized the concept of the biomarker, which has been used so far and which is now defined as a measurable element that correlates with a normal phenotype, pathologically changed (including cancerous) or resulting from the therapy applied. The new term “cancer proteomics” has also been introduced, i.e. the creation of tumor protein profiles including proteins in tumor cells, proteins in the microenvironment and proteins appearing in the body fluids of patients with neoplastic disease [28,29].

Thanks to the use of LC-MS, LC-MS/MS, MALDI-MS/MS and MALDI-TOF-MS, it is possible to identify and analyze selected peptides and proteins in detail, as well as study endogenous compounds that occur in very low concentrations [30]. What is worth underlining is that nowadays it is possible to identify proteins characteristic of neoplastic diseases *in vivo* and to visualize them [31].

There are also attempts to use mass spectrometry as a method of molecular imaging of tumor tissues. In this technique (imaging MS), TOF spectrometers ionize proteins that are on the surface of cells or tissues, and then create mass spectra of the proteins in various positions. The protein profiles obtained are correlated with the microscopic image and related to modern histopathological classifications. The number of proteomic studies on tumors is rapidly increasing. They include the biology of cancers, such as lung, breast, prostate, colon, ovarian or endometrial cancer [32–37]. In addition, the correlations with recognized prognostic factors are analyzed [38].

There have been reports in the literature about the potential use of proteomics to distinguish primary and metastatic cancers. Using mass spectrometry, it is also possible to identify post-translational modifications that are considered by some researchers to be key in the development of cancer and the bioimage phospholipids of cell membranes [39–41]. Nowadays, the main goal of cancer proteomics is to identify diagnostic, prognostic and predictive markers [1] and fully personalize the treatment of patients [34,42,43].

Unfortunately, many valuable and extremely interesting achievements of proteomics have no clinical implications, as their use would require the creation of complete biomarker panels and to assign them to specific pathological conditions, while maintaining the expected sensitivity and specificity of the results obtained. Similarly, most of the other valuable findings in medicine are resulting in a lot of new markers, although their low specificity considerably limits direct clinical use [44,45].

Atomic level cancer studies

Atomic level cancer studies appears to be a unique example of distal interdisciplinarity with a potential clinical application. The studies are based on highly advanced techniques from the mass spectrometry panel, especially isotope ratio mass spectrometry, which relates to the atomic level of the evaluation of tumor biology, which has unexpectedly appeared to relate the isotopic composition of cancer tissue to cancer progression and dissemination with potential clinical implications. The results also brought a new type of isotopic biomarkers [10,46–52], as well as an innovatory idea for personalized cancer management via isotope fractionation

processes [52]. It should be mentioned that this method is also used for the evaluation of non-cancerous human pathologies e.g. diabetes mellitus or sepsis [8,9].

Isotope Ratio Mass Spectrometry (IRMS) makes it possible to reveal the distinctiveness of the materials tested by assessing their isotopic composition. This method measures the heavier isotope ratio to a lighter solid isotope of a given element, which makes it possible to see the phenomenon of isotopic enrichment or depletion (increase or decrease in the amount of a heavier isotope) in the test material treated as a whole. There are a number of contemporary applications for this unique technique with the highest reliability and precision of determinations that have been documented; it is growing rapidly. They include geographic identification and biological origin of the samples and environmental changes in the history of the Earth, identification of food sources, nutrient circulation, water assessment, metabolism research, doping control, which reveal the common origin of a substance e.g. drugs, explosives, identification of GMOs, and monitor man-made environmental hazards.

Changes in the isotopic ratio of elements are extremely small and, for ease of use, are expressed by the value delta (δ) expressed in per mille. A relative measurement is used, i.e. one which alternaes between the sample measured and the standard, within one measurement cycle, and relates the measured isotopic composition of the sample to the isotopic composition of the standard adopted. The delta value, therefore, expresses the relative difference between the isotope ratio in the sample and in the standard. Measurements of such high precision are made using an Isotope Ratio Mass Spectrometer, adapted to the study of the isotopic ratios of light elements – hydrogen, carbon, oxygen, sulfur and nitrogen [53].

Despite the many advantages and the highest credibility, only a few reports on the use of isotope mass spectrometry seem to concern studies with potential clinical impact. They evaluate the pathological processes in modern humans. They focus on the cognitive or traditional, non-medical aspects of IRMS measurements, and the evaluation covers only the non-invasive or minimally invasive samples, not post-surgical materials [8,9,54–57]. Subsequent publications are also starting to describe attempts to initially assess biological materials in the course of cancer, but they focus on the measurement of the isotopic composition of metals using methods based on inductively coupled plasma mass spectrometry. Furthermore, the concept of these studies, which are based on a small number of cases, does not include histoclinical analyses or the search for potential relationships with the spectrum of prognostic factors recognized in modern oncology, depending on the cancer type [46,47,51].

