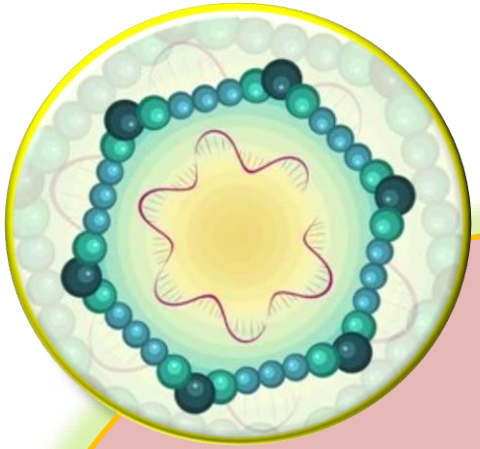

بسم الله الرحمن الرحیم



Parvovirus B19 After Kidney Transplantation

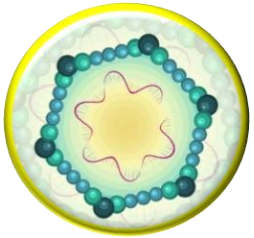
Dr .Maryam Pourkar Jadid
Nephrologist

Parvovirus B19

Parvovirus B19 is a single-stranded DNA virus .

In the transplant patient, the infection is mainly acquired from the donor organ or by reactivation of latent infection.

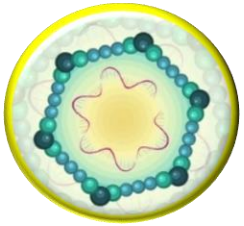
70% of parvovirus B19 infections occur in the three first months post-kidney transplantation ,remaining very rare beyond the first year post-kidney transplantation. The infection especially affects young male recipients (30 years old on average).



Key point 1: major diagnostic delay due to a nonspecific clinico-biological picture

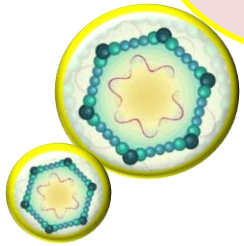
The initial clinical presentation is that of a non-specific and moderate pseudo-flu syndrome suggestive of any viral infection.

Clinical Presentations	Initial Biologic presentations
Fever(up to 48 hr)	Increased CRP
Asthenia	Negative Procalcitonin
Joint and muscle pains	Mild to Moderate AKI
Skin rashes	Leukopenia
Dizziness	Hepatic cytolysis
Profuse Sweating	Moderate Thrombocytopenia



Key point 1: **major diagnostic delay due to a nonspecific clinico-biological picture**

The anemia sets in, rapidly worsens, and the Hb declines to very low levels, around 6 g/dl, sometimes under 5 g/dl within a few days, and is associated with a significant drop in reticulocyte levels, a strongly suggestive sign of parvovirus B19 infection. This anemia requires treatment by high doses of erythropoietin, because it is typically resistant to erythropoietin therapy, sometimes with recourse to transfusion of packed red blood cells, and on average, it regresses a few weeks later after reduction of immunosuppression.



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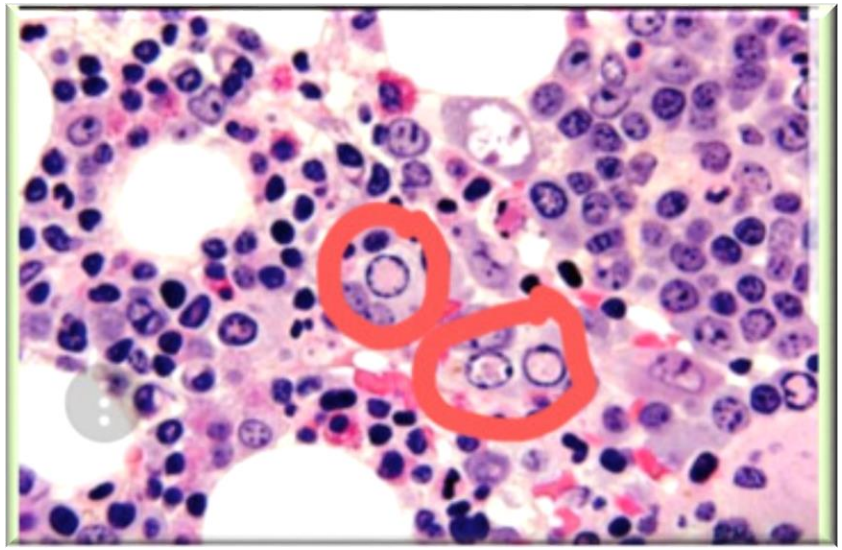
Bone marrow biopsy, which is not performed routinely, shows characteristic findings of pure red cell anemia (depletion of all erythroid elements except a few giant proerythroblasts with intranuclear inclusions).



