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Chapter 1

BASIC INFORMATION THE PEDIATRIST SHOULD KNOW ABOUT CONTRAST AGENTS IN RADIOLOGICAL IMAGING

Merter KEÇELİ[1]

INTRODUCTION

With the increase in the use of medical imaging in recent years, the use of radiological contrast material has increased significantly, although more limitedly in children. Therefore, clinicians involved in radiological practice as well as radiologists need to be familiar with the basic physical properties of radiological contrast agents, the advers effects of their usage, and the treatment of prolonged reactions. Radiologic contrast agents should be injected and eliminated from the body without additional effects on the patient. The contrast agents used are not completely safe to use. Undesirable effects range from simple physiological and mild allergic reactions to serious and life-threatening events. In all age groups, identification of patients likely to experience adverse effects with contrast agents should occur before approval of radiologic examinations. The principles regarding the use of contrast agents and associated adverse events are similar in children to adults. Predicting the incidence of reactions to contrast media in children is impossible because of the lack of controlled prospective studies. There are also many conflicting opinions as to why a true allergic reaction develops. Allergic reaction with the use of iodinated contrast media in children is more common than in adults. The incidence of acute allergic-like reactions due to intravenous administration of low-osmolality nonionic iodinated contrast material has been reported as 0.18% (1). Guidelines for prevention and treatment of allergic reactions in children are similar to those for adults (2). In children, radiological contrast media should be used when necessary due to renal immaturity and low glomerular filtration rate. Gadolinium-based contrast agents may therefore rarely cause nephrogenic systemic fibrosis (NSF) (3). It was first described in 1997 with

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CONCLUSION:

The increasing use of radiological imaging and contrast agents in children requires knowing the physical and chemical properties of these agents and being familiar with the treatment of their adverse-allergic effects. Although these responsibilities rest with radiologists, it is necessary for pediatricians to have knowledge of these agents as they are involved in imaging method and planning. In addition, clinicians may have to recognize and treat recurrent and late allergic reactions that develop with the use of contrast agents. The pediatrician who has acquired this information becomes more competent in the follow-up and treatment of pediatric patients who are more affected by adverse effects and allergic reactions and their consequences.

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Chapter 2

CUTANEOUS VASCULITIS

Adem ERTÜRK[1]

INTRODUCTION

Vasculitis is a condition characterized by partial or total occlusion of the vessel lumen, aneurysm formation, and inflammation of the vessel wall, resulting in impaired distal organ function. As a result of thinning of the vessel wall due to inflamed cells of the vessel wall, there is an increase in vascular permeability, vessel wall rupture, and hemorrhage in the affected organ (palpable purpura, pulmonary hemorrhage). There is narrowing or occlusion of the vessel lumen due to vascular intimal proliferation and intraluminal thrombus formation, and signs of ischemia or infarction develop in the affected organ, such as necrotic skin ulcers, mononeuritis multiplex, and major organ infarction. In cutaneous vasculitis, systemic vasculitis findings such as fever, weakness, fatigue, weight loss, widespread muscle pain, arthralgia, and oligoarthritis may also be seen (1).

In cases where cutaneous vasculitis is suspected, answers to the following questions should be sought:

-Is there a vasculitis-like (mimic) condition?

-Is there an underlying secondary cause?

-Is there organ involvement other than cutaneous?

-How can a diagnosis of vasculitis be confirmed?

-What type of vasculitis is present?

Cutaneous vasculitis typically targets the dermal and subcutaneous vessels of small or medium size, encompassing a diverse spectrum of conditions that vary in their extent, ranging from localized lesions to systemic manifestations (2).

The first International Chapel Hill Consensus Conference (CHCC) on the nomenclature of systemic vasculitides was held in 1994 to establish uniform terminology and definitions. In 2012, a revised version was developed (Table 1) (3,4).

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CONCLUSION

Since skin lesions occurring in systemic and cutaneous vasculitis may show similar clinical and pathological features, systemic involvement should be excluded before diagnosing cutaneous vasculitis. As with systemic vasculitides, cutaneous vasculitides' causes are heterogeneous and generally classified as primary (idiopathic) and secondary. Infections, drugs, autoimmune diseases and malignancies are the most important secondary causes. As in systemic forms, cutaneous vasculitis is diagnosed by presenting clinicopathological and laboratory findings. The prognosis of vasculitis limited to the skin is generally favourable. However, caution should be exercised in painful, itchy or ulcerated skin lesions and chronic or recurrent cases. Treatment selection should be determined according to the severity of symptoms, potential risks and the patient's comorbidities. Randomized controlled studies on treatment in cutaneous vasculitis are insufficient; additional studies, including multicenter randomized studies, are needed on this subject.

