

Rassegna

Review

# Myopericarditis during a primary Epstein-Barr virus infection in an otherwise healthy young adult. An unusual and insidious complication. Case report and a 60-year literature review

***Miopericardite in corso di infezione primaria da virus di Epstein-Barr in un giovane altrimenti sano. Una complicazione infrequente e insidiosa. Caso clinico e rassegna di 60 anni di letteratura***

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## ■ INTRODUCTION

As known, acute primary Epstein-Barr virus (EBV) infection often represents a pauci-symptomatic illness in early childhood, while it becomes responsible of a full-blown infectious mononucleosis usually in adolescents and young adults.

However, the association between EBV infection and a broad spectrum of benign and malignant diseases has been underlined in a comprehensive review recently published by the leading *New England Journal of Medicine* by K. Luzuriaga and coworkers [1]. Within infected tissues, the proteins expressed during the normal lytic and latent viral life cycle of EBV lead to cell alterations which support these EBV-related diseases. Although the early events of EBV infection are still poorly known, the increasing awareness of the viral processes which govern viral latency contributed to disclose some mechanisms by which EBV infection leads to cellular transformation, including the role played by EBV in prompting Burkitt lym-

phoma, Hodgkin's lymphoma, nasopharyngeal carcinoma, and multiple EBV-associated diseases, which may potentially involve an elevated number of organs and sites, and may also establish a life-threatening conditions, called "chronic active EBV infection", which takes advantage from a general or a selective deficit of immune defence [1, 2].

Complications linked with infectious mononucleosis other than the frequent acute satellite hepatitis associated with spleen enlargement prove infrequent in otherwise healthy subjects, but they occasionally may occur and present in form of a myriad of haematological, oncological, neurological, and cardiological disorders, as well as with lower respiratory tract manifestations [1-6]. For instance, an EBV infection expressing with predominantly, but polymorphic neurological signs and symptoms has been reported [7]. Moreover, the known oncological potential of EBV has been taken into careful account in the management of both immunocompetent hosts, and with a very different attitude in the immunocompromised patient with either

HIV disease, as well as in subjects suffering from malignant diseases and undergoing antineoplastic chemotherapy [8-10]. In these last patients group, a wide spectrum of clinical and pathological findings may encompass serious problems especially in terms of differential diagnosis. For instance, a very infrequent bilateral parotiditis due to EBV reactivation has been recently described, concurrently with a thymoma, whose viral aetiology had been suspected just after the retrieval of the concomitant EBV-related complication [10].

The most important disorders related to a primary EBV infection and infectious mononucleosis which may affect the heart as a whole, are represented by pericarditis and myocarditis, which may present concurrently or separately, and may complicate the disease course from its early onset, up to its late course.

In late 1984, B.J. Murray published a comprehensive review regarding the complications of infectious mononucleosis, which have been estimated to occur in around 5% of overall cases, and emphasized the possibility that they may precede, follow, or coincide with the usual signs and symptoms of disease. Sometimes, a complication may be the first manifestation of infectious mononucleosis, and these complications may become lethal in rare, but not negligible occurrences. From a pathogenetic point of view, an autoimmune response, a lymphocytic infiltrative reaction, a generalized oedema of the airways tissues, or a direct viral damage, are the most common conditions supporting organ damage, while spleen enlargement is the most frequent complication of primary EBV infection burdened by potentially severe complications (i.e. spleen rupture and bleeding) [4].

A rare case of self-limiting atypical myocarditis and pericarditis occurring in an otherwise healthy young adult affected by infectious mononucleosis is described, and is discussed on the ground of the existing literature evidence published from 1940s to present [11, 51].