IRMS as a tool of Earth sciences appears to be barely accessible and very expensive for medical research, although the method meets the highest requirements concerning scientific value, especially in medicine for the purposes of evaluations with potential clinical application [2].

In 2015, structured atomic level studies were shown to be applicable to the direct evaluation of cancer tissues growing in vivo [7,8], and in the same year, for the first time, the statistical significance of such estimations and their prognostic value was proved [52], highlighting the last previously undiscovered area of cancer biology.

The prognostic impact of atomic cancer tissue evaluation was confirmed in 2016 in two independent studies on Wilms tumor [10] and breast cancer [50]. Although recently discovered, the utility of IRMS studies for medical purposes and their clinical application have currently made this method the standard tool in the new rapidly developing field of atomic level studies of pathological processes.

Summary

The interdisciplinarity of atomic level studies of pathological tissues draws attention to previously unknown aspects of the biology of abnormal tissues. Primary attempts to estimate the stable isotope ratio in pathological tissues appear to be a potentially new method of understanding the biology of cancer. The changes of delta values (isotope depletion or enrichment) show the relationship with the fundamentals of cancer e.g. the promotion stage of neoplastic disease, and the mechanisms of its progression as well as the established prognostic biomarkers of the cancer types examined.

Isotope mass spectrometry cannot be perceived as a competitive technique in relation to the recognized research method, which is the microscopic evaluation of cancer tissue, but it seems to be a valuable supplement to it. A stable isotope ratio in tumor tissue appears to be a novel isotopic biomarker of cancer. Finally, an advanced multidisciplinary analysis of the results of isotope ratio assesment in cancer studies has brought unexpected conclusions and resulted in 'The Revolve(r) Heavy Nitrogen Theory of Death' being written, which explains the phenomena of the proliferation force of cancer cells [58].

Conclusions

Stable isotope profiling performed with the use of the highly advanced and credible isotope ratio mass spectrometry approach reveals a previously unknown area of pathological tissue biology. Overcoming interdisciplinary barriers opens a new branch of medical studies with a potential clinical

impact. The intriguing results of the first attempts and potential clinical implications should also be the focus of the next atomic level cancer studies projects.

The author declares no conflict of interests.

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Emergency surgery in the COVID era

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Abstract

We describe the case of a COVID-positive patient with a clinical diagnosis of acute appendicitis who was a prisoner at a maximum security facility without access to a prison surgical ward. The administrative and legal issues related to admitting and treating this patient on a standard surgical ward are briefly discussed.
Keywords: COVID, emergency surgery, acute appendicitis, prison healthcare

Case report

A 35-year-old inmate, accompanied by two armed prison guards, presented in the emergency department with clinical signs of acute appendicitis. After a standard preoperative workup he was deemed suitable for an emergency appendectomy. Following hospital policy at the time of the COVID pandemic a PCR test for COVID was performed. The test result was positive. The hospital had a designated COVID operating theatre as well as COVID beds in the ICU and the surgical and medical wards. However, no free beds were available at the time, nor were the wards prepared to allow the armed guards to stay with the inmate during the postoperative period.

Since in the same city there is a hospital of the Ministry of the Interior, the surgical ward of this hospital was contacted in order to receive instructions on how to handle the case (from a legal and administrative perspective, as from a medical perspective the case seemed pretty straightforward).

During a telephone conversation the surgeon on duty at the Ministry of the Interior hospital informed us that they did not have the organizational capabilities to take care of a COVID-positive inmate with the two armed guards that have to accompany the prisoner at all times. They suggested

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that in this situation the standard procedure would be to refer the patient to the nearest prison hospital.

The nearest prison hospital, located 180 km, away was contacted. The physician on duty agreed to accept the patient, but also informed us that this particular prison hospital had neither an operating theatre nor a surgical ward, so the only treatment they could provide the patient with would be non-surgical. Since the diagnosis of acute appendicitis with ensuing peritonitis is a clear surgical emergency, we asked for a prison hospital with a functioning surgical ward. As it turned out, in a country of 38 milion inhabitants, there is only one such facility, and it is located 632 km away from our hospital. Given the medical state of the patient, time spent talking to the other hospitals (three hours) and the impossibility of organizing transport for a COVID-positive inmate with two guards over a long distance, we decided to operate at our hospital.

The operation was performed in a designated COVID operating theatre. A laparotomy was performed. Due to a massive perforation at the base of appendix with severe inflammation of the cecum wall, a right colectomy was deemed necessary. After the operation, due to the lack of free COVID beds and also the legal requirement for two armed guards to be present at all times, one of the rooms in the surgical ward was prepared as an impromptu COVID room with two guards in COVID suits sitting in front of the room. The postoperative course was uneventful, and the patient returned to the maximum security prison after six days.