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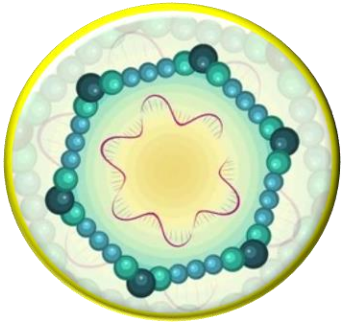
Intranuclear inclusions



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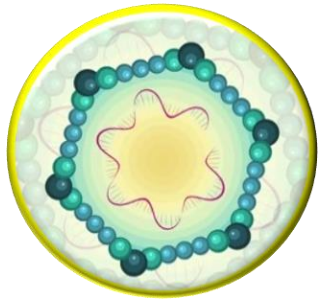
The clinical symptoms and laboratory findings warrant multiple sampling to search for bacterial, parasitic, or fungal source of infection, as well as samples for a variety of virus serology, especially for CMV and EBV, While parvovirus B19 infection is typically not investigated.

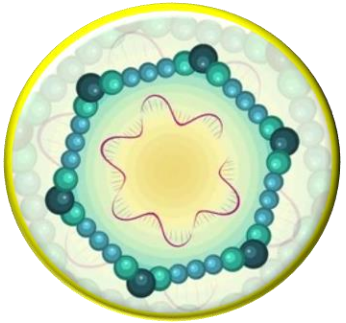
The clinical picture also suggests, again incorrectly, toxicity and/or a drug allergy. This results in a major diagnostic delay, leaving enough time for strong multiplication of parvovirus B19.



Key point 1: major diagnostic delay due to a nonspecific clinico-biological picture

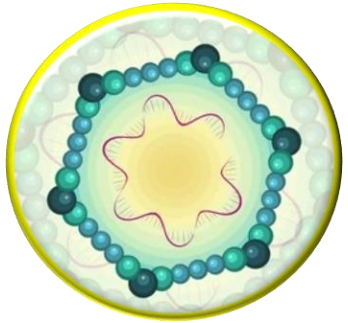
The diagnosis is generally made several weeks after the start of symptoms, thus explaining the high viral density, in RT-PCR assay often exceeding a billion copies/ ml .

The diagnosis of parvovirus B19 disease is based on serologic reaction to detect specific immunoglobulins, IgM or IgG, but due to a low sensitivity of these assays in immunocompromised patients, PCR remains the key diagnostic tool.



Key point 2: serum complement consumption is an early diagnostic biologic marker

Serum complement consumption is highly suggestive of post-transplant parvovirus B19 infection. However, serum complement is not part of the usual post-kidney transplant screening for infections. It is only requested if there is suspicion of recurrence or de novo nephropathy of the MPGN, lupus nephropathy, thrombotic microangiopathy, or infection-related glomerulonephritis.



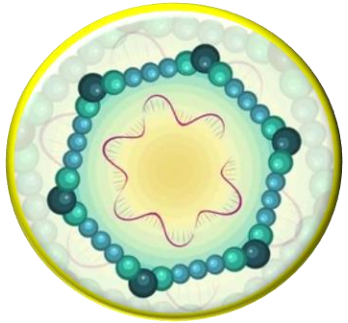
Key point 2: serum complement consumption is an early diagnostic biologic marker

The decreased levels of C3, C4 and the CH50 level are closely correlated with parvovirus B19 infection

The C4 level is usually more diminished than the C3 level in an acute parvovirus B19 infection.

The decrease of serum complement occurs early and concomitantly with a drop-in Hb.

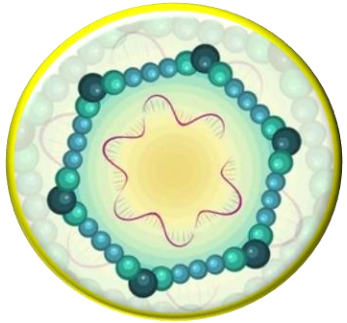
The two parameters tend to normalise in parallel.



