Increased incidence of acute parvovirus B19 infections in Marseille, France, in 2012 compared with the 2002–2011 period

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Abstract

Human parvovirus B19 occurs worldwide and causes mild or asymptomatic disease in the form of cyclic local epidemics usually occurring in late winter and early summer. In 2012, a dramatic increase in cases was observed in the Public hospitals system of Marseille, with a total of 53 cases reported. Here, we describe the characteristics of this outbreak and compare it with the local epidemiology of B19V infections observed during the 2002–2011 period.

Keywords: Epidemiology, outbreak, parvovirus B19, pregnant women, seasonality
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Background

Parvovirus B19 (B19V), genus *Erythrovirus*, family *Parvoviridae*, is distributed worldwide and causes fifth disease, polyarthralgia, anaemic crisis in children with underlying haematological diseases and intrauterine infections. B19V infections are common during childhood and in young adults [1]. Seasonal recrudescence is observed in spring and early summer.

Diagnostic Methods

Nucleic acid purification was performed with the EZ1 DSP Virus Kit onto the EZ1 Advanced XL biorobot (both from Qiagen, Hilden, Germany) from a volume of 200 μL including 10 μL of a mixture composed of bacteriophage T4 and MS2 for process monitoring as previously described [2]. Qualitative PCR was performed with the system described by Aberham *et al.* [3]. Quantitative PCR was performed with the same protocol, using calibration range on B19V DNA-positive samples [3]. IgM and IgG specific for B19V were tested using commercial ELISA tests (Biotrin International, Dublin, Ireland).

B19V cases during 2002–2011

Between 2002 and 2011, we tested annually an average of 1409 patients (range 788–1630 per year) for B19V. We detected an average of 23.2 cases (range 8–31) of acute B19V infections for a global frequency of cases of 1.65% of tested patients with yearly variations from 0.64% to 2.47%. Year by year data are presented in Fig. 1(a). The sex ratio was balanced in patients younger than 20 years. In contrast, in patients older than 20 years, females were over-represented (Fig. 1b). The majority of acute B19V cases affected young adults between 21 and 40 years (Fig. 1b). During the 10 years studied, most of the requests (52%) for B19V serology and PCR originated from paediatric haematology, infectious diseases, gynaecology and internal medicine. These four specialties diagnosed 64% of all the acute B19V infections. Each year, an increased incidence of acute B19V infections was noted between April and July with a peak in June (Fig. 1c). Seasonality was demonstrated by autocorrelation.

B19V cases in 2012

In 2012, we tested 1885 patients for B19V: 1735 were tested by serological tests IgG and IgM, 443 by qualitative PCR. Fifty-three acute B19V infections were diagnosed: 53 had a qualitative positive PCR, 49 B19V DNA were quantified (four were not available) and 49 presented positive IgM (four were not available). The detailed characteristics of these 53 cases are presented in Table 1. The mean age was 22 years (range 1–58 median: 25 years). A sex ratio of 0.36 (39 women for 14 men) was observed. The majority (n = 35, 66%) presented clinical/biological manifestations that were severe enough to require hospitalization; of the 18 remaining patients, seven patients were discharged after admission to the emergency ward, and nine were diagnosed after being seen as outpatients in gynaecology, paediatric haematology, infectious diseases or internal medicine. The patients were referred to paediatric haematology (n = 17), obstetrics (n = 10), emergency room

