RETROPERITONEAL NODAL APLASIA, ASPLENIA, CHYLOUS EFFUSION AND LYMPHATIC DYSPLASIA: AN ACQUIRED IMMUNODEFICIENCY SYNDROME?

L Carini, LD Meregaglia, C Galli, G Segalini, M Strada, J Jones, MH Witte and CL Witte

From the Departments of Medicine (LC, CG, CS) and Radiology (DM, MS) Bassini Hospital, Cinisello-Balsamo, Milano, Italy, the Department of Pediatrics (JJ), University of Colorado and National Jewish Hospital, Denver, Colorado, and the Department of Surgery (MHW, CLW), University of Arizona College of Medicine, Tucson, Arizona, USA

ABSTRACT

Two adult patients (one in Italy and the other in the USA) are described with similar findings of paraaortic nodal aplasia, asplenism, multiple serous and chylous effusions, and retroperitoneal lymphatic dysplasia. Although the clinical courses are incomplete, this unusual constellation of signs in the setting of normal peripheral lymph trunks suggest an acquired rather than inborn anomaly and possibly a variant acquired immunodeficiency syndrome.

Disorders of the lymphatic system are usually classified into disturbances of the tissue fluid-lymph circulation on the one hand and dysfunction of lymph nodes on the other (1). Deranged circulation of lymph is characterized further by edema or effusion (sometimes chylous) from either primary lymphatic obstruction (so-called lymphedema or low output failure) or from overproduction of lymph with accelerated but nonetheless insufficient lymph transport (i.e., high output failure) (2). Although seldom entirely discrete, edema of the former type arises in Milroy's disease and filariasis while trauma, thermal burns, and "cirrhotic" ascites are examples of the latter type (3). Occasionally, both processes con-

tribute prominently to tissue swelling ("mixed" anasarca) as in congestive heart failure where elevated systemic venous pressure accelerates lymph formation and concomitantly impedes lymph return (3). In contrast, disorders of lymph nodes are usually classified as hyperplasia and neoplasia (4). Whereas intense chemotherapy and irradiation (e.g., for control of malignant lymphoma) (5) and longstanding microfilarial (*W. bancrofti*) infestation (6) may obliterate regional lymph nodes, spontaneous disappearance of paraaortic lymph nodes and the spleen is most unusual.

We have recently encountered two adult patients (one in Italy and the other in the U.S.A.) with longstanding, poorly explained serous and chylous effusions who were found to have complete aplasia of retroperitoneal lymph nodes, absence of the spleen and visceral lymphatic dysplasia. Although the pathogenesis is obscure and no primary infectious agents have been isolated to date, the clinical presentations suggest a variant acquired immunodeficiency syndrome.

CASE REPORTS

1. A 57-year-old man developed, 9 years

earlier, mild exertional dyspnea and bilateral pleural effusions. Aspiration of straw-colored pleural fluid yielded at that time a protein content of 4g/dl but bacterial culture, cytology and a variety of blood examinations failed to reveal a causative process. Maintenance on low dose diuretic drugs promoted little subjective or radiologic change. Approximately 6 months before, progressive ascites developed. Physical examination disclosed bilateral pleural effusion (Fig. 1), pericardial effusion, prominent ascites, hydrocele, mild leg edema, and telangiectasia of the face, trunk, and legs. Laboratory examination showed a slightly decreased serum albumin and fluid

