Human *Parvovirus* and giant cell arteritis: A selective arteritic impact?

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ABSTRACT

Peak incidences of giant cell arteritis (GCA) following human Parvovirus epidemics were found in 2 previous epidemiological studies.

The incidence of GCA [temporal arteritis and polymyalgia rheumatica (TA + PMR)] was studied before and after a major epidemic of human Parvovirus in 1994. Clinical data from the National Patient Register showed a significant inversion of the TA/PMR ratio during a 12-month period after an HPV epidemic. The inversion of this ratio was due to an increase in TA. The change in the ratio was most pronounced in the regions with the epicenter of the epidemic.

In many areas of the world giant cell arteritis (GCA)is the most common form of vasculitis, and in the past several investigations have been carried out, to disclose one or more infections as the triggering mechanism. Two recent studies found a regular cyclic pattern in the incidence rates of GCA over time, suggesting a possible infectious cause (1, 2). In our studies covering the period 1982-94, we also described that these fluctuations in the incidence of GCA occurred synchronously in several regions of Denmark. Such findings could be logically interpreted to mean that one or more microbiological agents with epidemic outbreaks are influencing these cyclic and synchronous variations.

The clustering of cases of GCA in Denmark occurred in relation to two epidemics of *Mycoplasma pneumoniae* (2), but we also observed a clustering of cases of giant cell arteritis not related to epidemics of *Mycoplasma pneumoniae*. Two simultaneous peaks of positive temporal artery biopsies in two different regions in 1991 and one peak in 1994 in one general hospital stood apart, since they followed two major human *Parvovirus* epidemics.

Thus, our preliminary observations suggest that human *Parvovirus* may be involved in GCA; the severity of the infection depends mostly on the hematological status of the host due to the remarkable tropism of human *Parvovirus* for erythroid progenitor cells. It initiates its entry into red cells via the erythrocyte P antigen, a known blood group antigen. In relation to vasculitis the tissue distribution of the P antigen is of considerable interest, because it is present not only on erythrocytes, but also on a few other cells including endothelial cells (3). Although the virus has not been shown to replicate in endothelial cells, reports of sporadic cases of human *Parvovirus* infection in adults with systemic necrotizing vasculitis are consistent with its potential ability to infect endothelial cells (4). Human *Parvovirus* infection has been described in other vasculitides (5, 6) and in cerebral vasculitis in children as a rare complication of erythema infectiosum (7).

Given this background, we studied a major human *Parvovirus* epidemic and its possible impact on the incidence of GCA. Serological epidemiological surveillance data on infections causing epidemics in Denmark were obtained from Statens Seruminstitut (8).The incidence of GCA (hospitals are legally required to report all cases) was obtained from the national patient register from 1982-1997. Fourteen of the 16 regions in Denmark were evaluated. The number of temporal artery biopsies showing GCA was obtained from 5 Department of Pathology which provide all histological services for three regions, including the county in which the human *Parvovirus* epidemic began.

Sero-surveillance data show the occurrence in the fifth week of 1994 of a major epidemic of human *Parvovirus* which began in one county and afterwards spread to other regions and came to an end 6 months later (Fig. 1). Register-derived clinical data showed that the human *Parvovirus* epidemic was followed by a marked increase in the ratio between

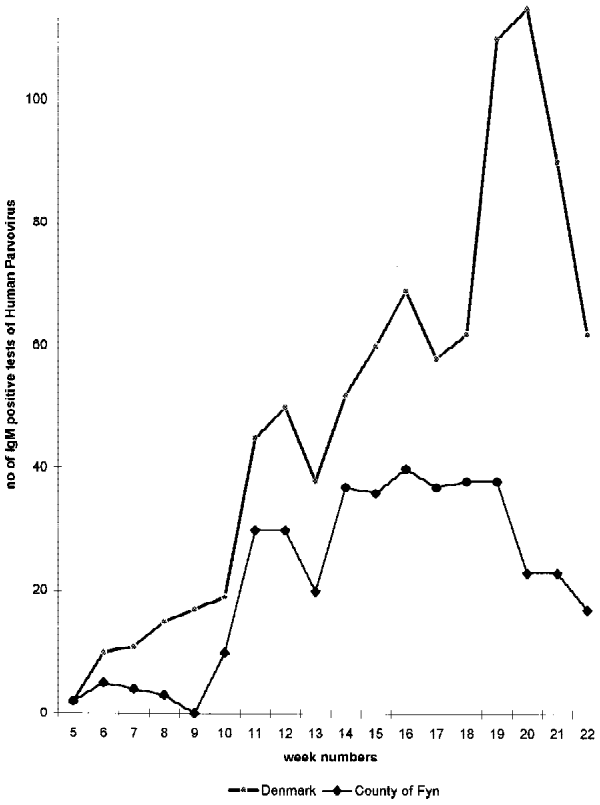

Fig. 1. Number of IgM positive tests of human *Parvovirus* registered during the epidemic for the county of Fyn and for the whole country at Statens Seruminstitut in 1994