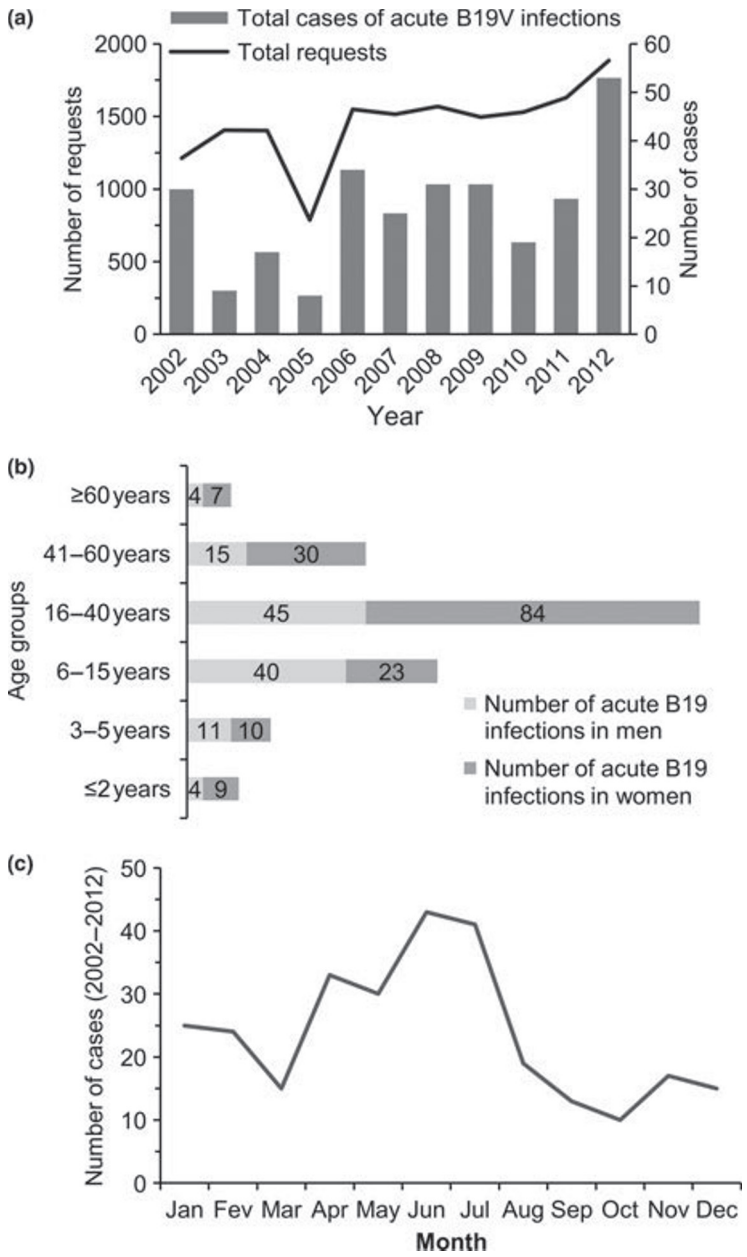

FIG. 1. (a) Requests for parvovirus B19-positive cases per year (Public Hospitals of Marseille, France 2002–2012). (b) Parvovirus B19 acute infections—Age and sex repartition (Public Hospitals of Marseille, France, 2002–2012). (c) Parvovirus B19 acute infections—Seasonnality (Public Hospitals of Marseille, France, 2002–2012).

(n = 7), internal medicine (n = 6), infectious diseases (n = 4), nephrology (n = 3), paediatrics (n = 2), oncology (n = 1), neurology (n = 1), dermatology (n = 1), and medical staff (n = 1). A total of 37.7% of cases affected children with a pre-existing condition such as sickle cell disease, hereditary spherocytosis, thalassaemia and Fanconi anaemia. Among the 11 pregnant women, six presented with severe complications and/or negative outcome (five hydrops fetalis and three pre-eclampsia). The six amniotic fluids were tested by qualitative PCR assay, and two were also tested through quantitative PCR assay (four were not available). In 2012, 20.7% and 24.5% of B19V acute infections involved pregnant women and children with an increased red blood cell turnover, respectively. The number of cases increased between April and July reaching an unprecedented high number of cases (n = 15) observed in July.