Discussion

Until quite recently, it was hard to imagine that a case report of acute appendicitis could be published in a contemporary medical journal. However, the advent of the COVID pandemic has changed our everyday practice to a great extent [1]. After more than three years we have become accustomed to constantly changing situations in hospitals. The influx of COVID patients, the necessity to test the patients and their families and preoperative difficulties with COVID-positive patients have become a new normal for us. The opening of new temporary hospitals and the creation of designated COVID hospitals on the basis of existing ones was supposed to be a way to prepare the medical community for all possible scenarios [2]. Unfortunately, not everything can be foreseen. The present case is surprising because it shows how one of the most common surgical emergencies can turn into an administrative disaster because of COVID hospital rules. From one point of view, there was a patient requiring surgery, and from another the legal requirement for the constant presence of two armed prison guards. When a COVID

infection was added to this equation it seemed almost impossible to solve [3]. The option that was chosen by our team was far from correct from the point of view of the COVID rules; the guards were exposed to an infected patient for too long and the isolation of the patient was very primitive. However, we feel that a surgical emergency needs to take priority over COVID rules. Sending a patient more than 600 km with a diagnosis of appendicitis seems nonsense [4]. Sending a surgical emergency from a surgical ward to a hospital without an operating theatre seems more like a scene from a Monty Python sketch. Unfortunately, from an administrative point of view these were the right things to do [5]. We decided otherwise and we were happy to save this patient from possible death due to a simple case of appendicitis. Which would be a real tragedy in the third decade of the 21st century.

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Upper GI bleeding as a first symptom of gallbladder cancer

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Abstract

An unusual case of gallbladder cancer with duodenal perforation presenting as massive upper gastrointestinal bleeding is described. A case of diagnosis and treatment of gallbladder cancer is briefly discussed.
Keywords: gallbladder cancer, upper gastrointestinal bleeding, cholecystectomy, surgery

Introduction

Gallbladder cancer is a relatively rare and aggressive cancer [1]. Clinical signs of gallbladder cancer include pain, jaundice, visible tumor in the right hypochondrial region, which are frequently associated with advanced stages of the disease [2]. Early diagnosis is usually made during standard laparoscopic cholecystectomy specimen evaluation or during imaging tests performed on otherwise healthy individuals [3]. Massive bleeding from a cholecysto-duodenal fistula caused by previously undiagnosed gallbladder cancer is an extremaly rare occurrence.

Case description

A previously healthy 62-year-old female was admitted with symptoms of gastrointestinal bleeding. After stabilizing the patient, a series of diagnostic tests were performed. Abdominal ultrasound revealed irregularly thickened duodenal pad walls (up to 7 mm), a small gallbladder (about 30 × 8 mm) with a closed lumen, with no visible deposits or gas bubbles in the lumen. A gastroscopy was performed, showing an abnormal tissue mass on the lower wall of the duodenal pad, most likely growing in from the outside, less

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likely a large polyp. Specimens taken showed infiltration of single atypical glandular tubules, and the diagnosis was made more specific using immunohistochemistry, which showed the presence of lesion cells, positive for markers CDX2, CK19, CK20, weakly positive for CK7, GATA3, negative for chromogranin, estrogen, and TTF1 and PAX8. A contrast-enhanced CT in the part adjacent to the bulbous part of the duodenum revelealed a thickened wall with visible ulceration, penetrating from the duodenum into the gallbladder. Due to a suspected gallbladder neoplasm with a cholecystoduodenal fistula, an MRCP was performed, which revealed a small gallbladder (10 × 24 mm) with irregular, thickened walls showing communication with the duodenal wall through a 7 mm diameter canal at the border of the pad and descending part – a fistula. The patient was scheduled for laparotomy, during which a cholecystectomy with wedge resection of the liver and partial resection of the duodenum "en bloc" was performed (Fig. 1 and 2). The postoperative course was uneventful and patient was discharged 6 days after surgery.

