G. D. Di Nucci
G. Mariani
P. Arcieri
R. Cerbo
L. Tarani
L. Bruni
M. C. Tozzi
P. Vignetti

Antiphospholipid syndrome in young patients. Two cases of cerebral ischaemic accidents

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Abbreviation *APS* antiphospholipid syndrome

Sir: In a recent issue of this journal, Ravelli et al. [8] reviewed the antiphospholipid syndrome (APS) in paediatric age, reporting 19 cases of juvenile thrombosis. Given the limited number of cases discussed in literature, we felt that a further report might be useful.

Cerebral ischaemic accidents are not frequent among children. In some instances one of the inhibitors of the coagulation pathway [antithrombin III, protein C, protein S] is lacking. This deficiency is genetically transmitted as an autosomal trait [6], and the condition is called "juvenile thrombophilia". The defect may also be acquired and associated with antiphospholipid antibodies or the "Lupus Anticoagulant" [3, 9, 10]. Antiphospholipid antibodies can be detected by clotting methods or by immunological techniques. The former include kaolin clotting time and other phospholipid dependent clotting assays with appropriate confirmation and specificity tests [2]. The latter are mainly solid-phase immuno assays (ELISA) to detect anticardiolipin antibodies and their Ig classes [3].

We observed two girls, one 21 months and the other 12 years old, who had experienced left hemiplegia due to cerebral infarction (shown by MRI). Their haemograms were normal, as were their blood chemistries (including APTT, fibrinogen, antithrombin III, protein C, protein S). Prothrombin time was prolonged in the second patient (PT ratio – 1.5, normal range 0.76–1.16). Both had prolonged kaolin clotting time ratios. The ELISA for anticardiolipin antibodies was negative in the second patient and positive at a low titre for the IgM subclass in the first patient (5.5 U MPL with normal values < 4.52 U MPL). Both cases fulfil the APS criteria [4], in so far as both cases showed cerebral thrombosis and antiphospholipid antibodies, with no evidence of auto-immune diseases or drug exposure.

APS is seldom diagnosed in young patients, perhaps because of the relative rarity of its clinical manifestations in children, which, when present, are similar to those described in adults [6]. Our cases, in contrast to those of others, showed no biochemical alterations (such as low levels of protein C or protein S) other than antiphospholipid antibodies [1], which are believed to be a risk factor for both arterial and venous thrombosis.

We therefore suggest that screening for APS by both clotting methods and immunochemical techniques, should be carried out even when thrombosis occurs in childhood [5].

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G. D. Di Nucci (✉) · G. Mariani
P. Arcieri
Centro Trombosi, Ematologia,
Dipartimento di Biopatologia Umana,
Università "La Sapienza",
V. Chieti, 7, I-00161 Roma, Italy

R. Cerbo
Servizio di Neuropsichiatria Infantile,
USSL L'Aquila, Italy

L. Tarani · L. Bruni · M. C. Tozzi
P. Vignetti
V Clinica Pediatrica,
Istituto di Clinica Pediatrica,
Università "La Sapienza", Roma, Italy

Themistocles Karpathios
Maria Kostaki
Sophia Drakonaki
Anastasia Garoufi
Soultana Siahanidou
Niki Spirou
Charalambos Theodoridis

An epidemic with influenza B virus causing benign acute myositis in ten boys and two girls

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Sir: Acute myositis is often caused by viral agents including the influenza A and B viruses [2, 5, 8, 9]. The affected patients are usually boys aged 4–10 years [2, 6, 11]. Myalgia involving mainly the calves and thighs follows an influenza-like illness and subsides rapidly without any specific therapy. Transient leukocytopenia and/or neutropenia have been described in association with viral myositis [5, 7, 9] but not as a constant finding. An epidemic with influenza B virus (Panama 45/90 strain) causing benign acute myositis, leukocytopenia and neutropenia in 12 patients (10 boys and 2 girls aged 4.5–11 years) is reported.

