Diaphragmatic weakness and myositis associated with systemic juvenile rheumatoid arthritis

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An unusual presentation of systemic juvenile rheumatoid arthritis in a young adult is reported. Among the major manifestations were severe muscle weakness and dyspnea, which were found to be due to myositis and diaphragmatic weakness. The evolution of the disease and its response to therapy are described.

On décrit un tableau clinique inhabituel de polyarthrite rhumatoïde générale juvénile observé chez un jeune adulte. On constatait parmi les manifestations importantes une faiblesse musculaire grave et de la dyspnée, attribuables à une myosite et à une faiblesse diaphragmatique. On décrit également l'évolution de la maladie et sa réponse au traitement administré.

Systemic juvenile rheumatoid arthritis (SJRA) in adults (Still's disease) is an uncommon disorder in which arthralgia and myalgia are almost always present.[1] However, myositis resulting in severe muscle weakness has not previously been reported. We describe a patient in whom generalized myopathy and diaphragmatic weakness were prominent features of SJRA.

Case report

An 18-year-old man was referred to our hospital for management of a pericardial effusion. He had initially been admitted to a regional hospital with a 4-day history of remittent fever, myalgia, weakness, pain in the right upper quadrant of the abdomen and progressive dyspnea and orthopnea.

During his 2-week stay in that hospital pleural effusions and pericarditis were found. His fever persisted, with daily temperature spikes, and he lost 5 kg of body weight. He received antibiotics and a 3-day course of corticosteroid therapy, but there was no improvement. When chest x-ray films showed enlargement of the cardiopericardial silhouette, he was transferred to our hospital.

The patient had no history of headache, cough, arthralgia, change of colour of the urine or contact with persons having tuberculosis. His temperature was 37.2°C in the morning and 39.6°C in the evening, his blood pressure was 130/60 mm Hg with no inspiratory decrease, and his pulse rate was 110/min. He preferred to remain sitting in bed, breathing shallowly, at a rate of 32/min. His jugular veins were not distended. The chest expansion was symmetrically decreased. The accessory respiratory muscles of the neck were being used, and the abdominal wall moved inwards during inspiration, particularly when the patient was supine. Dullness was noted at both lung bases, and breath sounds were absent. A loud pericardial rub was present. The liver was enlarged, spanning 15 cm, and tender. There was no hepatojugular reflux or peripheral edema. All the muscles were tender and weak. On a few occasions a discrete maculopapular rash was observed on the trunk and the proximal area of the extremities. Some of the lesions had a clear centre. There were no petechiae. Examination of the joints initially yielded normal results, but on the 10th hospital day painful swelling developed in the right wrist.

Urinalysis showed 2+ protein, 3+ blood and two to seven leukocytes and erythrocytes per high power field. The hematocrit was 36.6%, the leukocyte count 33.2 × 10^9/L (94% neutrophils) and the erythrocyte sedimentation rate 32 mm/h. The serum levels of urea nitrogen, glucose, creatinine, electrolytes, bilirubin, alkaline phosphatase, aspartate aminotransferase and lactate dehydrogenase were within normal limits. The serum creatine kinase level was 15 (normally less than 118) U/L and the serum aldolase level 6.7 (normally 0 to 3.1) U/L. The serum levels of immunoglobulins and the C3 and C4 components of complement were normal. Tests for rheumatoid factor and antinuclear antibody gave negative results, and the deoxyribonucleic acid (DNA) binding test had a normal result. No microorganisms were cultured from the blood.

A chest x-ray film showed bilateral small pleural effusions and a large cardiopericardial silhouette (Fig. 1). An electrocardiogram showed sinus tachycardia, the heart rate being 110/min, and widespread repolarization abnormalities. An echocardiogram confirmed the presence of a moderate pericardial effusion and showed small particles, consistent with fibrin balls, within the fluid. Pressures measured from a Swan–Ganz catheter were as follows: central venous 8 mm Hg, right ventricular 25/13 mm Hg, pulmonary arterial 22/13 mm Hg and pulmonary wedge 9 mm Hg.