aspirates displayed the following characteristics: 1) ascitic-milky, total protein 8g/dl, cholesterol 150mg/dl, triglycerides 720mg/dl, pH 8.0; 2) pleural - golden yellow, total protein 4 gm/dl, pH 8; 3) hydrocele — clear yellow, total protein 4g/dl, pH 7.5. Numerous lymphocytes and mesothelial cells were detected in these fluids. Fluid culture, cytology, and serum lupus erythematosus (LE) cell preparation and antinuclear antibody (ANA) factor were negative. Contrast radiographs of the small intestine were unremarkable. Bilateral dorsal pedal lymphangiography showed absent inguinal and retroperitoneal lymph nodes and unobstructed lymph trunks with
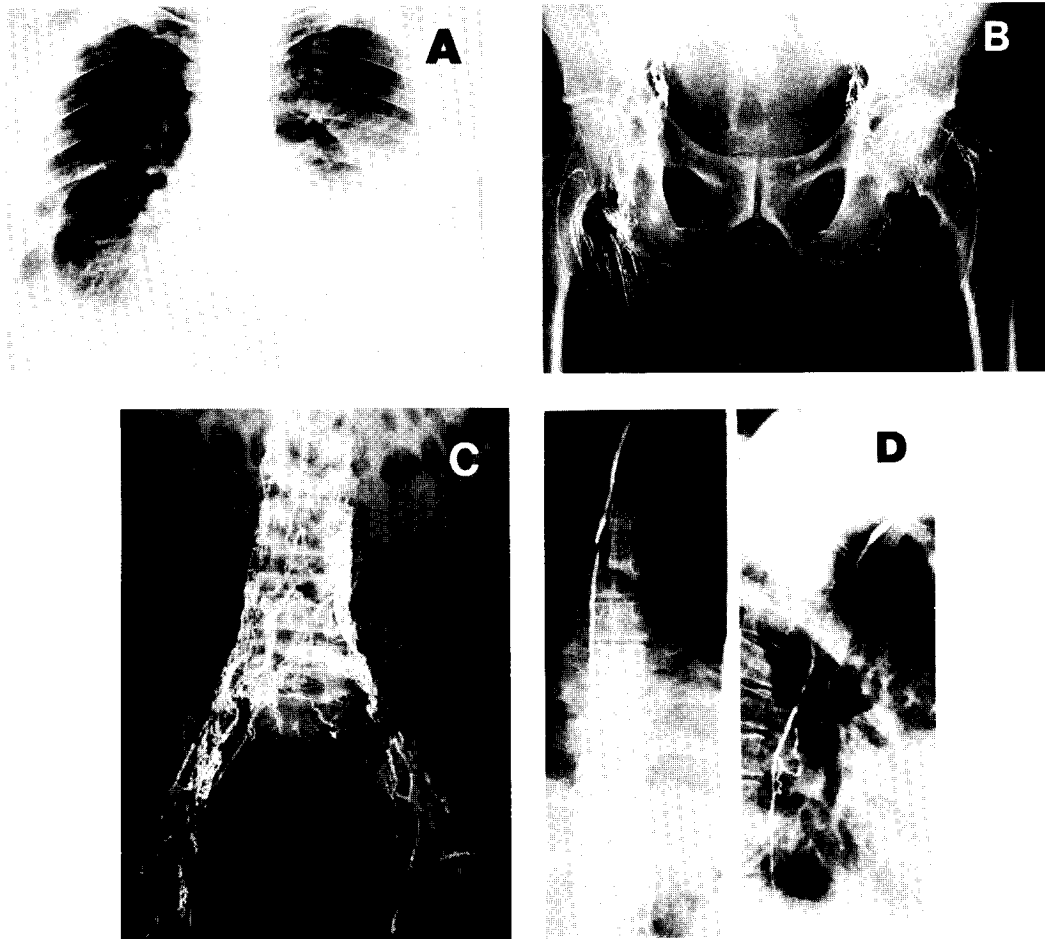

Fig. 1: Chest x-ray (A) and dorsal pedal lymphangiography (B-D) of 57 year old man with bilateral pleural effusions (A), intact peripheral lymph trunks, absence of inguinal (B) and paraaortic lymph nodes (C), dysplastic retroperitoneal lymphatics (C) and normal thoracic duct (D).

filling of the thoracic duct (Fig. 1). Twenty-four hours post-injection, plain films of the abdomen showed no residual contrast medium and specifically no lymph nodes. Computed tomography showed absence of the spleen, a finding corroborated by splenic scintigraphy (Fig. 2). Serum electrophoresis, immunodiffusion, response to mitogens, and blood T/B lymphocyte ratio were normal.

Fig. 2: Scintigraphy with 99mTc labeled red blood cells demonstrating a normal liver but absence of the spleen. (Patient 1).

Despite initial improvement with diuretic drugs and intravenous albumin infusion, ascites and pleural effusions worsened. Recently, he underwent pleurodesis for control of refractory pleural effusion and severe exertional dyspnea.