Comparison of B19V cases in 2012 versus the 2002–2011 period

The analysis of the characteristics of acute B19V infections observed in 2012 compared with the cases diagnosed during

TABLE 1. Characteristics of parvovirus B19 infection cases (Public Hospitals of Marseille, France, 2012)

Patient	Sex	Age (Years)	Clinical unit	Date (2012)	Amniocentesis	Sample tested by quantitative PCR	B19 viral load (copies/mL)	RBC (T/L)	Hb (g/dL)	Reticulocytes (G/L)	WBC (G/L)	Platelets (G/L)	Risk factor for severe acute B19 infection	Clinical signs
1	M	58	Infectious diseases	January 10	–	Serum	4.97E+05	4.51	14.8	–	6.06	228	HIV	–
2	F	28	Gynaecology	March 13	Yes	Amniotic fluid	1.12E+08	–	–	–	–	–	Pregnancy (12 weeks of gestation)	Hydrops foetalis leading to intrauterine fetal death for one of the two fœtuses
3	F	36	Gynaecology	April 3	No	Serum	2.47E+06	4.5	137	–	3.96	95	Pregnancy	Normal echography
4	M	12	Paediatric haematology	April 4	–	Edta	>5E+12	2.6	7.9	16	2.5	125	Sickle cell disease	–
5	M	6	Paediatric haematology	April 6	–	Edta	2.31E+06	1.9	6.5	1.9	3.1	26	Fanconi anemia	–
6	F	25	Nephrology	April 12	–	Edta	3.16E+05	3.3	8.6	–	8.56	299	Renal transplant recipient	Lymphadenopathy
7	F	9	Paediatric haematology	April 25	–	Edta	2.27E+11	3.5	8.4	24	2.7	66	Thalassemia	Fever asthenia
8	F	3	Emergency	April 27	–	Serum	7.33E+06	4	10.4	–	13.09	377	–	Fever
9	M	10	Paediatric heamatology	May 2	–	Edta	>5E+12	3.1	72	224	9.6	81	Thalassemia and sickle cell disease	–
10	F	27	Emergency	May 3	–	Serum	2.51E+08	4.6	13.1	14	4.2	90	–	Fever
11	F	24	Dermatology	May 13	–	Serum	3.98E+07	4.8	12.4	–	6.27	263	–	Cutaneous rash in socks
12	M	16	Pediatry	May 14	–	Serum	2.07E+08	5	14.4	–	3.6	183	–	Asthenia and arthralgia
13	F	40	Infectious diseases	May 18	–	Edta	5.02E+08	4	10.7	–	7.32	226	HIV and HCV coinfection	–
14	F	36	Gynaecology	May 18	No	Serum	2.70E+06	3.4	10.8	–	12	255	Pregnancy (second trimester)	Normal echography
15	F	43	Emergency	May 18	–	Serum	–	4.3	13	–	5	212	–	Fever and arthralgia
16	M	21	Paediatric haematology	May 29	–	Edta	3.61E+09	4.4	12	101	4.5	171	–	–
17	F	29	Gynaecology	June 4	Yes	Amniotic fluid	3.77E+10	2.9	8.2	–	12	224	Pregnancy (20 weeks of gestation)	Hydrops fetalis and preeclampsia syndrome
18	F	28	Gynaecology	June 5	No	Serum	1.42E+10	4.22	12.4	–	6.23	170	Pregnancy (18 weeks of gestation)	Normal echography, lymphadenopathy, asthenia and inflammatory syndrome
19	F	29	Gynaecology	June 8	Yes	Serum	4.48E+04	3.14	8.5	–	14.94	16.6	Pregnancy (20 weeks of gestation)	Preeclampsia syndrome hydrops foetalis
20	F	5	Paediatry	June 25	–	Serum	1.05E+06	3.69	10.8	–	16.72	277	Ivemark syndrome	–
21	F	47	Infectious diseases	June 29	–	Edta	3.24E+07	4.15	13.3	–	2.54	144	–	Fever, rash and discrete petechiae
22	F	33	Internal medicine	July 2	–	Edta	1.70E+04	4.49	13.3	45	4.8	266	–	Polyarthralgia, cutaneous rash and fever
23	F	4	Paediatry	July 5	–	Serum	2.00E+03	3.46	10.3	–	2	363	Past lymphoid acute leukemia B II and heterozygous sickle cell disease	–
24	F	33	Emergency	July 11	–	Serum	1.77E+07	4.14	13.2	–	5.94	217	–	Polyarthralgia and cutaneous rash
25	M	38	Emergency	July 12	–	Serum	2.01E+07	4.32	12.9	–	4	192	–	Distal and inflammatory arthralgia