## ■ CASE REPORT

An early-onset myocarditis and pericarditis linked to a primary EBV infection has been disclosed in a 20-year-old healthy young man who was initially hospitalized at a Cardiology Division, after making his preliminary screening at the Emergency Room. In fact, a baseline electrocardiogram disclosed a ST segment rise in

inferior-lateral sites, while a heart ultrasonographic assessment showed a minimal pericardial effusion and thickening, in absence of major deficits of the left heart ventricular kinetics. A treatment with amoxicillin plus aspirin (500 mg, twice daily) was recommended at the discharge occurred three days later, but after four more days our patient came back to the Emergency Room, and he was hospitalized due to hyperpyrexia (body temperature up to 39.5°C), diffuse arthromyalgia, and a prominent, non-itching macular-papular rash with a cranial-caudal extension, in absence of significant sore throat, pharyngodinia, and latero-cervical and local-regional lymphadenopathies, and with a slight hepatomegaly and splenomegaly. The laboratory examinations showed a mild increase of total leukocyte count (9,780 cells/ $\mu$ L), with increased lymphocyte (39.4%) and monocyte (10.3%) rate, completely normal erythrocyte, haemoglobin, and platelet levels, no coagulation abnormalities, while the biochemistry screening pointed out an isolated increase of serum transaminase (GOT 39, GPT 54 U/L), and gamma-GT levels (54 U/L), together with a rise of C-reactive protein value (5.95 mg/dL), with normal erythrocyte sedimentation rate (ESR) value, and no alterations of serum CPK and CPK-MB levels.

A search of anti-EBV antibodies tested positive, with elevated levels of specific IgM, and an initial IgG response, while all other microbiological investigations (including blood cultures, Widal-Wright serology, and Adenovirus, Cytomegalovirus, and Parvovirus B19 serum antibody search), tested negative. An abdominal ultrasonographic study demonstrated a mild liver and spleen enlargement, in absence of evident intrabdominal lymph nodes. After 7 days of hospitalization, our patient was discharged with an almost normal blood cell count (only a slight increase of the lympho-monocyte quota was present), and a completely normal serum biochemistry profile, save an increase level of serum transaminases (GOT 142, GPT 250 U/L), and serum gamma-GT (76 U/L), but with a fully normalized C-reactive protein level (0.69 mg/dL), and persistent, normal ESR, and normal serum levels of CPK and CPK-MB. The heart ultrasonography repeated 15 days after the first one showed the disappearance of pericardial effusion, a normal biventricular kinetic, and a minimal, residual pericardial thickening. Also chest X-ray and a repeated electrocardiography tested within normal limits.

A treatment with aspirin alone (at 500 mg, two times a day) was continued until an outpatient control was performed 10 days after the hospital discharge. At that visit, our patient felt well, neither electrocardiographic nor echocardiographic alterations were detected, and also serum transaminases returned within normal limits, so that aspirin treatment was interrupted. A subsequent follow-up visit conducted two months after hospital discharge, confirmed the complete disappearance of all clinical, instrumental and laboratory alterations observed during the complicated course of infectious mononucleosis.

## ■ DISCUSSION

Heart complications of infectious mononucleosis have been anecdotally reported since over 60 years ago [11]. In the large majority of the older cases, electrocardiographic findings were prominently described [12].

An isolated pericarditis was disclosed in a minority of cases, the first of them from Naples, Italy, in 1951, followed by one episode each reported even by the *New England Journal of Medicine*, and by the outstanding journal *JAMA*, in the same year 1953, and another case published by *Presse Médicale* in 1956 [13-16].

A complete overview of heart involvement by infectious mononucleosis was published for the first time in the United States, already in 1956 [17].

In the subsequent year (1957), together with another anecdotal case of pericardial involvement published by the *Archives of Internal Medicine*, an acute pericarditis was recognized for the first time as a possible, early clinical clue of infectious mononucleosis (as occurred in our patient) in a report of the outstanding journal *Annals of Internal Medicine* [18, 19].