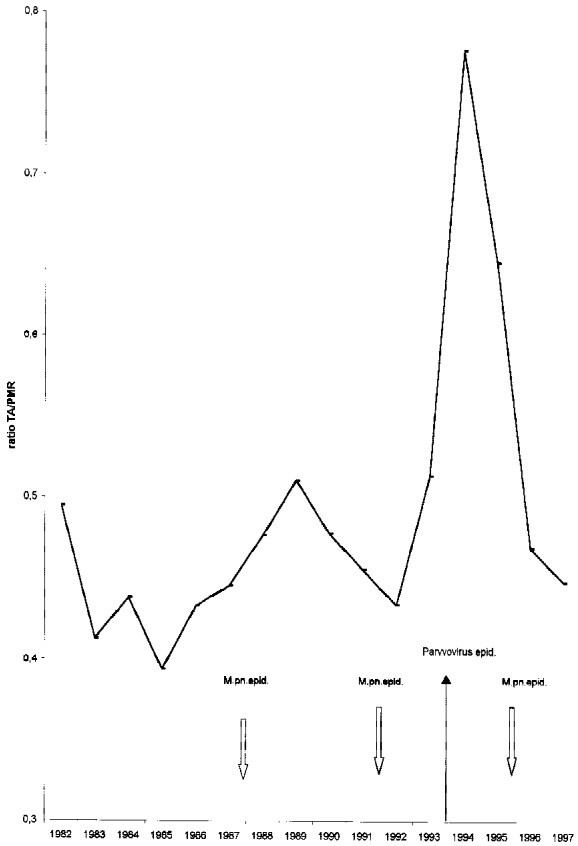

Fig. 2. Ratio of arteritis temporalis and polymyalgia rheumatica in 1982-96 as recorded by all hospitals in Dennark.Three epidemics of *Mycoplasma pneumoniae* and one of human *Parvovirus* are indicated by arrows.

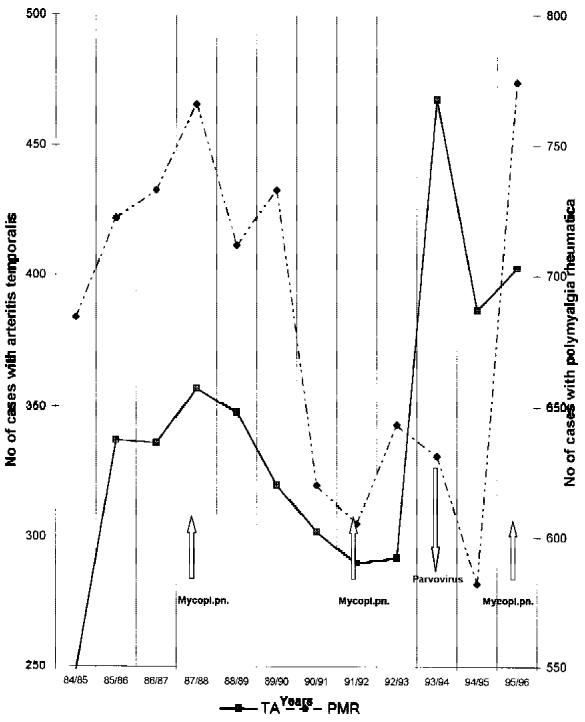

Fig.3. Number of cases recorded in the national patient register as arteritis temporalis/polymyalgia rheumatica (GCA) in Denmark. Arrows indicate epidemics of *Mycoplasma pneumoniae* and human *Parvovirus*.