Table 1 (*Continued*)

Patient	Sex	Age (Years)	Clinical unit	Date (2012)	Amniocentesis	Sample tested by quantitative PCR	B19 viral load (copies/mL)	RBC (T/L)	Hb (g/dL)	Reticulocytes (G/L)	WBC (G/L)	Platelets (G/L)	Risk factor for severe acute B19 infection	Clinical signs
26	F	34	Internal medicine	July 12	–	Serum	8.31E+06	4.16	11.7	–	5.96	317	–	–
27	F	27	Nephrology	July 13	–	Edta	4.65E+07	3.75	7.7	41	5.56	89	–	Proteinuria nephritic syndrome and distal arthralgia
28	F	28	Internal medicine	July 18	No	Serum	7.00E+03	3.77	11.5	72	8.96	212	Pregnancy (27 weeks of gestation)	–
29	M	6	Emergency	July 20	–	Serum	3.80E+04	4.57	12.1	–	16	421	–	Fever, polyarthralgia and lymphadenopathy
30	F	1	Paediatric hematology	July 20	–	Serum	3.45E+08	1.89	4.9	5.7	12	362	Hereditary spherocytosis	Asthenia
31	M	28	Nephrology	July 21	–	Edta	3.00E+06	3.63	10	11	5	24	–	Hemolytic and uremic syndrome
32	M	10	Paediatric haematology	July 23	–	Edta	4.46E+09	2.73	8	30	14	332	Sickle cell disease	Fever
33	F	24	Gynaecology	July 25	No	Serum	7.00E+03	4.23	13.6	–	9.34	238	Pregnancy (21 weeks of gestation)	Fœtal growth retardation, preeclampsia syndrome requiring therapeutic pregnancy interruption
34	F	14	Paediatric haematology	July 25	–	Edta	1.20E+04	2.47	8	4.9	0.95	100	Crohn's disease	–
35	F	32	Infectious diseases	July 30	–	Serum	–	–	–	–	–	–	–	Fever, cutaneous rash and polyarthralgia
36	F	24	Medical staff	July 30	–	Serum	4.08E+05	–	–	–	–	–	–	Arthralgia
37	F	32	Internal medicine	August 3	–	Serum	2.83E+05	–	–	–	–	–	–	Fever, arthralgia and cutaneous rash
38	F	7	Paediatric haematology	August 9	–	Serum	2.64E+06	3.49	9.7	433	5.9	207	–	–
39	F	17	Gynaecology	August 13	Yes	Serum	1.75E+05	3.71	11.8	–	7.87	296	Pregnancy (17 weeks of gestation)	Hydrops foetalis with ascitis, pericardia and prefrontal oedema
40	F	2	Emergency	August 28	–	Serum	2.84E+06	3.67	10.6	18	11	97	Beta thalassemia	–
41	F	26	Gynaecology	September 7	Yes	Serum	3.96+E10	3.46	11.3	–	10.42	222	Pregnancy (16 weeks of gestation)	Hydrops foetalis with prefrontal oedema
42	M	43	Internal medicine	October 25	–	Serum	–	4.18	12.9	–	6.87	250	–	–
43	F	15	Paediatric haematology	October 30	–	Serum	–	2.54	75	7.6	5.8	654	Sickle cell disease	–
44	F	35	Neurology	November 13	–	Edta	1.46E+07	3.73	11.5	–	5.3	417	–	Arms paresthesia, meningitic syndrome and occipital lymphadenopathy
45	M	11	Paediatric haematology	November 14	–	Serum	1.39E+03	4.64	13.3	269	5.7	513	Double heterozygous sickle cell disease	–
46	F	25	Gynaecology	November 15	No	Serum	7.57E+04	3.67	10.2	–	13	428	Pregnancy (33 weeks of gestation)	Cutaneous rash
47	F	36	Haematology	December 3	–	Edta	1.57E+04	3.22	10	325	3.22	274	Hereditary spherocytosis	–
48	M	5	Paediatric haematology	December 14	–	Edta	3.09E+07	2.27	79	1135	13	528	Glucose 6 phospho	–