At the same time, the first case series of cardiac complications of infectious mononucleosis was published, together with the first known "review of the literature" on this subject [20]. In fact, at the same time (year 1957), the well known satellite hepatitis caused by the primary infection with EBV was described in a patient who also suffered from a pericarditis [21].

Two comprehensive reviews on heart involvement which occurred during infectious mononucleosis were hosted by the *Archives of Internal Medicine* in 1958, and by *General Canadian Journal of Medicine* in 1959 [22, 23].

Between late fifties and early sixties, acute pericarditis was further discussed by United States and French Journals, and two more reports (again from the United States and France), underlined its possible early appearance in the course of this viral disease, as occurred in our patient [24-27].

Together with single case reports of self-limiting acute pericarditis occurring during an infectious mononucleosis coming from the United States, Italy, and France, one single patient with a disease complicated by an acute, constrictive epicarditis was described for the first time in 1961 by the outstanding journal *Circulation* [28-31].

During the late sixties, an English review article focused on cardiac presentation of infectious mononucleosis, while a 14-page-long review was dedicated to infectious mononucleosis-associated acute pericarditis by the prestigious French journal *Archives de Maladies de Coeur et Vaisseaux* [28, 33].

The first case report of the seventies greatly enlarged the scenario of the known heart complications of infectious mononucleosis. A particular young patient with pericarditis as the sole clinical manifestation of infectious mononucleosis was reported by the leading paediatric journal *American Journal of Diseases in Childhood*, and one case of focal myocarditis mimicking a myocardial infarction deserved relevant space in the outstanding journal *Chest* [34, 35].

Paralleling the increasing awareness of cardiac complications during infectious mononucleosis, during mid-seventies up to the year to 1980, a single case report of myocarditis and pericarditis was hosted by a general journal like *JAMA*, while *Archives de Maladies de Coeur and Vaisseaux* published another contribution, which underlined the possible severity of myocardial complications [36, 37]. An acute, severe myopericarditis was also observed in Croatia, together with another severe case of pericarditis, respiratory distress, and inappropriate antidiuretic hormone secretion, described in the United States in a patient already affected by Gaucher's disease [38, 39]. Infectious mononucleosis-associated myocarditis was analyzed in depth by the German author K.H. Dathe in 1975, who speculated that a combined mechanisms of a direct tissue tropism of EBV, summed up to a late immunological reaction, could be the pathological origin of this complication [40]. In the late seventies, a case of complete heart block during EBV myocarditis was

reported by the journal *Pediatrics*, as a relevant sequela of an otherwise benign disease like infectious mononucleosis [41]. Later, a fatal case of myocarditis was described in 1977 on the journal *Chest*: an otherwise healthy 14-year-old girl developed a sudden, refractory ventricular fibrillation during her apparently non-complicated course of infectious mononucleosis, with the histopathology picture demonstrating an extensive lymphoid-histiocytic infiltration of the myocardium [42]. Probably due to a mounting awareness of the non-negligible frequency and the potential severity of infectious mononucleosis complications, a 12-page comprehensive review by R.J. Hoagland was directed to general practitioners in 1975 [3].

In the year 1983, an observational study which assessed the aetiology of "mild" acute infection myocarditis in young men (a cohort of 126 consecutive conscripts), based only on serial electrocardiographic changes during an acute infection, and specific serologic studies, ranked infectious mononucleosis at the fifth place after Adenovirus, Vaccinia, and Influenza A, beta-haemolytic streptococci, and preceding Mycoplasma, Chlamydia, Influenza B, Coxsackievirus, Parainfluenza, and mumps virus; no specific signs and symptoms were detected in patients with a concurrent primary EBV infection [43]. In the same year (1983) an early, benign myopericarditis had its onset with a severe chest pain in a 17-year-old boy, so that the Author claimed the introduction of infectious mononucleosis among the potential differential diagnosis of an acute onset, severe chest pain in young adults [44].