2. A 24-year-old woman developed progressive ascites in conjunction with fatigue, malaise, and chronic cough. Since age 12 years she had recurrent bronchopneumonia, particularly of the right lung. Between 14 and 17 years, she had multiple episodes of sinusitis, upper respiratory infections, abdominal distension, puffiness of the face and hands, diarrhea, and high fever. Eight years earlier laparotomy disclosed chylous ascites, hepatic scarring, retroperitoneal and visceral lymphadenopathy (follicular hyperplasia, histologically) and a nodular but small spleen. Because of severe hypogammaglobulinemia, she intermittently received antibiotic drugs, corticosteroids, and gamma globulin infusions. Between 1976-1980 laboratory findings showed mild to moderate hypoalbuminemia (2.5-3.5g/dl), severe hypogammaglobulinemia with low or undetectable plasma titers of IgA and IgG. Liver-spleen scintiscan (99mTc sulfur-colloid) initially showed the spleen as reduced in size but repeat scintigraphy 2 years later showed nonfunction or asplenia. The platelet count fluctuated between $700x10^3$ and $1.375x10^3$/cu.mm. while the peripheral smear consistently revealed leukocytosis ($\sim$12,000/mm^3) with many atypical lymphocytes. In 1982 chest x-ray disclosed bilateral pulmonary infiltrates and right-sided pleural effusion (Fig. 3). Repeat liver-spleen scintiscan, ultrasonography and abdominal computed tomography each confirmed absence of the spleen (Fig. 4). Quantitative immunoelectrophoresis showed diffuse hypoglobulinemia (IgE — < .5g/dl; IgG — 4mg/dl; IgA — <1m/dl; IgM — 16mg/dl). Because of persistent albeit intermittent diarrhea, malabsorption studies were carried out. Whereas D-xylose absorption was normal, intravenous injecton of ^{51}Cr chloride (which binds to serum albumin) showed a 15.4% excretion in the stool (normal < 1%) and 25% in the urine (normal > 55%) (7) consistent with protein-losing enteropathy. This abnormality was consistent with 4 trials of gammaglobulin which yielded a protein half-life of only 5½ days (normal 21-28 days). Small bowel radiographs were unremarkable and jejunal biopsy showed microscopically only focal mucosal atrophy. Blood T/B lymphocytes revealed 67% T lymphocytes (helper 26%; suppressor 35%) and 8% B lymphocytes. Response to mitogens (phytohemagglutinin, concanavalin A, pokeweed) was decreased. Dorsal pedal lymphangiography revealed normal peripheral trunks (Fig. 3) but irregular, fine retroperitoneal lymphatics with absence of paraaortic nodes and a normal thoracic duct (Fig. 3). By 24 hours retroperitoneal contrast medium was virtually gone, and notably no nodes were seen. Aspiration of pleural fluid yielded a total protein of 3.1g/dl. No acid-fast bacilli were seen or cultured. Blood LE cells and ANA were negative. Because of persistent

right pleural effusion a pleurectomy was done in 1981 but recurrent ascites and peripheral edema persisted. Over the past several months she developed subacute bacterial endocarditis with multiple system emboli, progressive weight loss and died in extreme inanition. Autopsy confirmed near total absence of mediastinal and intra-abdominal nodes and extreme atrophy of the spleen.

DISCUSSION

Despite differences in clinical presenta-tion, the similarity and rarity of derange-ment in the lymphatic system including its "fixed" cellular elements (the nodes) and the spleen are so striking as to suggest a common pathologic process. Both patients exhibit complete involution of paraaortic lymph nodes, absence of the spleen, multi-ple serous and chylous effusions, and an ir-regular, fine network of retroperitoneal lym-phatics. Although congenital agenesis of the spleen is associated with a variety of other congenital anomalies (8), coexistent lymph nodal and truncal hypoplasia is ex-tremely rare (9). Moreover, lymphatic
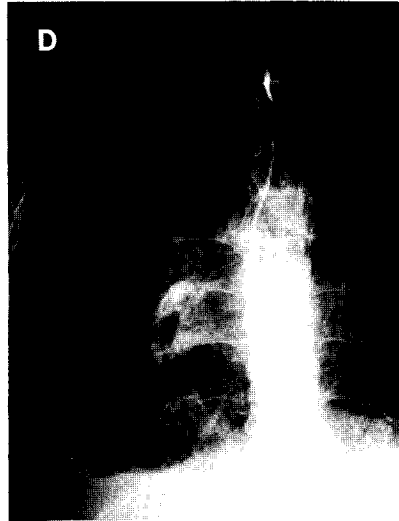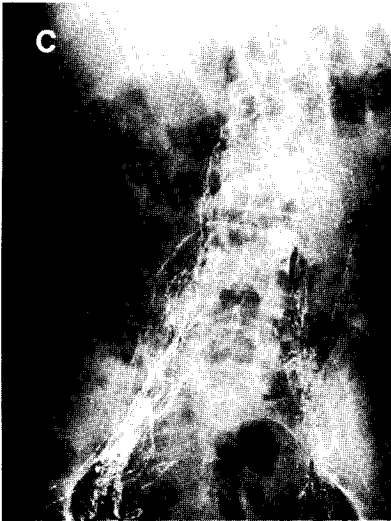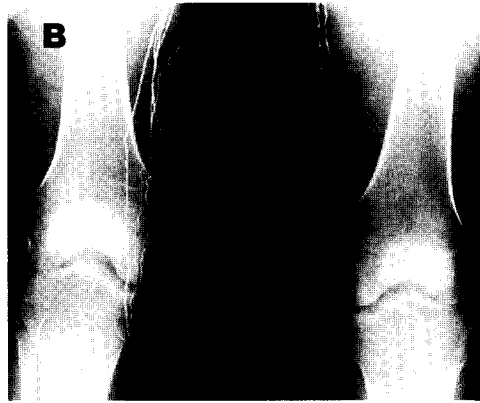