Table 1 (*Continued*)

Patient	Sex	Age (Years)	Clinical unit	Date (2012)	Amniocentesis	Sample tested by quantitative PCR	B19 viral load (copies/mL)	RBC (T/L)	Hb (g/dL)	Reticulocytes (G/L)	WBC (G/L)	Platelets (G/L)	Risk factor for severe acute B19 infection	Clinical signs
49	M	7	Paediatric haematology	December 14	–	Edta	1.78E+10	2.6	93	511	7.7	387	deshydrogenase deficit	–
50	F	1	Paediatric haematology	December 14	–	Edta	2.41E+08	2.34	69	7	5.8	319	Glucose 6 phospho deshydrogenase deficit	–
51	F	4	Paediatric haematology	December 17	–	Bone marrow aspirate	9.41E+07	2.2	64	20	15	375	Glucose 6 phospho deshydrogenase deficit	–
52	F	2	Paediatric haematology	December 19	–	Edta	4.12E+07	4.82	13	9.6	7.2	478	Hereditary spherocytosis	–
53	F	37	Internal medicine	December 20	–	Serum	6.70E+04	4.3	12.9	43	5.44	232	Hereditary spherocytosis	–

the 2002–2011 period indicated that the number of acute B19V cases was significantly higher in 2012 (binomial test, $p < 0.001$; Fig. 1a). In contrast, no difference could be shown in the composition of the two populations with more than half of acute B19V infections diagnosed in young adults (21–40 years old; Fig. 1b). During the two periods, the higher rate of hospitalization suggested that symptomatic and severe infections are more often seen in females than in males. Finally, the epidemiology was identical for both periods with an increased number of cases during spring and summer, with a peak in June–July (Fig. 1c), as previously reported [4,5].

Conclusion

In 2012, in the Public Hospitals of Marseille, we noticed an increased number of cases of B19V infection relative to that observed during the ten previous years (2002–2011). We recorded 53 acute B19V infections, which represented a 71% incidence increase compared with the average incidence per year reported during the 2002–2011 period. From 2002 to 2012, (i) the annual number of B19V tests was constant; (ii) the distribution of B19V cases was similar; and (iii) the techniques used for diagnosis of B19V infection in the laboratory were unchanged. Therefore, the increased number of B19V infections noticed in 2012 was not biased by modified recruitment of patients, by number of annual tests, or by technical modifications. However, in samples with high concentration of B19V, the immunoglobulins may be complexed to virus particles and not be detectable in ELISA. Thereby, acute B19V infection might be significantly underdiagnosed. There is no bias in our study because the same algorithm was used for the entire study period. In 2013, the procedure was changed to test all samples by PCR. The unexpectedly high number of acute B19V infections in 2012 was also noticed in England and Wales [6]. As described previously, cases can be sporadic or can occur in clustered outbreaks. B19V infection occurs more frequently between late winter and early summer. Where reportable, communities have documented not only seasonality to B19V infections, but also cycles of local epidemics with case numbers that can peak every 4–10 years [4–7]. In epidemic periods, particular awareness should be granted to pregnant women who could develop complications such as pre-eclampsia and hydrops fetalis [8–10].

Transparency Declaration

The authors have declared no conflicts of interest.

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