In late 1984, BJ Murray published a review on the complications of infectious mononucleosis, which were estimated to occur in around 5% of overall cases when carefully searched, and emphasized the possibility that these complications may precede, follow, or coincide with the usual disease signs and symptoms. Sometimes, a complication may be the first manifestation of infectious mononucleosis, and in infrequent cases a complication may become lethal. From a pathogenetic point of view, an autoimmune response, a lymphocytic infiltrative reaction, a generalized oedema of the airways tissues, or a spleen enlargement, have been reported as the most frequent complications of primary EBV infection [4].

In the year 1985, pericardial effusion was still reported as the only manifestation of infectious mononucleosis from the United Kingdom, and

other atypical case reports have been described in small series from Hungary, and from Denmark [5, 45, 46].

Also a Canadian group assessed the cardiac effects of common viral illnesses (evaluated with both electrocardiographic and ultrasonographic findings), in 32 healthy patients matched with a comparable control group [6]. A small pericardial effusion was found in even 17 patients out of 32 affected by a number of viral illnesses, but mild and transient electrocardiographic alterations and/or self-limiting defects of left ventricular kinesis were found in small minority of cases, and were not linked to EBV infection in particular [6]. On the other hand, an irreversible auriculo-ventricular blockade requiring the implant of permanent pacemaker, occurred during the acute phase of infectious mononucleosis in a 29-year-old male, underlined the infrequent possibility to suffer from non-reversible conduction disturbances during infectious mononucleosis [47].

In the year 1993, three patients affected by a Kawasaki's-like coronary artery disease had EBV detected by molecular biology techniques in cardiac and aortic tissues, showing a possible role of this chronic active infection in prompting coronary artery aneurisms during this infrequent, but potentially severe pediatric disorder [48].

After nearly one decade of an apparent decline of literature reports regarding infectious mononucleosis and the heart involvement, in the year 2002 a 26-year-old male who developed a methicillin-resistant *Staphylococcus aureus* endocarditis on a bicuspid aortic valve, which occurred in the acute phase of an infectious mononucleosis, and required cardiac surgery and a prolonged antimicrobial treatment, was presented and discussed, although the relationship with the underlying viral disease was not clarified [49].

In the year 2006, a severe myopericarditis occurring during a primary EBV disease was diagnosed in a 18-year-old male patient from Serbia, and documented through a transvenous endomyocardial biopsy, and treated with non-steroidal antiinflammatory agents, beta-blockers, antibiotics, and other supportive agents [45]. An autoimmune pathway (perhaps mediated by complement activation), was postulated as the potential pathogenetic mechanism, as opposed to a direct viral damage [50].

The most recent available literature contribution of the year 2008, reported a case of active

myocarditis occurring in a patient with chronic active EBV infection, which is a potentially life-threatening condition characterized by chronic or recurrent infectious mononucleosis-like symptoms, burdened by a proportionally elevated rate of organ and site complications, including cardiac ones; this clinical occurrence has been carefully studied by virological, immunological, histopathological, and instrumental examinations, including a positron emission tomography (PET) [51]. EBV-encoded RNA sequences have been shown by *in situ* hybridization, and a predominant T-lymphocyte infiltrate characterized the histopathological picture.

## ■ CONCLUSIONS

In our experience, an otherwise healthy young man suffered from a symptomatic pericarditis and myocarditis documented through instrumental examinations, around one week before developing an atypical infectious mononucleosis (characterized by liver and spleen enlargement, prominent fever, but not pharyngodinia, and cervical lymph node enlargement), in association with a diffuse macular-papular cutaneous rash probably prompted by the concur-

rently administered amoxicillin treatment. We herewith underline a careful attention to all caregivers of infectious mononucleosis (especially general practitioners, paediatricians, ear, nose, and throat specialists, infectious disease specialists, and emergency room physicians), to consider also heart complication among rare, but possibly relevant and infrequently life-threatening complications of a primary EBV infection, in healthy patients too. In fact, these complications may occur in any different phase of infectious mononucleosis, and might even precede the clinical syndrome, as in our case, which also presented with atypical clinical features, making even more difficult its prompt recognition. Due to the usual self-limiting and benign course of these complications in otherwise healthy subjects, a careful clinical and instrumental monitoring and an eventual treatment with aspirin is deemed sufficient, to avoid the rare, but potentially severe heart damage anecdotally reported by the international literature.