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Chapter 3

HANTAVIRUS INFECTIONS

Cihan SEMET[1]

INTRODUCTION

Hantaviruses are a diverse group of RNA having a place in the Bunyaviridae family, named after the Hantan River in South Korea, from which this virus was first isolated in 1970 (1). The link between the virus and hemorrhagic fever with renal syndrome (HFRS) was first discovered during the Korean War, when in excess of 3,000 soldiers affiliated with the United Nations were afflicted with an illness, resulting in sickness and death (2).

Since then, numerous strains of Hantaviruses have been identified worldwide, each associated with a specific rodent species. The principal transmission mode to humans is inhaling aerosolized virus in rodent urine, feces, or saliva (3). They are considered significant zoonotic pathogens, causing two major human diseases, namely HFRS, mainly in Europe and Asia, and Hantavirus Cardiopulmonary Syndrome (HCPS) in the Americas (4).

Despite ongoing research, no specific antiviral treatments or vaccines against Hantavirus infections exist. Thus, they pose significant threats to public health, particularly in endemic regions. Hantaviruses' prevalence and geographical distribution appear much more significant than previously thought, increasing the potential for human exposure and subsequent disease (5).

BIOLOGY AND CLASSIFICATION OF HANTAVIRUS

Hantaviruses are viruses composed of a non-recombinant RNA genome. The genetic makeup of the pathogen is trifurcated into three distinct regions, specifically the small (S), medium (M), and large (L) segments. The S segment encodes the nucleocapsid (N) protein involved in encapsulating the viral genome and infection. The M segment encodes two envelope glycoproteins, Gn and Gc, which play essential roles in bacterial entry and penetration; the L segment

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Nevertheless, these ailments continue to present a significant obstacle to public health on account of their extensive prevalence, elevated fatality rate, and dearth of targeted antibodies and responses (7).

Comprehensive and multidisciplinary research is required to gain insights into multiple aspects of Hantavirus infections. This includes a deeper understanding of virus-host interactions, which can reveal the complex dynamics of how these viruses subvert host immune responses, replicate, and cause disease (5).

Research to identify predictors of severe disease, such as biomarkers or specific clinical characteristics, could facilitate early intervention strategies and improve patient outcomes. Furthermore, studying the socio-ecological factors contributing to outbreaks can help formulate better preventive measures and risk assessments (23).

Efforts toward developing specific antiviral treatments and vaccines should remain a priority. This includes the design and testing of potential therapeutic candidates and the establishment of infrastructure for conducting clinical trials in areas where outbreaks occur (25).

In conclusion, the global impact of hantavirus infections underscores the need for continuous and coordinated efforts in research, public health interventions, and education. Efforts such as these play a crucial role in the management of the impact of perilous pathogens on human health. This is particularly significant in a world that is progressively influenced by environmental transformations and population shifts (26).

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Chapter 4

HEAD AND NECK PARAGANGLIOMAS: IMAGING FINDINGS

Yeliz GÜL[1]

Introduction

Head and neck paragangliomas (HNPs) are hypervascular, slow-growing, mostly benign neoplasms that arise from paraganglionic cells of the autonomic nervous system (1). It is estimated to make up 3% of all paragangliomas (PGLs), 0.6% of all head and neck cancers and 0.03% of all tumours (1,2). HNPs can be of sympathetic or parasympathetic paraganglionic origin. The majority of HNPs originate from parasympathetic paraganglia, are usually biochemically silent and less than 4% of them secrete catecholamines (3).

Etiology and Genetic

HNPs are particularly high risk in women aged 50-70 years who are exposed to chronic hypoxia living at high altitudes. They can be sporadic or inherited. About 30- 40% of HNPs are hereditary, usually develops in the carotid body, and up to 80% is multifocal, tending to occur earlier than sporadic paragangliomas (2,4-6).

