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RARE JUVENILE PRIMARY SYSTEMIC VASCULITIS

WHAT IS IT?

Vasculitis is an inflammation of blood vessels. Vasculitides cover a wide group of diseases. Primary vasculitis means that the blood vessels are the main part of the body effected by the disease. The name and classification of vasculitis depends upon the size and type of blood vessels involved.

HOW COMMON IS IT?

Some of the primary vasculitides are realtively common paediatric diseases (e.g. Henoch-Schönlein purpura or Kawasaki disease), while the diseases described below are rare and their exact frequency is not known.

What are the causes of the disease? Is it inherited? Is it contagious? Can it be prevented?
Diseases in this group do not usually run in the family. The majority of the patients do not have affected family members and it is very unusual for siblings to get the same disease. It is likely that a combination of different factors plays a part in causing the disease. Various genes, infections and environmental factors may contribute to disease development.
These diseases are not contagious and cannot be prevented.

WHAT HAPPENS TO BLOOD VESSELS IN VASCULITIS?

The blood vessel walls are attacked by the body's immune system, causing inflammation. If the vessel walls are injured or inflamed, blood clots start forming inside the blood vessels causing narrowing or even closure.
The inflammatory cells inside blood vessels travel from the blood stream, across the vessel walls, causing more damage to the vessel and surrounding tissue.

Changes visible in tissue biopsies (small samples of tissue removed from the effexted area) include the presence of inflammation in the vessel walls and variable degrees of its destruction. The resulting vessel abnormalities in arteries are detectable on angiography (a radiological investigation procedure that allows us to see the blood vessels).
Decreased blood supply through narrowed or blocked vessels or, less frequently, vessel rupture with bleeding may damage the tissues. Involvement of the vessels supplying vital organs like the brain or heart could be a very serious condition. Widespread (systemic) vasculitis is usually accompanied by general symptoms like fever, or malaise, as well as abnormal laboratory tests detecting inflammation (ESR, CRP).

What are the main symptoms?

Disease symptoms vary significantly according to the blood vessel type involved and the severity of organ involvement.

HOW IS IT DIAGNOSED?

Diagnosis of vasculitis is rarely straightforward. The symptoms might resemble other paediatric disorders. The diagnosis is based on expert evaluation of clinical symptoms, together with the results of blood and urine tests and imaging studies (e.g ultrasonography, x-ray, CT scan, MRI scan and angiography) and, where appropriate, confirmed by tissue biopsy findings. Due to the rarity of these diseases, it is often necessary to transfer the child to the centre where paediatric rheumatology is available, along with other paediatric expertise.

Can it be treated?

Yes, vasculis can be treated. In the majority of properly treated patients, disease control and remission can be achieved.

What are the treatments?

The treatment of vasculitis is long term and complex. The main goal is to get the disease under control as soon as possible and to maintain control long term, while avoiding unnecessary drug side effects.

Corticosteroids have proven most effective, in combination with immunosuppressive drugs (cyclophosphamide), in induce remission. Drugs regularly used in maintenance therapy include azathioprine, methotrexate and cyclosporine A, together with low-dose prednisone. Various other drugs have also been used to suppress the immune system and fight inflammation. They are chosen on a strictly individual basis when other common drugs have failed. They include biological agents, colchicine and thalidomide.

In longer term corticosteroid therapy, osteoporosis can be prevented by sufficient calcium and vitamin D intake. Drugs that effect blood clotting may be prescribed (low-dose aspirin) and in cases of hypertension blood pressure lowering agents.

Physiotherapy may be needed to improve musculoskeletal dysfunction. Psychological and social support for the patient and the family may be needed.

Check-ups

The main purposes of regular check ups is to evaluate the activity of the disease, check the effectiveness of treatment and to check for possible side effects. The frequency and type of check-up depend on the type and severity of the disease and on the drugs given. In the early stage of the disease, check-ups will be frequent and become less frequent as soon as disease control is achieved.

There are several ways of evaluating the activity of vasculitis. The disease is evaluated by clinical examination, together with an analysis of the child's reported complaints. Blood and urine tests are performed to detect activity of inflammation, changes in organ functions and potential drug side effects. Based on individual internal organ involvement, various other investigations might be performed by various specialists, including imaging studies.

HOW LONG WILL THE DISEASE LAST FOR?

Rare, primary vasculitides are long-term, often life-long, diseases. They can start as an acute, often severe, or even life-threatening condition and subsequently evolve into a more chronic disease.