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*Keywords:* infectious mononucleosis, Epstein-Barr virus infection, myocarditis, pericarditis.

## SUMMARY

An otherwise healthy young man had infectious mononucleosis detected after an atypical clinical onset, including myocarditis and pericarditis. Our patient slowly but completely recovered from his cardiac complications after the course of his primary Epstein-Barr infection, as shown by periodi-

cal electrocardiographic and ultrasonographic studies, and a simple treatment with aspirin alone. Our case report is briefly reported, and discussed with regard to the existing literature, which has recorded such complications since the mid 1940s.

## RIASSUNTO

*In un giovane altrimenti sano, la diagnosi di mononucleosi infettiva veniva posta dopo un esordio di malattia atipico, caratterizzato da miocardite e pericardite. Al termine del decorso dell'infezione primaria da virus di Epstein-Barr, la complicazione cardiaca andava incontro a lenta, ma completa guarigione, come docu-*

*mentato da periodici controlli elettrocardiografici e ultrasonografici, con un semplice trattamento a base di sola aspirina. Il caso clinico viene da noi presentato e discusso sulla base delle evidenze di letteratura esistenti, che riportano tali complicazioni a partire dalla metà degli anni '40.*

## REFERENCES

- [1] Luzuriaga K., Sullivan J.L. Infectious mononucleosis. *N. Engl. J. Med.* 362, 1993-2000, 2010.
- [2] Kutok J.L., Wang F. Spectrum of Epstein-Barr virus-associated diseases. *Annu. Rev. Pathol.* 1, 375-404, 2006.
- [3] Hoagland R.J. Infectious mononucleosis. *Prim. Care* 2, 295-307, 1975.
- [4] Murray B.J. Medical complications of infectious mononucleosis. *Am. Fam. Physician* 30, 195-199, 1984.
- [5] Timar L., Budal J., Gero A., Lakos A., Rapi K. Complications of infectious mononucleosis in childhood. *Orv. Hetil.* 126, 2647-2650, 1985.
- [6] Montague T.J., Marrie T.J., Bewick D.J., Spencer C.A., Kornreich F., Horacek B.M. Cardiac effects of common viral illnesses. *Chest* 94, 919-925, 1988.
- [7] Luchi S., Del Bono L., Vincenti A., Messina F., Scasso A. Neurological disorder associated to EBV: three case reports. *Le Infezioni in Medicina* 3, 182-185, 1997.
- [8] Bellissima P., Tricoli D., Platania S. CD30 (ki-1) antigen expression in acute infectious mononucleosis. *Le Infezioni in Medicina* 4, 228-232, 1998.
- [9] Manfredi R., Sabbatani S., Gianelli U., Marinacci G. Epstein-Barr virus associated nasopharyngeal carcinoma and local polymorphic B-cell lymphoproliferative disorder in a patient with HIV disease. *J. Intl. Assoc. Physicians AIDS Care* 6, 255-259, 2007.
- [10] Giordano S., Diego Pampinella D., Alù M., Agostara B., Romano A. EBV reactivation in a patient undergoing chemotherapy for invasive thymoma. *Le Infezioni in Medicina* 3, 195-198, 2007.
- [11] Geraghty F.J. Heart complications in infectious mononucleosis; report of a case. *South Med. J.* 39, 693-696, 1946.
- [12] Evans W.F., Graybiel A. Electrocardiographic evidence of cardiac complications in infectious mononucleosis. *Am. J. Med. Soc.* 211, 220-226, 1946.
- [13] De Fazio V., Marsico F. Cardiac complications in infectious mononucleosis: case of pericarditis. *Progr. Med. (Napoli)* 7, 545-550, 1951.
- [14] Miller H., Uricchio J.F., Phillips R.W. Acute pericarditis associated with infectious mononucleosis. *N. Engl. J. Med.* 249, 136-140, 1953.
- [15] Soloff L.A., Latuchni J. Infectious mononucleosis associated with symptoms of acute pericarditis. *J. Am. Med. Assoc.* 152, 1530-1531, 1953.