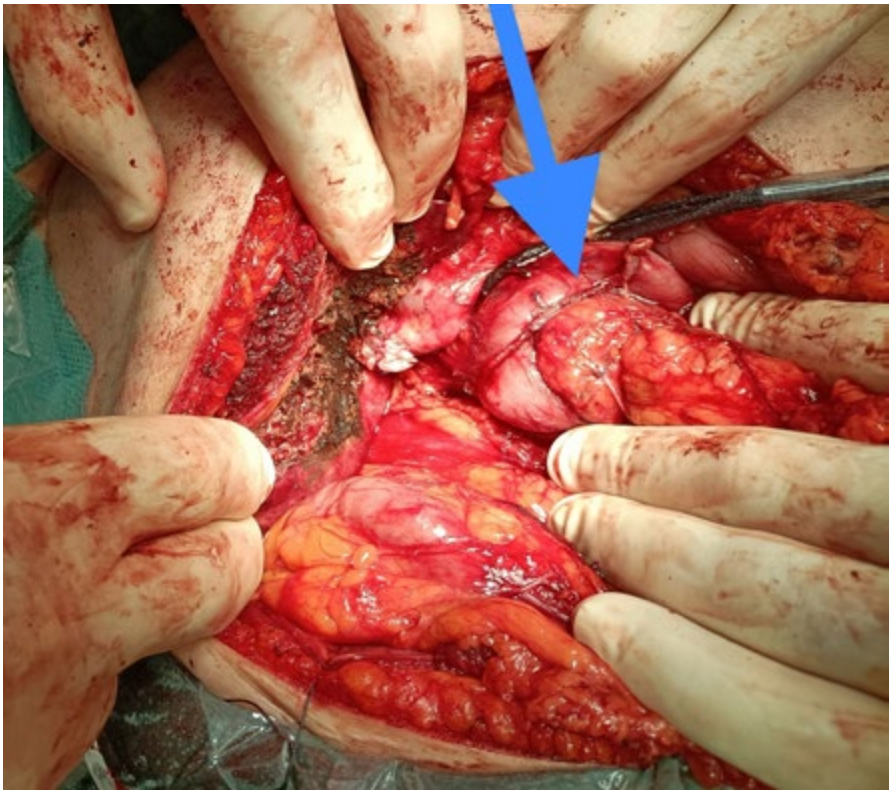

Fig. 1. The operative field after excision of the specimen. The Pringle manoeuver can be noted as well as the staple line on the duodenal wall. The arrow points to the duodenal staple line. Photo courtesy dr Bogdan Kopacz.

Fig. 2. The specimen with part of the duodenum clearly visible with staple line and liver tissue. The gallbladder is hidden between the duodenal wall and liver wedge. Photo courtesy dr Bogdan Kopacz.

Discussion

Gallbladder cancer (GBC) is the most common malignant neoplasm of the biliary tract and the sixth most common of the gastrointestinal tract [1,4]. GBC is very aggressive, with a 5-year survival rate of only 19% [5,6]. It affects women disproportionately more than men, which may be associated with women's greater propensity for gallstones [7]. It develops from the mucosa of the gallbladder and its early development is usually asymptomatic, which is why it is usually detected at an advanced stage [8]. Risk factors for gallbladder cancer are old age, with the highest incidence rate reported >75 years of age, female gender [9], obesity, gallstones, gallbladder polyps, porcelain gallbladder [10] (although this has recently been debated [11]), chronic inflammation associated with Salmonella and Helicobacter Pylori infection, primary sclerosing cholangitis, environmental exposure to heavy metals, cigarette smoking, individual variability of the pancreaticobiliary duct junction, genetic predisposition, poor dietary habits or drinking untreated water [12]. High-resolution ultrasonography remains the diagnostic

standard, but a large proportion of tumors are detected incidentally intraoperatively or during routine pathologic evaluation of a gallbladder resected for gallstones [8]. The most common symptoms of GBC include pain, discomfort in the right upper abdominal quadrant, weight loss, jaundice, palpable tumor, malaise and fever [2,12]. Early detection of GBC increases the likelihood of a complete recovery. Prognostic factors include depth of infiltration, histologic grade, presence of lymph node metastasis, size of liver infiltration, and presence of venous, lymphatic and peri-neural infiltration [13]. Cholecystectomy is the treatment of choice for T1 tumors [14], while T2 tumors require liver wedge resection. In the case of T4 gallbladder cancer, radical resection is rarely achieved. Surgery for metastatic disease is discouraged [3,15]. In the available literature we were not able to find any case of massive gastrointestinal bleeding as a first sign of gallbladder cancer. Interestingly, radical surgery with resection of the liver and part of the duodenum was feasible in our patient, thus making long-term survival possible.

Conclusion

Locally advanced gallbladder cancer can present as massive gastrointestinal bleeding due to duodenal infiltration.