Key point 3: the immunoglobulins and the reduction of immunosuppression make up the cornerstone of treatment

(IVIG) associated with a reduction of immunosuppression make up the cornerstone of therapeutic management of post-kidney transplantation parvovirus B19 infection.

American Society of Transplantation recommends 400 mg/kg/day of IVIG for 5 consecutive days and a reduction of immunosuppression at the time of the parvovirus B19 infection diagnosis. One course of IVIG is usually sufficient, but sometimes recourse to a second and/or third course is possible but rare.



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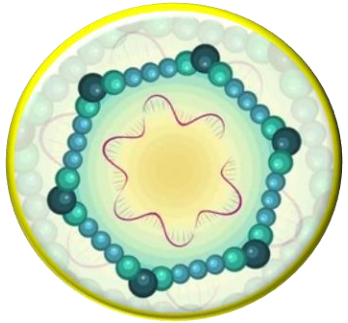
Besides institution of IVIG treatment, the mycophenolate dose is reduced by 50% and the T0 target of tacrolimus is lowered to 5 mg/ml.

If the viremia persists, consideration must be given, according to the immunologic risk of the patient, to decreasing T0 Tacrolimus to 3-4 mg/ ml, discontinuing mycophenolate, or switching to cyclosporine or an m-TOR inhibitor.



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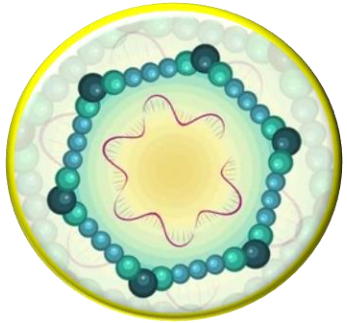
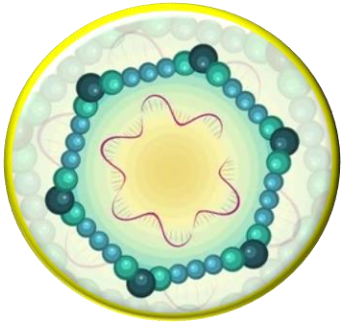
Because of the diagnostic delay and excessively high PCR values of parvovirus B19, viral clearance is only obtained several weeks or even months after diagnosis. Clinical improvement, however, may be observed a few days after initiation of treatment, i.e. reduction of immunosuppression and/or immunoglobulins.



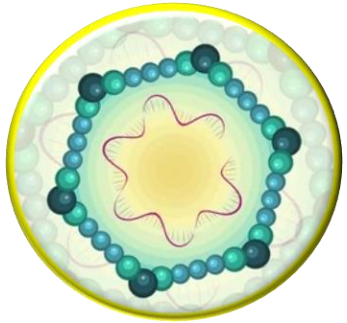
Key point 4:watch out for other viral infections, particularly CMV, EBV, and BKV

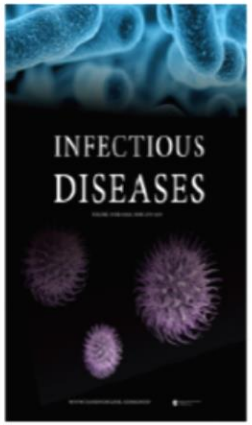
The onset of a parvovirus B19 infection indicates strong immunosuppression. The concomitant presence of other viral infections is frequent and must be systematically monitored, particularly CMV, EBV, BKV, and HHV-6. CMV is the most frequent viral infection in this context and is found in 75% of patients with a PCR positive for parvovirus B19 . A PCR for CMV must be systematically requested upon diagnosis of parvovirus B19 infection and redone monthly, and at the least suspicious sign.



TAKE HOME MASSAGE

- Severe, regenerative anemia associated with serum complement consumption in a young kidney transplant recipient during the first months post-kidney transplantation should be seen as a signal of parvovirus B19 infection and a reason to rapidly order a PCR test.
- The reduction of immunosuppression is the rule and IVIG will be set up if the PCR is too high or the clinicobiological picture severe. Rigorous monitoring needs to be maintained to detect any relapse of the parvovirusB19 infection or the onset of parvovirus B19-related glomerulopathy.





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Parvovirus B19 in kidney transplantation: key points and essential pitfalls to know

Yassamine Bentata

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