= Henoch ? Schönlein purpura =

Henoch ? Schönlein purpura (HSP) , also known as IgA vasculitis , anaphylactoid purpura , purpura rheumatica , and Schönlein ? Henoch purpura , is a disease of the skin , mucous membranes , and sometimes other organs that most commonly affects children . In the skin , the disease causes palpable purpura (small hemorrhages) , often with joint pain and abdominal pain . With kidney involvement , there may be a loss of small amounts of blood and protein in the urine (hematuria and proteinuria) , but this usually goes unnoticed ; in a small proportion of cases , the kidney involvement proceeds to chronic kidney disease . HSP is often preceded by an infection , such as a throat infection .

HSP is a systemic vasculitis (inflammation of blood vessels) and is characterized by deposition of immune complexes containing the antibody immunoglobulin A (IgA) ; the exact cause for this phenomenon is unknown . It usually resolves within several weeks and requires no treatment apart from symptom control , but may relapse in a third of cases and cause irreversible kidney damage in about one in a hundred cases .

= = Signs and symptoms = =

Purpura , arthritis and abdominal pain are known as the " classic triad " of Henoch ? Schönlein purpura . Purpura occur in all cases , joint pains and arthritis in 80 % , and abdominal pain in 62 % . Some include gastrointestinal hemorrhage as a fourth criterion ; this occurs in 33 % of cases , sometimes , but not necessarily always , due to intussusception . The purpura typically appear on the legs and buttocks , but may also be seen on the arms , face and trunk . The abdominal pain is colicky in character , and may be accompanied by nausea , vomiting , constipation or diarrhea . There may be blood or mucus in the stools . The joints involved tend to be the ankles , knees , and elbows , but arthritis in the hands and feet is possible ; the arthritis is nonerosive and hence causes no permanent deformity . Forty percent have evidence of kidney involvement , mainly in the form of hematuria (blood in the urine) , but only a quarter will have this in sufficient quantities to be noticeable without laboratory tests . Problems in other organs , such as the central nervous system (brain and spinal cord) and lungs may occur , but is much less common than in the skin , bowel and kidneys .

Of the 40 % of patients who develop kidney involvement , almost all have evidence (visible or on urinalysis) of blood in the urine . More than half also have proteinuria (protein in the urine) , which in one eighth is severe enough to cause nephrotic syndrome (generalised swelling due to low protein content of the blood) . While abnormalities on urinalysis may continue for a long time , only 1 % of all HSP patients develop chronic kidney disease . Hypertension (high blood pressure) may occur . Protein loss and high blood pressure , as well as the features on biopsy of the kidney if performed , may predict progression to advanced kidney disease . Adults are more likely than children to develop advanced kidney disease .

= = Pathophysiology = =

Henoch ? Schönlein purpura is a small @-@ vessel vasculitis in which complexes of immunoglobulin A (IgA) and complement component 3 (C3) are deposited on arterioles , capillaries , and venules . As with IgA nephropathy , serum levels of IgA are high in HSP and there are identical findings on renal biopsy ; however , IgA nephropathy has a predilection for young adults while HSP is more predominant among children . Further , IgA nephropathy typically only affects the kidneys while HSP is a systemic disease . HSP involves the skin and connective tissues , scrotum , joints , gastrointestinal tract and kidneys .

= = Diagnosis = =

The diagnosis is based on the combination of the symptoms , as very few other diseases cause the

same symptoms together . Blood tests may show elevated creatinine and urea levels (in kidney involvement) , raised IgA levels (in about 50 %) , and raised C @-@ reactive protein (CRP) or erythrocyte sedimentation rate (ESR) results ; none are specific for Henoch ? Schönlein purpura . The platelet count may be raised , and distinguishes it from diseases where low platelets are the cause of the purpura , such as idiopathic thrombocytopenic purpura and thrombotic thrombocytopenic purpura .

If there is doubt about the cause of the skin lesions , a biopsy of the skin may be performed to distinguish the purpura from other diseases that cause it , such as vasculitis due to cryoglobulinemia ; on microscopy the appearances are of a hypersensitivity vasculitis , and immunofluorescence demonstrates IgA and C3 (a protein of the complement system) in the blood vessel wall . However , overall serum complement levels are normal .

On the basis of symptoms , it is possible to distinguish HSP from hypersensitivity vasculitis (HV) . In a series comparing 85 HSP patients with 93 HV patients , five symptoms were found to be indicative of HSP : palpable purpura , abdominal angina , digestive tract hemorrhage (not due to intussusception) , hematuria and age less than 20 . The presence of three or more of these indicators has an 87 % sensitivity for predicting HSP .

Biopsy of the kidney may be performed both to establish the diagnosis or to assess the severity of already suspected kidney disease . The main findings on kidney biopsy are increased cells and Ig deposition in the mesangium (part of the glomerulus , where blood is filtered) , white blood cells , and the development of crescents . The changes are indistinguishable from those observed in IgA nephropathy .

HSP can develop after infections with streptococci (? @-@ haemolytic , Lancefield group A) , hepatitis B , herpes simplex virus , parvovirus B19 , Coxsackievirus , adenovirus , Helicobacter pylori , measles , mumps , rubella , Mycoplasma and numerous others . Drugs linked to HSP , usually as an idiosyncratic reaction , include the antibiotics vancomycin and cefuroxime , ACE inhibitors enalapril and captopril , anti @-@ inflammatory agent diclofenac , as well as ranitidine and streptokinase . Several diseases have been reported to be associated with HSP , often without a causative link . Only in about 35 % of cases can HSP be traced to any of these causes .