A biopsy of one of the skin lesions showed an acute perivascular inflammation in the upper layer of the dermis; the results of immunofluorescence testing for immunoglobulins and complement were negative.

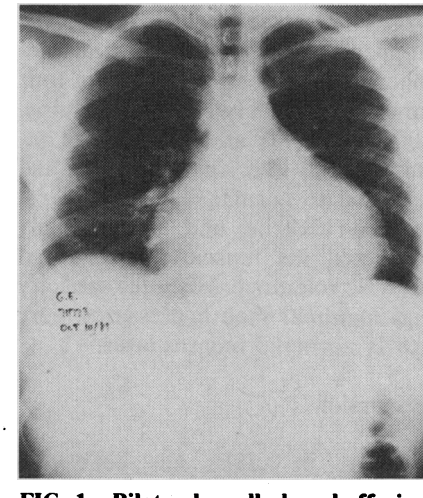

FIG. 1—Bilateral small pleural effusions (mainly subpulmonic), elevation of hemidiaphragms and large cardiopericardial silhouette 2 weeks after onset of illness.

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On the 10th hospital day electromyograms of the left deltoid, the left gluteus medius and the tibialis anterior showed no spontaneous activity, but during recruitment all the motor unit potentials were of small amplitude and most were of short or normal duration and polyphasic, which suggested myopathy. In the fourth week after admission a biopsy of the left biceps showed mild regenerative activity. There were a few mononuclear cells around the veins and granular immunofluorescence with IgG in the microvasculature. Electron microscopy showed no dense deposits or inclusion bodies. A joint scan showed a symmetrically increased uptake of the radiotracer in the elbows, shoulders and acromioclavicular joints.

The results of pulmonary function tests performed 3 weeks after admission are listed in Table I. The arterial blood gas values while the patient was sitting and breathing room air were as follows: partial pressure of oxygen 84 mm Hg, partial pressure of carbon dioxide 30 mm Hg and pH 7.49. Fig. 2 shows the pressures measured from gastric and esophageal balloons during tidal breathing and after maximal static inspiration from functional residual capacity.

Treatment was started with acetylsalicylic acid (ASA), up to 6.5 g/d, which resulted in a serum salicylate level of 1.8 mmol/L, and with indomethacin, 100 mg/d. The patient's temperature decreased slowly. Nine days after the start of treatment the serum aspartate aminotransferase level rose to 2220 U/L. Treatment with ASA was stopped, and the dose of indomethacin was increased to 150 mg four times a day. Hydroxychloroquine, 400 mg/d, was added after the results of the liver function tests had returned to normal. The patient remained afebrile and progressively recovered his muscle strength and exercise tolerance. His vital capacity and maximal mouth pressures were nearly normal 3 months later.

Discussion

SJRA in adults has been discussed in recent reviews.[1,2] The patient we have described had numerous features of this disorder, including the typical remittent fever, Still's rash, pleuropericarditis, monoarthritis, anemia and marked leukocytosis. Hepatomegaly and abnormal results of liver function tests are also recognized features of SJRA, as is the exacerbation of the liver function abnormalities in some cases by treatment with ASA.[2,3]

Myalgia is almost always present in adults with SJRA. The recent discovery of the muscle release of prostaglandin E2 induced by leukocytic pyrogen may account for the myalgia.[4] Muscle weakness is usually considered to be secondary to the pain. In our patient, however, the degree of muscle weakness appeared to be out of proportion to the severity of the myalgia. Although the serum creatine kinase level was normal, the serum aldolase level was twice the upper limit of normal. We did not look for myoglobinuria, but its presence was suggested by the finding of 3+ blood and only a few erythrocytes per high power field in the urine. The electromyograms and the muscle biopsy specimen showed nonspecific changes consistent with mild myositis. Bujak and associates[5] reported that 7 of their 10 patients with SJRA underwent muscle biopsy and that the muscle fibres were normal in all instances; however, a perivascular accumulation of inflammatory cells was noted in 2 of the patients. The serum creatine kinase and aldolase levels were normal in all 10 patients, and none of the patients had muscle weakness.