Hereditary HNPs are mainly associated with germline mutations in the enzyme succinate dehydrogenase (SDH), a multiprotein complex consisting of SDHB, SDHC, SDHD, SDHA and SDHAF2. SDH subunit mutation is frequently associated with bilateral or multifocal parasympathetic HNPs (4-6).

While sporadic HNPs are usually benign, the risk of malignancy increases in the presence of SDHB mutation. Malignancy is most commonly found in vagal PGLs (10-19%) and metastases are often to cervical lymph nodes. Distant metastases are very rare, such as in the lungs, liver and bones (1,5). There are no known histopathological criteria defined for malignancy. Malignant paraganglioma is

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Chapter 5

HISTORY OF TYPE 1 DIABETES MELLITUS AND CURRENT TREATMENT METHODS

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1. INTRODUCTION

1.1. Type 1 Diabetes And Its History

In recent years, especially in parallel with technological developments, the sedentary lifestyle has increased in humans, and this situation has paved the way for the increase of health problems that arise in parallel with the sedentary lifestyle. These diseases are called "diseases of our age" as these diseases are increasing in modern society. Since the increase in diseases brought by modern society life threatens countries' health expenditures, diseases threaten both individual health and economic structure. One of the diseases described as the disease of our age is the type I diabetes (2). Type I diabetes is shown among the most common endocrine system diseases today (3).

Diabetes; is defined as a chronic and metabolic disease characterized by hyperglycemia that occurs as a result of insulin effect, insulin secretion, or defects in both of these factors (4-6). Diabetes, when defined more broadly, is a metabolic and endocrine disorder characterized by chronic hyperglycemia, which occurs in parallel with the deficiency of insulin hormone in the organism or develops as a result of insulin absence/insufficiency, causing deterioration in fat, protein, and carbohydrate metabolism (7). As can be understood from the definitions made, diabetes is not an isolated disease, but a heterogeneous disease that includes different physiopathological elements, has a genetic background and prepares the ground for glucose intolerance (8). Type I diabetes, on the other hand, is defined as a metabolic disease characterized by hyperglycemia and insulin deficiency,

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2.Conclusion

Blood glucose level is one of the main factors used in the diagnosis and diagnosis of type I diabetes and that patients should pay attention to in their daily lives. For this reason, regular testing of blood glucose levels is one of the traditional methods of supporting the treatment during the disease process. When factors that cannot be changed, such as genetic factors and family history, are put aside, changing daily life habits of children and adolescents in the protection of type I diabetes reduces the risk factor of type I diabetes and positively affects daily life activities, sick individuals. In this context, exceptionally healthy nutrition physical activity is among the protective factors in type I diabetes. The literature shows that research findings on this subject also include physical activity and eating habits among effective methods in combating type I diabetes.

In recent years, it is seen that current treatment approaches are widely used in type I diabetes patients, especially in parallel with the developments in the field of medicine. Pancreas transplantation, which eliminates the need to use insulin throughout the patients' lives, is the leading treatment method, and it is recommended to use this method, especially in patients with severe problems during the treatment process. In addition, although stem cell therapy is seen to be quite effective in the treatment of type I diabetes, phase studies are also continuing in the fight against type I diabetes.

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Chapter 6

LATENT TUBERCULOSIS INFECTION

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INTRODUCTION

Tuberculosis is an infectious disease that primarily affects the lungs (1). The etiologic agent is the bacterium Mycobacterium tuberculosis most likely existed before the emergence of man on Earth (1). The genus Mycobacterium has been estimated to have evolved more than 150 million years ago. The skeletal malformations of tuberculosis are evident in Egyptian mummies from 2400 BC, and Pott's lesions are documented (2). Tuberculosis (TB) is as old as mankind and has been a persistent challenge throughout human history (1).

Since it is a contagious disease that often lasts throughout life and causes tubercles to form in various regions of the body, it has significant societal ramifications (2). Nearly one-third of people on earth are TB bacillus carriers, which puts them at risk of getting the disease and makes tuberculosis a major public health burden (3). Before the name was coined "tuberculosis" in the middle of the 19th century, the terms consumption and phthisis were used in the 17th and 18th centuries (1). Intimate links between the disease and the spread of particularly unfavorable socioeconomic conditions throughout the Industrial Revolution included exceedingly deplorable working conditions, overcrowding and poorly ventilated dwellings, subpar sanitation, hunger, and other risk factors (2). There was a significant scientific debate at the start of the 19th century about various hypotheses regarding the etiopathological origin of phthisis, debating whether it should be considered an infectious disease, a hereditary disease, or a form of cancer (2). On the other hand, scrofula, tubercles, and phthisis were discussed as distinct disease entities or symptoms of the same sickness (1,3).