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CASE REPORTS

Strangulated epiplon in the inguinal canal as an atypical presentation of Amyand hernia

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Abstract

An Amyand hernia is defined as a vermiform appendix located within the inguinal canal. It is a rarely seen condition with complications that are even more uncommon. We report the case of an Amyand hernia containing a strangulated epiplon and vermiform appendix.
Keywords: Amyand hernia, appendicitis, inguinal hernia

Case report

A 59-year-old female patient recently referred by a surgical outpatient center for acute appendicitis was admitted onto the surgical ward and prepped for an urgent appendectomy. Prior to admission, the day before she had been admitted to the emergency room for abdominal pain located in the lower right quadrant. Since the patient presented with an atypical history for appendicitis, no signs of peritoneal inflammation, and laboratory results within or close to normal range, she was prescribed antibiotics, painkillers and dismissed from the hospital. Upon admission to surgery the patient's vitals were normal, body temperature was non-febrile, she had an elevated CRP level 41 mg/l with a normal leukocyte count, and physical examination strongly indicated peritonitis. The patient was operated on using a laparoscopic approach. An orientational 360 degree revealed the greater omentum adhering to the anterior abdominal wall, which was freed revealing a small part of the greater omentum and appendix located within the inguinal canal (Fig. 1) which were reducible using standard laparoscopic instruments. The appendix was inflamed along the part located in the inguinal

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canal but showed no signs of necrosis or perforation. It was noted that a part of the greater omentum within the canal was strangulated and necrotic. Both the appendix and necrotic element of the greater omentum were excised and removed through the main trocar. The postoperative course proceeded with no complications and the patient was dismissed on the second postoperative day.

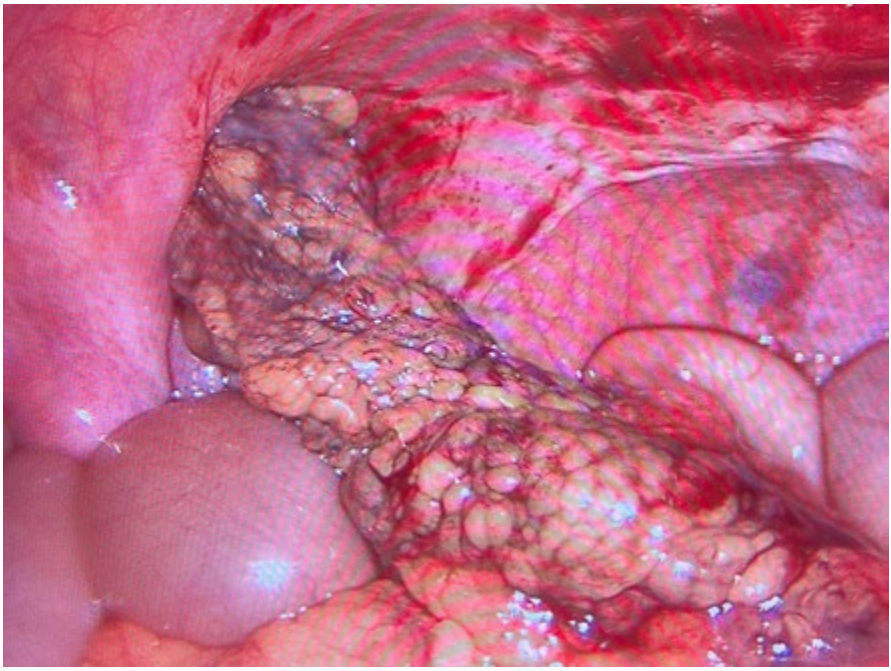

Fig. 1. Strangulated epiplon inside the right internal inguinal ring. The appendix can be seen on the right

Discussion

Various types of hernia, including abdominal, inguinal and femoral hernias, often contain a piece of omentum or a part of the bowel. A hernia of this type is seen in less than one percent of hernias, with complications seen in even fewer cases [1]. An incarcerated inguinal hernia is one of the most commonly performed surgical procedures, and acute appendicitis is one the most common causes of pain in the right iliac fossa [2,3]. When both cases are present, a proper diagnosis must be obtained to progress with the best treatment option in mind. Amyand hernias are classified into four types, and in this case the patient presented with a type two Amyand hernia: acute appendicitis within an inguinal hernia with no abdominal sepsis. Classification

type one is characterized by a lack of acute appendicitis and in types 3 and 4 sepsis and other related abdominal pathologies are present. In this case, the recommended treatment option would be to perform an appendectomy and repair the hernia with no mesh placement. It is the inflammatory status of the appendix that determines a favorable outcome of any mesh placement. In this case, no hernia repair was performed, but was planned for in the near future [3,4]. The internal inguinal ring with the round ligament of the uterus was clearly seen after reduction of the hernia [Fig. 2].

Fig. 2. Right internal inguinal ring after reposition of the epiplon. Round ligament of the uterus can be seen on the left

It is worth mentioning that Claudius Amyand was a French Huguenot in exile in England, working as a military surgeon at St. George's Hospital in Westminster, London. He operated on an 11-year-old boy for a right inguinal hernia complicated by a fecal fistula. The operation performed by Claudius Amyand is important for two reasons. First, it is the earliest description of a hernia involving the appendix. Second, it is the earliest documented appendicectomy in the history of surgery. To commemorate Amyand's achievement, an inguinal hernia containing the appendix is referred to as Amyand's hernia [5].