The dyspnea in our patient is unlikely to have been due to either the bilateral pleural effusions, which were small and not associated with pleuritic pain, or the pericardial effusion, as there was no clinical or hemodynamic evidence of tamponade or heart failure. However, it could be explained by the diaphragmatic weakness, which was suggested by the clinical and physiologic findings:[6,7] the paradoxic movement of the abdominal wall during tidal breathing, the reduction in vital capacity, which worsened when the patient was supine, and the marked

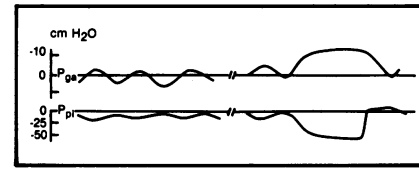

FIG. 2—Left: Simultaneous tracings of gastric (P_{ga}) and pleural (P_{pl}) pressures during tidal breathing 3 weeks after onset of illness, showing negative P_{ga} during inspiration. Right: Same pressures during maximal static inspiration; transdiaphragmatic pressure, $P_{ga} - P_{pl}$, 64 cm H_2O.

Table I—Results of pulmonary function tests done 3 and 15 weeks after onset of illness

Measure	Results: Predicted	Results: Measured: At 3 weeks	Results: Measured: At 15 weeks*
Lung volumes (L)			
Vital capacity			
Patient sitting	**5.58**	**2.42**	**4.79**
Patient supine		**1.91**	**4.40**
Functional residual capacity	**3.99**	**3.10**	**3.33**
Right ventricular volume	**1.87**	**2.44**	**1.40**
Total lung capacity	**7.45**	**4.86**	**6.19**
Flow (L/s)			
Forced expiratory volume at 1 second	**4.50**	**2.20**	**3.85**
Maximal midexpiratory flow rate	**4.80**	**1.25**	**3.93**
Diffusing capacity of the lung for carbon monoxide (mL/min•mm Hg^{-1})	**37.4**	**21.3**	**36.7**
Maximal mouth pressures (cm H_2O), patient sitting			
Inspiratory	**−124 ± 44**	**−61**	**−109**
Expiratory	**233 ± 84**	**130**	**140**
Transdiaphragmatic pressure (cm H_2O), patient sitting	**76–177**	**64**	**ND**

***ND = not determined.**

decrease in the maximal inspiratory pressure. The negative gastric pressure during inspiration confirms the clinical observation. The transdiaphragmatic pressure during maximal static inspiration, measured 3 weeks after the onset of the illness, was reduced. However, given the large variability in the diaphragmatic pressure among healthy subjects and in the way the pressure is measured,[8] we do not think that its measurement added much to the clinical evaluation.

Diaphragmatic weakness is known to occur in polymyositis and dermatomyositis;[9,10] however, we are unaware of measurements of respiratory muscle strength in these conditions. Respiratory system involvement may include aspiration pneumonia secondary to dysphagia. Previous reports have described an "elevated sluggish diaphragm"[11] and unexplained dyspnea[12] associated with systemic lupus erythematosus. Gibson and colleagues,[13] in their review of 30 patients with systemic lupus erythematosus, found low lung volumes in 13 patients, and the transdiaphragmatic pressure was grossly abnormal in 4 of the 5 patients in whom it was measured. They postulated that recurrent pleurisy resulted in splinting and wasting of the diaphragm. In our patient it is reasonable to postulate that the diaphragmatic "myositis", similar to the disorder of the peripheral muscles, accounted for the diaphragmatic weakness.

A systematic search for evidence of respiratory muscle weakness may uncover similar cases when myopathy is a prominent feature of SJRA.

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Addendum

Since we submitted this paper, Martens and colleagues have described 7 of 26 consecutive patients with systemic lupus erythematosus who had evidence of respiratory muscle weakness (*Chest* 1983; 84: 170–175). They ascribed it to a more generalized yet subclinical muscle disorder due to systemic lupus erythematosus.■