The exact cause of HSP is unknown , but most of its features are due to the deposition of abnormal antibodies in the wall of blood vessels , leading to vasculitis . These antibodies are of the subclass IgA1 in polymers ; it is uncertain whether the main cause is overproduction (in the digestive tract or the bone marrow) or decreased removal of abnormal IgA from the circulation . It is suspected that abnormalities in the IgA1 molecule may provide an explanation for its abnormal behaviour in both HSP and the related condition IgA nephropathy . One of the characteristics of IgA1 (and IgD) is the presence of an 18 amino acid @-@ long " hinge region " between complement @-@ fixating regions 1 and 2 . Of the amino acids , half is proline , while the others are mainly serine and threonine . The majority of the serines and the threonines have elaborate sugar chains , connected through oxygen atoms (O @-@ glycosylation) . This process is thought to stabilise the IgA molecule and make it less prone to proteolysis . The first sugar is always N @-@ acetyl @-@ galactosamine (GalNAc) , followed by other galactoses and sialic acid . In HSP and IgAN , these sugar chains appear to be deficient . The exact reason for these abnormalities is not known .

= = = Classification = = =

Multiple standards exist for defining Henoch ? Schönlein purpura , including the 1990 American College of Rheumatology (ACR) classification and the 1994 Chapel Hill Consensus Conference (CHCC) . Some have reported the ACR criteria to be more sensitive than those of the CHCC .

More recent classifications , the 2006 European League Against Rheumatism (EULAR) and Pediatric Rheumatology Society (PReS) classification , include palpable purpura as a mandatory criterion , together with at least one of the following findings : diffuse abdominal pain , predominant IgA deposition (confirmed on skin biopsy) , acute arthritis in any joint , and renal involvement (as evidenced by the presence of blood and / or protein in the urine) .

= = Treatment = =

Analgesics may be needed for the abdominal and joint pains . It is uncertain as to whether HSP needs treatment beyond controlling the symptoms . Most patients do not receive therapy because of the high spontaneous recovery rate . Steroids are generally avoided . However , if they are given early in the disease episode , the duration of symptoms may be shortened , and abdominal pain can improve significantly . Moreover , the chance of severe kidney problems may be reduced . However , some evidence suggests that steroids do not decrease the likelihood of developing long @-@ term kidney disease .

Evidence of worsening kidney damage would normally prompt a kidney biopsy . Treatment may be indicated on the basis of the appearance of the biopsy sample ; various treatments may be used , ranging from oral steroids to a combination of intravenous methylprednisolone (steroid) , cyclophosphamide and dipyridamole followed by prednisone . Other regimens include steroids / azathioprine , and steroids / cyclophosphamide (with or without heparin and warfarin) . Intravenous immunoglobulin (IVIG) is occasionally used .

= = Prognosis = =

Overall prognosis is good in most patients , with one study showing recovery occurring in 94 % and 89 % of children and adults , respectively (some having needed treatment) . In children under ten , the condition recurs in about a third of all cases and usually within the first four months after the initial attack . Recurrence is more common in older children and adults .

= = = Kidney involvement = = =

In adults , kidney involvement progresses to end @-@ stage renal disease (ESRD) more often than in children . In a UK series of 37 patients , 10 (27 %) developed advanced kidney disease . Proteinuria , hypertension at presentation , and pathology features (crescentic changes , interstitial fibrosis and tubular atrophy) predicted progression . About 20 % of children that exhibit nephrotic or nephritic features experience long permanent renal impairment .

The findings on renal biopsy correlate with the severity of symptoms : those with asymptomatic hematuria may only have focal mesangial proliferation while those with proteinuria may have marked cellular proliferation or even crescent formation . The number of crescentic glomeruli is an important prognostic factor in determining whether the patient will develop chronic renal disease .

In ESRD , some eventually need hemodialysis or equivalent renal replacement therapy (RRT) . If a kidney transplant is found for a patient on RRT , the disease will recur in the graft (transplanted kidney) in about 35 % of cases , and in 11 % , the graft will fail completely (requiring resumption of the RRT and a further transplant) .

= = Epidemiology = =

HSP occurs more often in children than in adults , and usually follows an upper respiratory tract infection . Half of affected patients are below the age of six , and 90 % are under ten . It occurs about twice as often in boys as in girls . The incidence of HSP in children is about 20 per 100 @,@ 000 children per year , making it the most common vasculitis in children .

Cases of HSP may occur anytime throughout the year , but some studies have found that fewer cases occur during the summer months .

= = History = =

The disease is named after Eduard Heinrich Henoch (1820 ? 1910) , a German pediatrician (nephew of Moritz Heinrich Romberg) and his teacher Johann Lukas Schönlein (1793 ? 1864) , who described it in the 1860s . Schönlein associated the purpura and arthritis , and Henoch the

purpura and gastrointestinal involvement . The English physician William Heberden (1710 ? 1801) and the dermatologist Robert Willan (1757 ? 1812) had already described the disease in 1802 and 1808 , respectively , but the name Heberden ? Willan disease has fallen into disuse . William Osler was the first to recognise the underlying allergic mechanism of HSP .