Conclusion

Special consideration for surgeons when diagnosing inguinal hernia with a possible diagnosis of an Amyand hernia. When diagnosing an inguinal hernia, surgeons should consider the possibility of the presence of an Amyand hernia.

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Patient with previously misdiagnosed total situs inversus

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Abstract

Background: The case of 30 years-old patient with recently diagnosed dextrocardia is discussed hererin.
Material and methods: Dextrocardia, a specific anomaly of heart position in the chest, usually associated with situs inversus and sometimes by Karteneger's syndrome was diagnosed in the patient by careful physical examination proven by electrocardiography and imaging.
Results: Specific ECG changes were crucial to recognize the syndrome. The patient presented total situs inversus in physical examination. The case is a good exemplification of frequent dextrocardia oversight, since it has not been found during previous 30 years by medical professionals, including both pediatrician and occupational medicine specialist.
Conclusions: The attention should be always turned to make a proper diagnosis because it allows to recognize properly additional diseases as well as avoid misdiagnosis in future.
Keywords: ECG, dextrocardia, total situs inversus

Introduction

Dextrocardia with situs inversus is a congenital syndrome in which the organs are mirrored or reversed. It can be correlated with Kartagener's syndrome (sinusitis and bronchiactases). It was first described in the first half of the 17th century by Hieronymus Fabricius and Marco Aurelio Severino [1].

If dextrocardia is associated with isomerism, polysplenia syndrome is likely to be diagnosed. Most patients with situs inversus are asymptomatic [2]. When these patients develop new symptoms or conditions, such as coronary artery disease or hypertension, they are treated like the general population, but diagnosing them can be more difficult [3,4].

Case description

A 30-year-old patient with an unknown history of dextrocardia came in (he was admitted to the out-patient cardiology unit) to have his blood pressure

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(BP) assessed. He had found elevated BP by chance when he checked it up together with his family over Easter. He had had no cardiologic symptoms before.

The patient had had an ECG performed on two previous occasions for occupational medicine, and both times there was a problem with the ECG machine and it had to be redone on another machine.

The standard ECG (Fig. 1) was notable for inverted P waves in the lateral leads (I and aVL), suggesting rightward atrial electric forces and no R wave progression. There were also T wave inversions in I and aVL, which are also consistent with dextrocardia, but less specific than the other findings.

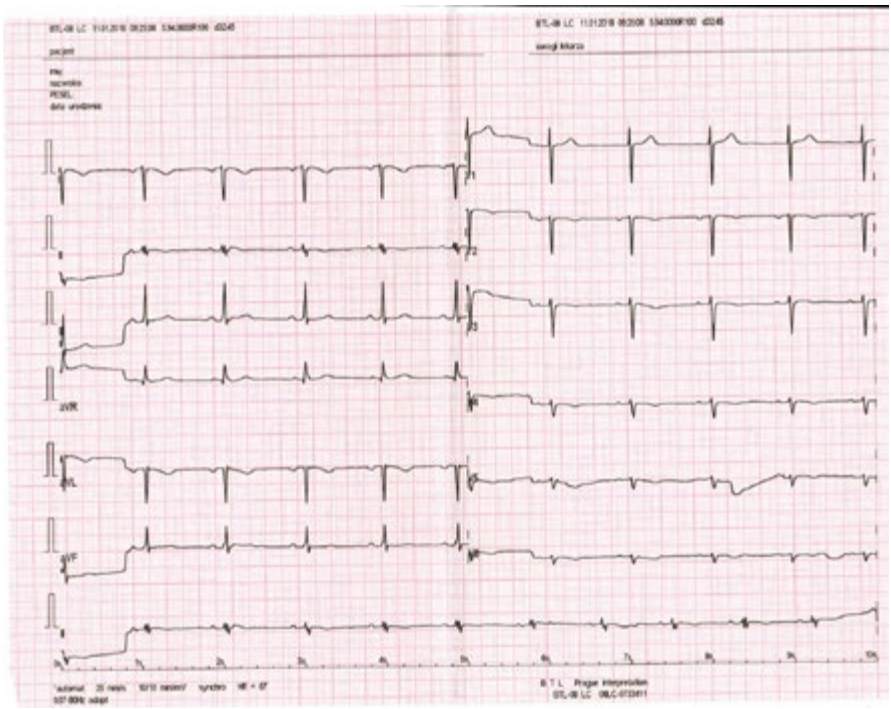

Fig. 1. The standard ECG

At the cardiologist's office an ECG with right-sided precordial leads (Figure 2 and 2a) was performed. The right-sided precordial lead ECG showed normalized R wave progression. These summations of ECG findings are suggestive of dextrocardia. In addition to this, an apical impulse was palpated in the right 5th intercostals space, 1.75 cm lateral to the right midclavicuar line. The lower liver span was palpated in the left upper quadrant of the abdominal cavity.