- [16] Celice J., Plas P., Peltier A., Papazian S. Cardiac localization of acute pericarditis type by infectious mononucleosis. *Presse Méd.* 64, 425-426, 1956.
- [17] Hoagland R.J. Cardiac involvement in infectious mononucleosis. *Am. J. Med. Sci.* 232, 252-257, 1956.
- [18] Shugoll G.I. Pericarditis associated with infectious mononucleosis. *Arch. Intern. Med.* 100, 630-634, 1957.
- [19] Roseman D.M., Barry R.M. Acute pericarditis as the first manifestation of infectious mononucleosis. *Ann. Intern. Med.* 47, 351-356, 1957.
- [20] Webster B.H. Cardiac complications of infectious mononucleosis; a review of the literature and report of five cases. *Am. J. Med. Sci.* 234, 62-70, 1957.
- [21] Jacobson S.M. Infectious mononucleosis complicated by hepatitis and pericarditis; a case report. *Md. State Med. J.* 6, 186-190, 1957.
- [22] Fish M., Barton H.R. Heart involvement in infectious mononucleosis. *Arch. Intern. Med.* 101, 636-644, 1958.
- [23] Hutchinson I. Cardiac involvement in infectious mononucleosis. *Med. Serv. J. Can.* 15, 306-313, 1959.
- [24] Cohen F.B., Goldman J. Acute pericarditis complicating infectious mononucleosis. A report of two cases. *J. Newark Beth Isr. Hosp.* 12, 234-243, 1961.
- [25] Gerbaut P., Hadot S., Pernot C., Lorrain J. Pericarditis during infectious mononucleosis. *Arch. Mal. Coeur Vaiss.* 51, 184-191, 1958.
- [26] Gardner C.C. Jr. Acute pericarditis as the initial manifestation of infectious mononucleosis. *Am. J. Med. Sci.* 237, 352-358, 1959.
- [27] Albeaux-Fernet M., Chabot J., Moreau P. Acute pericarditis. Initial manifestation of infectious mononucleosis. *Bull. Mem. Soc. Med. Hop. Paris.* 113, 1054-1059, 1962.
- [28] Burch G.E., Walsh J.J., Demasi C.J. Pericarditis due to infectious mononucleosis. *Am. Heart J.* 67, 421-422, 1964.
- [29] Colonna A., Solinas P. On two cases of acute benign idiopathic pericarditis in the course of infectious mononucleosis and herpes zoster. *Riforma Med.* 79, 1037-1043, 1965.
- [30] Treppoz M., Gallet M., Van Stratten L. A case of acute pericarditis in infectious mononucleosis. *Lyon Med.* 219, 707-222, 1968.
- [31] Wilson D.R., Lenkei S.C., Paterson J.F. Acute constrictive epicarditis following infectious mononucleosis; case report. *Circulation* 23, 257-260, 1961.
- [32] Dales M. Cardiac presentation of infectious mononucleosis. *J. R. Coll. Gen. Pract.* 16, 324-327, 1968.
- [33] Salvador M., Leclau J., Lesbre J.P., Galinier F., Mériel P. Acute pericarditis in the course of infectious mononucleosis. *Arch. Mal. Coeur Vaiss.* 62, 1023-1036, 1969.
- [34] Shapiro S.C., Dimich I., Steier M. Pericarditis as the only manifestation of infectious mononucleosis. *Am. J. Dis. Child.* 126, 662-663, 1973.
- [35] Miller R., Ward C., Amsterdam E., Mason D.T., Zelis R. Focal mononucleosis myopericarditis simulating myocardial infarction. *Chest* 63, 102-105, 1973.
- [36] Hugdins J.M. Infectious mononucleosis complicated by myocarditis and pericarditis. *JAMA* 235, 2626-2627, 1976.
- [37] Bensald J., Monassier J.P., Catanzano R., Marsaud G., Bouquier J.J., Grosogeat Y., et al. Severe myocarditis in infectious mononucleosis. *Arch. Mal. Coeur Vaiss.* 70, 773-779, 1977.
- [38] Bodo A., Stanic R., Ardeljian J. Acute myopericarditis in infectious mononucleosis. *Med. Pregl.* 33, 35-38, 1980.
- [39] Gribetz A.R., Kasen L., Teirstein A.S. Respiratory distress, pericarditis and inappropriate antidiuretic hormone secretion in a patient with infectious