All 12 patients were living in Athens and were admitted to the second Department of Paediatrics of the Children's Hos-

pital "P. and A. Kyriakou" from 7 February to 15 April 1991. During the same period an influenza B epidemic caused by the strain Panama 45/90 was noticed in Athens. All patients had had an influenza-like illness with fever, cough, headache, chills, rhinorrhea and vomiting (Table 1) 2–5 days prior to their admission. Myalgias involving mainly the calves appeared soon after the viral symptoms subsided.

On admission all the children were afebrile and alert. No true muscle weakness was apparent but they were reluctant to use the affected muscles on account of pain rather than weakness. Ten were unable to walk. Reflex changes and sensory deficits were not found. Hepatomegaly was noticed in 8 and splenomegaly in 4 children. Eight children had injection of the pharynx and 7 mild cervical adenitis. No other abnormalities were noticed.

Creatine kinase (CK), aldolase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), leukocyte, neutrophil and platelet count were estimated every other day until their values returned to normal. Throat swabs for cultures were obtained from all the patients.

All children had leukocytopenia and neutropenia (Table 2). In 8 children leukocytopenia and neutropenia were noticed in full blood counts performed on admission. In the remaining 4 patients leukocytopenia and neutropenia were revealed in the second blood count performed 2 days later. Thrombocytopenia was noticed in 7 children. CK and/or aldolase were raised in all patients. SGOT and/or SGPT were elevated in 10 patients. The strain Panama 45/90 of influenza B virus was isolated from throat swabs in 3 children (Table 2). Serum antibody titres for the same strain were not determined. Haemoglobin, urea, electrolytes, calcium, phosphate, alkaline phosphatase, glutamyl transferase, C – reactive protein, erythrocyte sedimentation rate, anti-streptolysin O titre, antinuclear factor, bacterial cultures from throat swabs, chest X-rays and urinalysis, were all normal.

All patients were treated with bed rest. Their symptoms improved dramatically within 48 h and resolved completely in 4–5 days. Serum CK, aldolase, SGOT, SGPT, white blood cell and platelet count returned to normal within a week.

The diagnosis of myositis in our patients was based on the typical clinical features and the raised serum muscle enzymes. Electromyography and muscle biopsy were not justified since the process was benign and resolved rapidly. We believe that the myositis was caused by a virus. This concept is supported by the clinical picture of prodromal illness, the rapid and complete resolution of myositis without any specific therapy and the predominance of boys aged 4–11 years. Presumably the strain Panama 45/90 of influenza B was the responsible agent as it was isolated in 3 patients from throat swabs taken after the onset of myositis. It is postulated that if the swabs were taken during the acute phase of the viral illness a higher incidence of positive cultures would have been obtained. Moreover the cases of myositis occurred concurrently with an influenza B epidemic in the Athens area caused by the same viral strain. The increase of serum SGOT and SGPT in our patients could be attributed to the myositis itself or to hepatic damage as 8 out of 12 children had hepatomegaly. The latter seems unlikely since serum alkaline phosphatase, glutamyl transferase, prothrombin and activated partial thromboplastin time were normal and SGOT and SGPT values returned rapidly to normal in parallel with CK and aldolase. Transient or even chronic leukocytopenia and neutropenia are often caused by viral agents including influenza A or B viruses, Epstein Barr virus and Parvovirus B19. All the patients in our