Robert Koch, a renowned scientist, succeeded in isolating the tubercle bacillus and announced this amazing discovery in 1882 (1). Also, there is still just one vaccination available to combat tuberculosis (TB), the Bacille Calmette-Guérin

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population, particularly those of LTBI. Both six and nine months of isoniazid are preferred regimens recommended in the guidelines. These guidelines may be used by physicians, healthcare organizations or policymakers.

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Chapter 7

ORAL ANTIAGGREGANT AGENTS IN CARDIOLOGY

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INTRODUCTION

Hence thrombus formation resulting in vascular obstruction is one of the challenging issues in cardiology, great effort has been given to obtain an efficient anti-aggregation in order to reduce ischemic events. Three stages are essential in the formation of vascular thrombus. First, circulatory blood has to encounter a thrombogenic spot in the vessel. Then, platelet adhesion- activation -aggregation processes occur via various receptor stimulation and various substrate secretion, which creates a vicious circle with further increase in aggregation. In the last stage, clotting mechanism involves in the process to build a thrombus. There are different anti-platelet agents inhibiting different pathways to create anti-aggregation effect. In this chapter, orally active anti-platelet agents will be reviewed.

I. THE 'GOOD OLD' ASPIRIN

Although extract of willow bark, which contains natural salicylic acid, has been consumed as a remedy for treating pain and fever for centuries, the synthetic form, acetylsalicylic acid or commonly known as aspirin, has been given to the market in the beginning of 1900 by the firm Bayer as a painkiller medicine, with no adequate knowledge of mechanism of action.

Mechanism of action

It took more than 70 years to unveil the mechanism of action. That aspirin decreases the prostaglandin production, has been shown by Vane in 1971. Thereafter, the mechanism has been explained as aspirin irreversibly acetylates the enzyme 'cyclooxygenase' (COX) in platelets and inhibits thromboxane (TX) formation, which is related to its anti-thrombotic effect (1-3). Our current knowledge about aspirin is that the molecule is absorbed fast in the upper gastro-intestinal tract and inhibits the platelet aggregation in one hour. It is critical to remember, that

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hour after discontinuation. Similar to ticagrelor, transient dyspnea may also seen as an unfavourable side effect during cangrelor treatment (21,23).

Clinical implications for P2Y12 inhibitors

Widespread use of coronary invasive treatments creates the need for better anti-aggregation strategies to prevent adverse events such as stent thrombosis or ischemic events. In this manner, dual anti-platelet therapy known as DAPT, including low dose aspirin with concomitant P2Y12 inhibitor, became a standard in current cardiology practice. DAPT is intensively studied to constitute a standardized therapy in cardiology to balance adverse ischemic and bleeding risks. Prasugrel and ticagrelor are more potent drugs than clopidogrel, however both drugs have higher gastro-intestinal bleeding risk than clopidogrel. Current guidelines recommend ticagrelor and prasugrel as a part of DAPT, beginning with a loading dose in the treatment of acute coronary syndromes requiring percutaneous coronary intervention (PCI) with a class 1B recommendation level. Clopidogrel as a part of DAPT and beginning with a loading dose in the treatment of patients with stable coronary artery disease treated with PCI or patients with acute coronary syndrome, who cannot receive ticagrelor or prasugrel (previous intracranial bleeding, indication for anticoagulation etc) is recommended with a level of class 1A (25). Current different European guidelines such as 2017 DAPT in coronary artery disease and 2020 acute coronary guidelines give a higher priority to ticagrelor and prasugrel than clopidogrel in the management of acute coronary syndromes however clopidogrel remains still as the first choice when stable coronary artery disease requires a percutaneous intervention. All the recent recommendations underline that the duration of DAPT should be personalized (can be as short as 1 month or long as 2 years on specific demands of individual profile) balancing the patients ischemic and bleeding risks (19,20,25).