Fig. 3: Chest x-ray (A) and dorsal pedal lymphangiography (B-D) of 24-year-old woman with lung fibrosis and effusions (A), intact peripheral lymph trunks (B), absence of paraaortic lymph nodes with dysplastic retroperitoneal lymphatics (C) and normal thoracic duct (D).
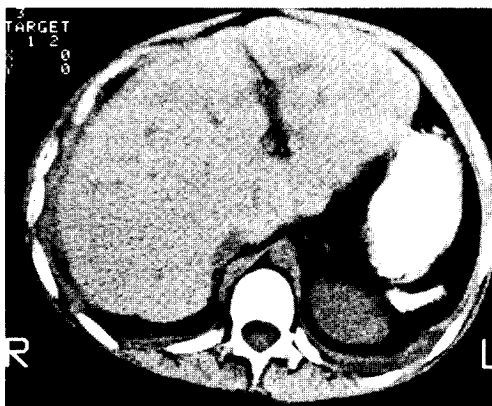
Fig. 4: Abdominal computed tomography (Patient 2) showing absence of the spleen, a finding confirmed by scintigraphy (technetium sulfur-colloid) and ultrasonography.

dysplasia most commonly occurs in the lower extremities with chronic lymphedema. Yet, peripheral edema in these adult patients was mild or absent and lymphangiography showed intact leg lymphatics. For these and other reasons the findings suggest an acquired etiology. Thus in patient 1, symptoms of effusion first appeared at 48 years, an unexpected time of onset for congenital nodal aplasia and lymphatic dysplasia. Prompt disappearance of intralymphatic contrast despite dysplastic channels also does not support retarded lymph flow or primary lymphedema. On the other hand, patient 2 despite a childhood onset originally displayed lymph node hyperplasia and presence of the spleen (albeit small) which over an 8-10 year interval was transformed into lymph nodal aplasia and asplenia. Anatomically, she, too, had fine irregular paraaortic lymphatics which nonetheless readily cleared contrast suggesting intact lymph flow. These findings differ from primary lymphedema syndromes, and it appears more likely that fluid extravasation from disrupted lymph ducts or abnormally permeable lymph nodes aggravated by mild to moderate hypoalbuminemia was responsible for intrathoracic and intraperitoneal effusions. Indeed in patient 2 this pathomechanism probably accounted for the protein-losing enteropathy despite the inability to visualize the leakage site on lymphography.

If the constellation of signs and symptoms are in fact acquired what is the likely underlying process? Progressive nodal aplasia and disappearance of the spleen strongly suggest acquired immunodeficiency and available data is consistent with this viewpoint. For example in AIDS (acquired immune deficiency syndrome commonly linked to homosexuality) initial clinical presentation is often lymph node hyperplasia (11). Later, however, during the course of the disease, inflammatory infiltration with progressive architectural disruption and cellular depletion culminates in involution of the thymus, lymph nodes, and spleen (12). The clinical picture then consists of profound immunosuppression and development of opportunistic infections and ultimately Kaposi's sarcoma and B cell lymphoma (11,12). Whereas patient 2 exhibited severe hypogammaglobulinemia and longstanding infectious complications, these derangements probably relate to ongoing intestinal loss of protein rather than defective antibody synthesis. To date, patient 1 has not manifest defective cell-mediated or humoral immunity despite notable lymph node aplasia and asplenia and thus the pathophysiologic explanation is still unclear. If, however, the findings represent a variant acquired immunodeficiency syndrome, progressively impaired immune surveillance increases the risk of opportunistic infection (which probably accounted for the death of patient 2) as well as occult malignancy (13).

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