Table 1 Prodromal symptoms of 12 children with acute myositis

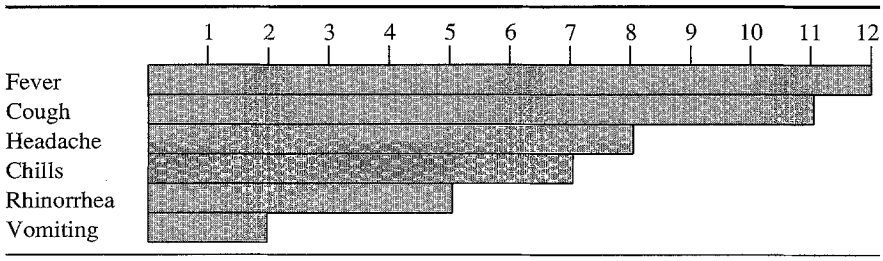

Table 2 Laboratory findings of 12 children with acute myositis

Case No	CK[a] (iu/l)	aldolase[a] (iu/l)	SGOT[a] (iu/l)	SGPT[a] (iu/l)	leukocyte[b] count/mm^3	neutrophil[b] count/mm^3	platelet[b] count/mm^3	viral culture
1	84	10	285	63	2500	825	127000	Nil
2	600	17.8	100	50	1800	738	200000	Nil
3	6348	189	467	153	2400	864	127000	Nil
4	1414	Nd[c]	7	17	2000	780	128000	Nil
5	94	17	55	111	2680	880	199000	Nil
6	1648	7.8	114	32	2500	182	124000	infl B/Panama 45/90
7	1320	16.4	90	36	2300	644	171000	Nil
8	331	9.9	26	26	3900	1404	170000	Nil
9	118	8	29	19	3200	1376	128000	infl B/Panama 45/90
10	736	12	42	16	4900	1323	127000	Nil
11	2140	14.2	102	31	2000	880	92000	Nil
12	2396	28.2	112	30	4000	920	191000	infl B/Panama 45/90
Normal range	Up to 80	Up to 7.6	Up to 27	Up to 27	> 5000	> 1500	> 150000	

[a] Highest value, [b] lowest value, [c] not done

study had leukocytopenia and neutropenia. In acute viral myositis according to our knowledge [1, 5–11] only 24 out of 63 and 4 out of 49 studied patients had leukocytopenia and neutropenia respectively. This difference between our results and those reported in the literature could be attributed to different causative viral strains or to a different methodology applied. The latter is supported by the fact that in 4 of our patients the initial blood count was normal and only a second blood count performed 2 days later, revealed the leukocytopenia and neutropenia. Thrombocytes were checked on the same occasions but mild thrombocytopenia was found only in 7 of our patients. The mechanisms by which viruses induce neutropenia [3, 4] are incompletely understood. It is postulated that neutropenia in these patients may be the result of a number of processes including suppression of myelopoiesis by the infecting agent, excessive neutrophil margination along endothelial surfaces, increase in the peripheral destruction of leukocytes, activation of C_5 to C_{5a} complement or production of circulating antineutrophil auto-antibodies. We did not study the pathogenesis of neutropenia in our patients.

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T. Karpathios (✉) · M. Kostaki
S. Drakonaki · A. Garoufi
S. Siahanidou · C. Theodoridis
Second Department of Paediatrics,
"A. and P. Kyriakou" Children's Hospital,
Thivon and Levadias,
GR-11527 Athens, Greece
Tel.: (01)77.09.450, Fax.: (01)77.74.127

N. Spirou
Hellenic Institute "Pasteur", Athens, Greece

Ben C. J. Hamel

Familial primary pulmonary hypoplasia

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Sir: With much interest we read the paper by Frey et al. on familial isolated pulmonary hypoplasia [1]. We know of another family with two male siblings with this condition. The first case was born at 35 weeks after an uneventful pregnancy and delivery. The amount of amniotic fluid was normal. Birth weight was 2770 g. He died a few hours after birth due to respiratory failure. Autopsy revealed very small, non-expanded lungs with a normal bronchi/alveoli ratio. No other abnormalities were found.

His brother was born at 39 weeks after an uneventful pregnancy and delivery. There was no oligo- nor polyhydramnios. Birth weight was 3435 g and length 52 cm. He too died because of respiratory failure after 1 h. At autopsy a combined lung weight of 12 g was found with a body weight/lung weight ratio of 0.0035 (normal > 0.012 [2]). The bronchi/alveoli ratio was normal. No other abnormalities were found. Their parents are healthy and in seven generations not consanguineous; they have two healthy sons. Family history is not contributory.

Though in the first case pulmonary hypoplasia is strictly speaking not proven, there is in our opinion no doubt that both cases had primary pulmonary hypoplasia, suggesting a genetic aetiology. It is too early to differentiate between a multifactorial or a monogenic cause. In the latter case autosomal recessive inheritance seems the most likely, but as in our family, X-linked transmission cannot be ruled out.

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B. C. J. Hamel
Department of Human Genetics,
University Hospital, P.O. Box 9101,
NL-6500 HB Nijmegen, The Netherlands,
Tel.: 31-80-613946, Fax: 31-80-565026