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Chapter 8

SPLEEN STRUCTURE AND MICRO ANATOMY

Danış AYGÜN[1]

Spleen is ovoid in shape and as big as one's own fist, with a soft consistency and purplish color. Although it is the largest lymphoid organ and has important functions in the lymphatic system, it is not a vital organ.

The spleen, which is approximately 12 cm long, 7 cm wide and 3-4 cm thick in adults and weighs approximately 150 grams, varies between individuals in both size and weight. It can even vary in the same person at different times. For example, while it is about 17 g in a newborn , it reaches up to 170 g at the age of 20 (1). In Figure 1, spleens belonging to two different cadavers are seen.

spleen, regio hypochondriac It is deep seated in sinistra . It is protected by the lower part of the rib cage, but this close protection of the ribs can be damaging in cases such as rib fractures.

Two extreme parts of the spleen - extremitas anterior and extremitas posterior , two face- facies diaphragmatica and facies visceralis , and its two edges- margo superior and margo There is inferior (Figure 2a and 2b).

facies The diaphragmatica is adjacent to the lower surface of the diaphragm and to the left 9th-11th ribs through the diaphragma . The long axis of the spleen is parallel to the 10th rib . facies diaphragmatica , diaphragma It is convex to match its concavity , curved to fit the body structures of the ribs , and its upper part is curved medially . facies visceralis is hilum splenica , facies gastrica , facies renalis and facies It consists of colica parts. hilum splenica is the slit through which nerves and splenic vessels enter and exit the spleen, which is not covered by the peritoneum. hilum The splenicum is adjacent to the tail portion of the pancreas and forms the left border of the bursa omentalis . facies gastrica , facies , where the posterior aspect of the stomach sits renalis facies , where the anterior aspect of the left kidney sits colica da flexura coli These are the faces on which the sinistra sits (Figure 3).

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Chapter 9

THE ROLE OF MicroRNAs IN COVID-19 INFECTION

Burcu GÜRER GİRAY[1]

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) causes The recent novel coronavirus disease (COVID-19) in the infected hosts. Although it primarily affects the cardiovascular system and immune system, many more systemare inflicted in addition to the respiratory system. The changes caused by miRNAs (MICRORNAS) on COVID-19 disease at the molecular levels are examined. The study give details about interactions among SARS-CoV-2 RNA, viral miRNAs and all coding and non-coding host RNAs by utilizing bioinformatic analysis. Host miRNAs are attracted towards viral genome and this leads to important modifications in the cellular miRNA gene expression. It is recommended that miRNAs diminish the impulse transmission pathway control with in SARS-CoV-2 infection. The entangled clinical disease symptoms can be clarified via the the interaction of viral miRNAs from SARS-CoV-2 with genes contained in transcription regulation and chromatin organization. Comprehending the role of miRNAs in COVID-19 disease pathogenesis will aid to enhance treatment alternatives. Currently studies are performed on extracellular vesicles (extracellular vesicles) being generated from mesenchymal stem cells in which special miRNAs are added to avert excessive cytokine production in COVID-19 disease.

The unique activities of the cell, basic building block of living organisms, are performed by extremely sensitive and interconnected many control mechanisms. The protein synthesis that executes cellular activities depends on the sequential occurrence of a series of molecular reactions. It was understood that many small molecules, besides ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) macromolecules, take part at distant levels in the regulation of transcription and translation with the expanded molecular biology studies. The methylation of DNA

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role in the control of "A disintegrin and metalloproteinase domain 17 (ADAM17)", an enzyme that plays a role in the activation of TNF-a cytokine and IL-6 receptors. It has been reported that estrogen hormone increases the expression of miR-222 (6). The studies aimed to identify miRNAs that play a role in the antiviral defense mechanism and to use them as a treatment option. Understanding the role of miRNAs in the immune response in COVID-19 disease, identifying miRNA target genes and regulating miRNA activity may contribute to the prevention of the disease and the development of an effective treatment (10).

CONCLUSION

It is aimed to identify miRNAs that play a role in the anti-viral defense mechanism and to use them as a treatment option. Understanding the role of miRNAs in the immune response in COVID-19 disease, identifying miRNA target genes and regulating miRNA activity may contribute to the prevention of the disease and the development of an effective treatment.

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