What is the long-term prognosis (predicted course and outcome) of the disease?
The prognosis of rare primary vasculitides is highly individual. It depends not only on the type and extent of vessel involvement, but probably on the interval between disease onset and the start of treatment as well as the response to therapy. The risk of organ damage is related to the duration of active disease. Damage to the vital organs can have life-long consequences. With proper treatment, clinical remission is often achieved within the first year. The remission could be life-long, but often long-term maintenance therapy is needed. Periods of disease remission may be interrupted with disease relapses requiring more intensive therapy. There is a relatively high mortality rate amongst children who do not receive treatment. Due to its rarity, exact data on long-term evolution and mortality are scarce.

How could the disease affect the child and family daily life?
The initial period, when the child is unwell and the diagnosis is yet to be made, is usually very stressful for the whole family.
Understanding the disease and its therapy helps the child and family to cope with unpleasant diagnostic and therapeutic procedures and frequent hospital visits. Once the disease is under control, home life can usually return back to normal.

What about school?
Once the disease is reasonably controlled, patients are encouraged to go back to school as much as they can. It is important to inform the school about the child's condition so that it can be taken into account.

What about sports?
Children are encouraged to take part in their favourite sporting activities once disease remission is achieved. Recommendations might vary according to the presence of organ functional impairment, including the muscles and joints.

What about diet?
There is no evidence that special diets could influence disease course and outcome. A healthy, well balanced diet is recommended. While on corticosteroid treatment sweet food, fat and salt should be limited in order to minimise the side-effects of steroids.

Can climate influence the course of the disease?
Climate is not known to influence the course of the diseases. In case of impaired circulation due to vasculitis, mainly in fingers and toes, exposure to cold can make the disease worse.

What about infections and vaccinations?
Some infections may have a more serious outcome in individuals treated with immunosuppressive drugs. In case of contact with chickenpox or shingles, you should contact your physician immediately in order to receive anti-virus drug and specific anti-virus immune globulin. The risk of ordinary infections may be slightly higher in treated children. They can also develop unusual infections from agents that do not affect

individuals with fully functioning immune systems. Antibiotics (co-trimoxazol) are sometimes administered for long periods to prevent lungs from infection with the bacteria called Pneumocystis, which can be a life-threatening complication in immunosuppressed patients.
Live vaccines (e.g. parotitis, measles, rubella, poliomyelitis, tuberculosis) should be postponed in patients receiving immunosuppressive treatments.

What about sexual life, pregnancy, birth control?
In sexually active adolescents, birth control is important as the majority of drugs used may damage the developing baby. There are concerns that some cytotoxic drugs (mainly cyclophosphamide) might affect the ability to have a child. This depends mainly on the total (cumulative) dose of the drug received over the period of treatment and occurs less frequently when the drug is administered in children or adolescents.

POLYARTERITIS NODOSA

What is it?
Polyarteritis nodosa (PAN) is a form of vasculitis that destroys blood vessel walls, affecting mainly medium and small sized arteries. Multiple vessel walls are affected in a patchy distribution. Inflamed parts of the artery walls become weaker and, under the pressure of the blood stream, small nodules (aneurysms) form along the artery. Cutaneous (skin) polyarteritis affects mainly the skin, not internal organs. Microscopic polyarteritis is a form of the disease that affects smaller sized vessels.

How common is it?
PAN is very rare in children, with an estimated number of new cases per year of one per one million children. It affects boys and girls equally, more commonly around none to 11 years of age. Mainly in adults, PAN may be associated with hepatitis B virus infection.

What are the main symptoms?
Since every tissue and organ in the body contain blood vessels, there are many symptoms connected with this disease. However, for unknown reasons, certain tissues and organs seem to be more frequently affected than others. The most common symptoms are:
1) Prolonged fever.
2) Aching muscles and joints.
3) Abdominal pain.
4) Painful, red and lumpy skin lesions, or other skin manifestations including purplish skin mottling (livedo reticularis).
5) Testicular pain in boys.
Vasculitic skin lesions may be present. Mainly in cutaneous polyarteritis, peripheral arteries (supplying fingers, toes, ears and nose) may be affected, causing insufficient blood supply with a risk of tissue loss. The child may appear vaguely unwell; tired, lethargic, with some weight loss and a persistent fever. Or they may become unwell very quickly, with severe pain, dramatic skin lesions and drowsiness. Since all these signs and symptoms occur in many other childhood diseases, the diagnosis is made by excluding other possibilities, particularly infection.

Kidney involvement can cause the presence of blood and protein in urine, or raised blood pressure (hypertension). In microscopic polyarteritis kidney involvement, together with lung disease, are the most common symptoms. Involvement of arteries supplying the gut often causes abdominal pain and discomfort, together with an impairment of bowel movements and a resorption of nutrients.
The nervous system can also be affected to a variable degree, as well as any other organ. Laboratory tests show marked inflammation in the blood and anaemia. If the disease is associated with a streptococcal infection, this can also be detected in a blood test.