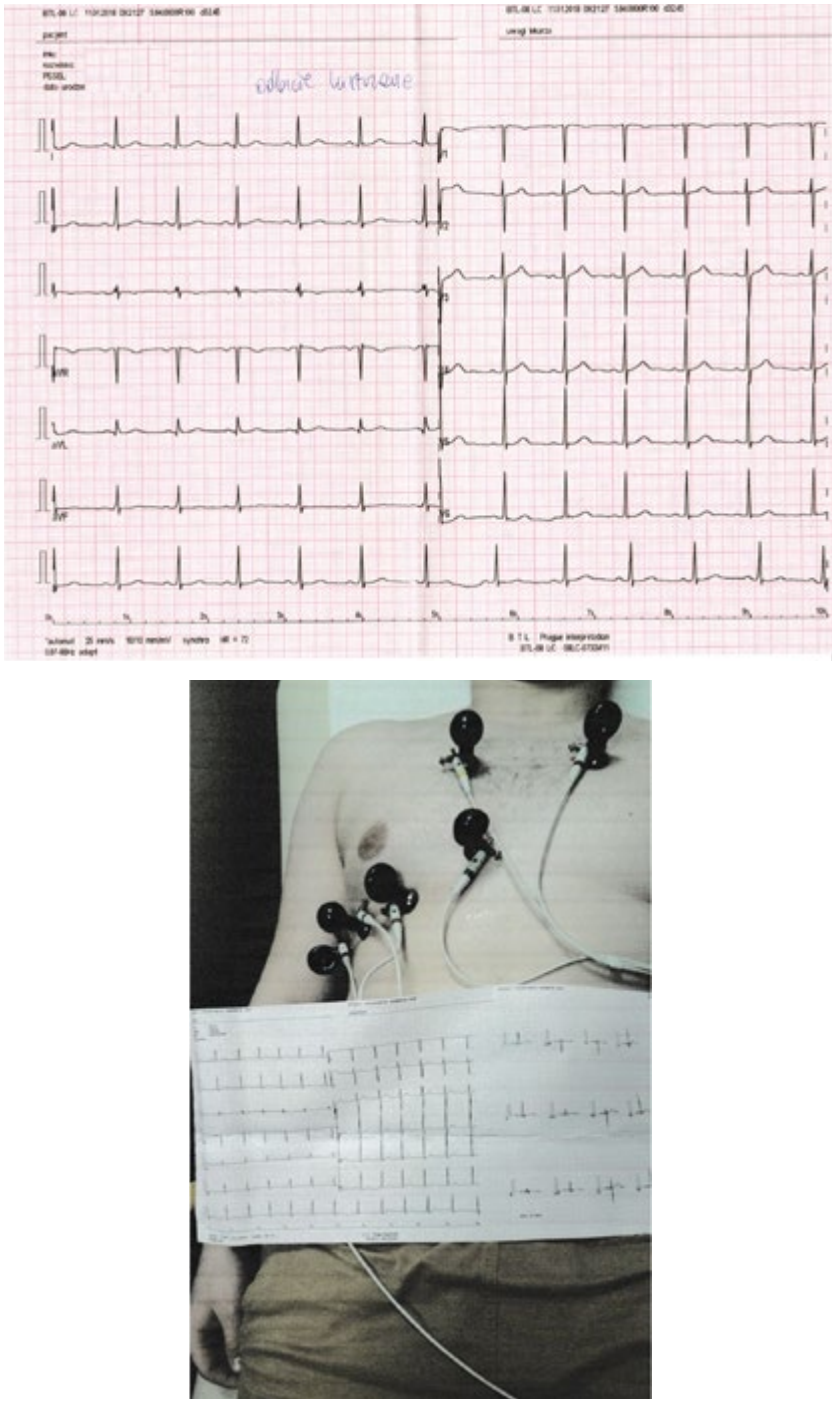

Fig. 2, 2a. ECG with right-sided precordial leads

Fig. 3. Chest radiography

IMAGES: A 12-lead surface electrocardiography (ECG) with both standard precordial leads (Figure 1) and right-sided precordial leads (Figure 2) was performed. The standard ECG was notable for inverted P waves in the lateral leads (I and aVL), suggesting rightward atrial electric forces and no R wave progression. The right-sided precordial lead ECG showed normalized R wave progression. These summations of ECG findings are suggestive of dextrocardia. There were also T wave inversions in I and aVL, which are also consistent with dextrocardia but less specific than the other findings. The patient subsequently underwent echocardiography, which comfirmed dextocardia with proper anatomy and function.