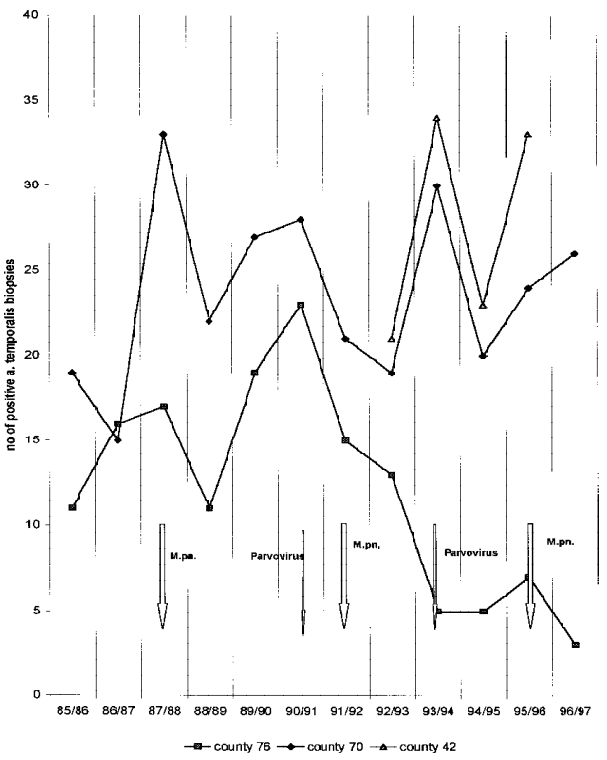

Fig. 4. Number of temporal artery biopsies showing giant cell arteritis from three regions during a 12-year period.

temporal arteritis (TA) and polymyalgia rheumatica (PMR) (Fig. 2) due to an increase in the incidence of TA cases and a simultaneous decrease in the incidence of PMR (Fig. 3). The median TA/PMR ratio for the whole country was not significantly changed (median ratio 1992-1993: 0.5, CI: 0.4-0.6; for 1994-95: 0.6, CI: 0.4 - 0.9; and for 1996-97: 0.5, CI: 0.4-0.7). The change in ratio was observed simultaneously in 9 of the 14 (65%) counties during 1994, but only in 27% of the regions in the year preceding and the year following 1994/95 ($p < 0.05$).

The TA/PMR ratio was highest in the region of the epicenter (ratio 1.1), in the two neighbouring regions (ratio 0.9) and in the two regions with high population densities (ratio 0.85), as compared with the other regions where the change in ratio was > 0.5 (ratio 0.56). This change began approximately one month after the outbreak and lasted for 12 months. Histological signs of GCA were found in 249 temporal artery biopsies during the epidemic period. The incidence of positive biopsies increased synchronously in the epidemic period, but only in 2 of the 3 counties investigated compared with the similar periods before and after the epidemic (Fig. 4).

While a causal relationship still remains to be established, the synchronous pattern of the increase in the incidence of temporal arteritis is specific evidence that microbiological agents with an epidemic pattern can trigger some cases. It is important to note that intravenous immunoglobulin may be useful in the treatment of chronic human *Parvovirus* infection.

References

1. SALVARANI C, GABRIEL SE, O'FALLON WM, HUNDER GG: The incidence of giant cell arteritis in Olmsted County, Minnesota: Apparent fluctuations in a cyclic pattern. *Ann Intern Med* 1995; 123: 192-4.
2. ELLING P, OLSSON AT, ELLING H: Synchronous variations of the incidence of temporal arteritis and polymyalgia rheumatica in different regions of Denmark; association with epidemics of *Mycoplasma pneumoniae* infection. *J Rheumatol* 1996; 23: 112-9.
3. BROWN KE, HIBBS JR, GALLINELLA G, *et al.*: Resistance to parvovirus B19 infection due to lack of virus receptor (erythrocyte P antigen). *N Engl J Med* 1994; 330: 1192-6.
4. FINKEL TH, TOROK TJ, FERGUSON PJ, *et al.*: Chronic parvovirus B19 infection and systemic necrotising vasculitis: opportunistic infection or aetiological agent? *Lancet* 1994; 343: 1255-8.
5. NIKKARI S, MERTSOLA J, KORVENRANTA H, VAINIONPAA R, TOIVANEN P: Wegener's granulomatosis and parvovirus B19 infection. *Arthritis Rheum* 1994; 37: 1707-8.
6. STAUD R, CORMAN LC: Association of parvovirus B19 infection with giant cell arteritis. *Clin Infect Dis* 1996; 22: 1123
7. NUNOUE T: Parvovirus B19 encephalopathy. *In*: *VIIth International Parvovirus Workshop*. Heidelberg. Deutscher Krebsforschungszentrum. 1997: 73.
8. Communication from the National Center of infectious diseases, Statens Seruminstitut, Copenhagen, June 1994.