- mononucleosis and Gaucher's disease. *Mt. Sinai J. Med.* 47, 589-591, 1980.
- [40] Dathe K.H. Carditis in mononucleosis. *Z. Gesamte Inn. Med.* 30, 32-35, 1975.
- [41] Reitman M.J., Zirin H.J., DeAngelis C.J. Complete heart block in Epstein-Barr myocarditis. *Pediatrics* 62, 847-849, 1978.
- [42] Frishman W., Kraus M.E., Zabkar J., Brooks V., Alonso D., Dixon L.M. Infectious mononucleosis and fatal myocarditis. *Chest* 72, 535-538, 1977.
- [43] Karjalainen J., Heikkila J., Nieminen M.S., Jalanko H., Kleemola M., Lapinleimu K., *et al.* Etiology of mild acute infectious myocarditis. Relation to clinical features. *Acta Med. Scand.* 213, 65-73, 1983.
- [44] Cheng T.C. Severe chest pain due to infectious mononucleosis. *Postgrad. Med.* 73, 149-150, 1983.
- [45] Mozes B., Pines A., Holtzman E., Frankl O. Pericardial effusion as the sole manifestation of infectious mononucleosis. *J. Infect.* 11, 149-151, 1985.
- [46] De Heide L., Hazenberg B.P. Infectious mononucleosis, different from usual. *Ned. Tijdschr. Geneesk.* 131, 2281-2283, 1987.
- [47] Marc M.O., Anconina J., Dodinot B., Perrin O., Meyer L., Selton-Suty C., *et al.* Irreversible auriculo-ventricular block of viral origin. *Ann. Cardiol. Angeiol. (Paris)* 42, 23-24, 1993.
- [48] Kikuta H., Sakiyama Y., Matsumoto S., Hamada I., Yazaki T., Nakano M. Detection of Epstein-Barr virus DNA in cardiac and aortic tissues from chronic, active Epstein-Barr virus infection associated with Kawasaki's disease-like coronary artery aneurisms. *J. Pediatr.* 123, 90-92, 1993.
- [49] Sakahashi H., Takazawa A., Toyama A., Haida T. Active infective endocarditis due to methicillin-resistant *Staphylococcus aureus* in the acute phase of infectious mononucleosis. *Jpn. J. Thorac. Cardiovasc. Surg.* 50, 249-251, 2002.
- [50] Mijailovic Z., Carnovic P., Gajovic O., Tomasevic S.. Myopericarditis during acute Epstein-Barr virus infection: a case report. *Med. Pregl.* 59, 490-493, 2006.
- [51] Takano H., Nakagawa K., Ishio N., Daimon M., Kobayashi Y., Hiroshima K., *et al.* Active myocarditis in a patient with chronic active Epstein-Barr virus infection. *Int. J. Cardiol.* 139, e11-e13, 2008.