Results

Because of possible anomalies [5], the patient subsequently underwent an echocardiography which confirmed dextocardia with proper anatomy and function. The patient also underwent an ultrasound examination of the abdomen to check for possible anomalies. All organs were normal but located on the opposite side. The patient was prescribed ACEI to control his blood pressure. After a few days of treatment the blood pressure was normalized.

Summary: For the diagnosis of dextrocardia a proper physical examination supported by a properly interpreted ECG is crucial [6,7]. An appropriate diagnosis can help avoid misleading symptoms of typical diseases.

Conclusions

We confirmed the presence of dextrocardia with situs inversus using chest radiography (Fig. 3) and abdomen ultrasound.

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MRI diagnosis of a rare subtype of kidney cancer

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Abstract

Mucinous tubule and spindle cell carcinoma (MTSCC) of the kidney is a rare renal tumor generally considered of low malignant potential. Radiological diagnosis of the MTSCC is frequently difficult as those tumors tend to present as more discrete changes than those typical for classical renal cell cancer. The radiological diagnosis of a MTSCC can be challenging. It is important to establish correct diagnosis preoperatively in order to qualify patients for NSS.
Keywords: Mucinous tubule and spindle cell carcinoma, Radiological diagnosis of the MTSCC

Introduction

Mucinous tubule and spindle cell carcinoma (MTSCC) of the kidney is a rare renal tumor generally considered of low malignant potential. Described for the first time in 1996 [1] and recognized by WHO in 2004 [2], it is frequently managed by partial kidney resection, also known as nephron sparing surgery (NSS) [3]. Radiological diagnosis of the MTSCC is frequently difficult as these tumors tend to present as more discrete changes than those typical of classical renal cell cancer [4].

Imaging

Rare type of renal cancer can be easily mistaken for benign leasions especially in young adults. Regarding mucinous tumors, some sequences may mimic cysts and normal tissue. The most striking feature is their low value on ADC maps, which is a hallmark of high-cellularity and very suggestive of malignancy.

On coronal T2 weighted scans, lesions are difficult to identify, but on ADC maps they are clearly visible with low values (DWI does not show increased diffusion).

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Clinical course

The patient was referred for surgery. A NSS procedure was performed. A 3.2 cm × 2.7 cm tumor was noted on the pathology report with a 0.8 mm free margin from the remaining healthy kidney tissue. The final diagnosis was T1a Mucinous tubular and spindle cell carcinoma with immunohistochemistry results of CD 10 (-) and CK 7 (+).

Conclusion

The radiological diagnosis of a MTSCC can be challenging. It is important to establish correct diagnosis preoperatively in order to qualify patients for NSS.

Fig. 1. MRI view of the right kidney mass

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Haematoma, soft tissue, or bone tumor? Differential diagnosis of an iliac crest mass in a child

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Abstract

A differential diagnosis of a right iliac crest mass in a 15-year-old boy is shortly discussed. The importance of cancer awarness and adequate diagnostic procedures are underlined.
Keywords: sarcoma, children, differential diagnosis

Introduction

Sarcomas originate in the bone or soft tissue and constitute about 20% of all solid malignancies in children. Bone sarcomas represent 10% of this number and pelvic girdle is the site of the disease in some 15% of cases [1]. The cornerstone of treatment is a margin-free surgical resection with neoadjuvant or adjuvant treatment depending on the histopathology report [2]. Patients with pelvic sarcomas tend to present at advanced stages of the disease and at the time of diagnosis the tumor is relatively large [3]. This is not infrequently caused by delays in the correct treatment, which in turn is a result of a lack of cancer awareness in parents and – even more worryingly – in primary care physicians.

The clinical presentation

A 15-year-old boy was referred for a consultation due to a mass in the right iliac crest (Fig. 1). The mass had been noted 3 months previously, and since then it had been diagnosed as a post-traumatic hematoma; the boy was limping on his right leg. Clinical examination revealed a large unmovable mass strictly related to the pelvis. A simple X-ray revealed multiple exostoses and popcorn calcification of the right iliac wing (Fig. 2).

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The patient was immediately referred for further staging and surgical resection.

Conclusion

Any pathological mass in the soft tissues or skeletal treatment must be suspected of malignancy and adequate diagnostic procedures should be implemented as soon as possible.

Fig. 1. A right iliac crest mass is clearly visible

Fig. 2. The right iliact crest mass is confirmed on X-ray

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