HOW IS IT DIAGNOSED?
PAN is diagnosed by excluding all other possible causes of fever in childhood. This means that infections need to be excluded. The diagnosis is then suspected by the persistence of the above clinical signs and evidence of marked inflammation in the blood. The diagnosis is confirmed by the demonstration of narrowing and aneurysms in blood vessels on an angiogram. The presence of inflammation of blood vesels in a skin or kidney biopsy can also confirm the diagnosis.

TAKAYASU ARTERITIS
WHAT IS IT?
Takayasu arteritis (TA) affects large arteries, predominantly the aorta and its branches and the main lung (pulmonary) artery branches. Sometimes the terms granulomatous, or large-cell vasculitis, are used to describe the main microscopic feature of small nodular lesions, formed around a special type of large cell in the artery wall.

How common is it?
TA is considered the third most frequent systemic vasculitis in children (after Henoch-Schönlein purpura and Kawasaki disease). Although described world-wide, it is extremely rare in the white (Caucasian) population. It affects girls more frequently than boys.
WHAT ARE THE MAIN SYMPTOMS?
Early disease symptoms include fevers, loss of appetite, weight loss, muscle and joint pain and night sweats. Laboratory markers of inflammation are increased. As the artery inflammation progresses, signs of diminished blood supply can be found. Loss of peripheral limb pulses, differences in the blood pressure in different limbs, murmurs over the narrowed arteries and sharp extremity pain are common signs. High blood pressure may be caused by narrowing of the arteries supplying the kidneys and chest pain can be due to lung involvement.
Various neurological and eye symptoms may reveal disturbed blood supply to the brain.

How is it diagnosed?
Ultrasound examination is useful in detecting the involvement of major arterial trunks close to the heart, but it often fails to show involvement of more peripheral arteries. Usually, visualisation of all main arteries, together with lung arteries, is necessary to evaluate the extent of arterial involvement.

WEGENER'S GRANULOMATOSIS

What is it?
Wegener's granulomatosis (WG) is a chronic systemic vasculitis affecting small and medium size blood vessels, most often those in the upper airways (nose and sinuses), lower airways (lungs) and kidneys. The term granulomatosis refers to the microscopic appearance of the inflammatory lesions that form small multi-layered nodules in and around the vessels.

How common is it? Is the disease in children different from the disease in adults?
WG is an uncommon disease, especially in childhood. An estimation of the number of new patients in a year would be one to two in one million children. More than 97 % of reported cases occur in the white (Caucasian) population. Both sexes are affected equally in children, although in adults men are affected slightly more than women.

What are the main symptoms?
In a large proportion of patients, the disease presents with sinus congestion that does not improve with antibiotics and decongestants. There is a tendency to nasal septum crusting, bleeding and ulcerations, sometimes causing deformity.
Inflammation in airway below the glottis can cause narrowing of the trache, leading to a hoarse voice and respiratory problems. The presence of inflammatory nodules in the lungs give the symptoms of pneumonia with short breath, coughing and chest pain.
Kidney involvement is initially present in only a small proportion of patients, but it becomes more frequent as the disease progresses. Inflammatory tissue can gather behind the eyes pushing them forward, or it can be present in the middle ears. General symptoms, such as weight loss, increasing fatigue, fevers and night sweats are common as in skin vasculitis, along with joint pain, or arthritis.
Not all patients experience the full spectrum of organ involvement, as described above. Limited WG means that the disease is limited to the orbit and the respiratory tract, without involvement of the kidney.

How is it diagnosed?
Clinical symptoms of inflammatory lesions in the upper and lower airways, together with kidney disease suggest WG.
Blood tests include increased non-specific inflammatory markers (ESR, CRP) and, in the majority of patients, an antibody called ANCA (Anti-Neutrophil Cytoplasmic Antibody) can be detected.

OTHER VASCULITIDES AND SIMILAR CONDITIONS
1) Cutaneous leucocytoclastic vasculitis (also known as hypersensitivity or allergic vasculitis) usually implies blood vessel inflammation caused by an inappropriate reaction to a sensitising source. Drugs and infections are common triggers of this condition in children. It usually affects small vessels and has a specific microscopic appearance in the skin biopsy.
2) Hypo-complementemic urticarial vasculitis is characterised by an often itchy, widespread rash, resembling hives, that does not fade as fast as common skin allergic reactions.

3) Churg-Strauss syndrome (allergic granulomatosis) is an extremely rare type of vasculitis in children. Various vasculitis symptoms in the skin and internal organs are accompanied with asthma and increased numbers of one type of white blood cells called eosinophils.
4) Primary angiitis of the central nervous system affects small and medium brain arteries. Major neurological symptoms are stroke or fits.
5) Cogan's syndrome is a rare disease characterised by the involvement of eyes and inner ear with photophobia, dizziness and hearing loss. Symptoms of more widespread vasculitis may be present.