

hemorrhage and/or purpura fulminans, occurring during the first two weeks of life. An increased risk of thrombosis in the fine blood vessels within the germinal matrix is probably associated with a risk of neonatal intracranial hemorrhage. In our patient, intracranial hemorrhage along with the recurrent miscarriage history of her mother strongly suggested the possibility of a thrombotic disorder.

Neonatal colonic perforation is extremely rare. A state of increased coagulability may be a significant factor in the pathogenesis of colonic ischemia [2]. Ischemic perforation in the colon has been reported in an adult patient with antiphospholipid syndrome [3]. Perioperative management of the patient was challenging because of the competing risks of bleeding and recurrent thrombosis. Administration of aPC concentrate seems appropriate for both the treatment and prophylaxis of thrombosis, without increasing the risk of bleeding [4].

It is challenging to screen for inherited protein C deficiency in neonates because their levels are lower than reference levels in adults. It may be useful to compare protein C and protein S levels, a low protein C and protein S ratio may be more diagnostic than low levels alone [5].

In conclusion, this case highlights the importance of recognizing congenital protein C deficiency in early neonates who experience intracranial hemorrhage or colonic perforation.

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## IgG4-related Disease at Rectovesical Pouch Mimicking Inflammatory Myofibroblastic Tumor

Fever of unknown origin frequently remains a diagnostic challenge. Immunological diseases account for about 20- 30% cases of these fevers. We report the case of a boy who presented with high fever for 2 months and was finally diagnosed as a case of IgG4-related disease at the rectovesical pouch.

**Keywords:** *Inflammation, Pyrexia of unknown origin, Positron emission tomography.*

**I**gG4-related disease is an immune-mediated chronic inflammatory condition characterized by tissue infiltration with lymphocytes and IgG4-secreting plasma cells with various degrees of fibrosis [1]. It is

a relapsing–remitting disease associated with a tendency to mass forming, tissue destructive lesions in multiple sites with systemic symptoms like fever and allergies.

A 9-year-old boy presented to us with intermittent fever for 2 months (102<sup>0</sup>-103<sup>0</sup>F, usually 2 peaks/day). Other than mild pallor, systemic examination was normal. Investigations showed hemoglobin of 8.2 g/dL, total leukocyte count 12.4x10<sup>9</sup>/L (Neutrophil 80%, Lymphocyte 10%) with persistently high C-reactive protein (270, 301 and 276 mg/L on three separate occasions done at an interval of 5 days) and elevated platelet count (820x10<sup>9</sup>/L). Serum ferritin was 657 ng/mL (Normal 7-84 ng/mL). Urea, creatinine, serum electrolytes, liver function test, Lactate dehydrogenase, uric acid, procalcitonin, and urine microscopic examination were normal; cultures showed no growth. Scrub typhus, tuberculin skin test, sputum for acid fast bacilli (AFB) and Cartridge based nucleic acid amplification test (CBNAAT), brucella IgM,

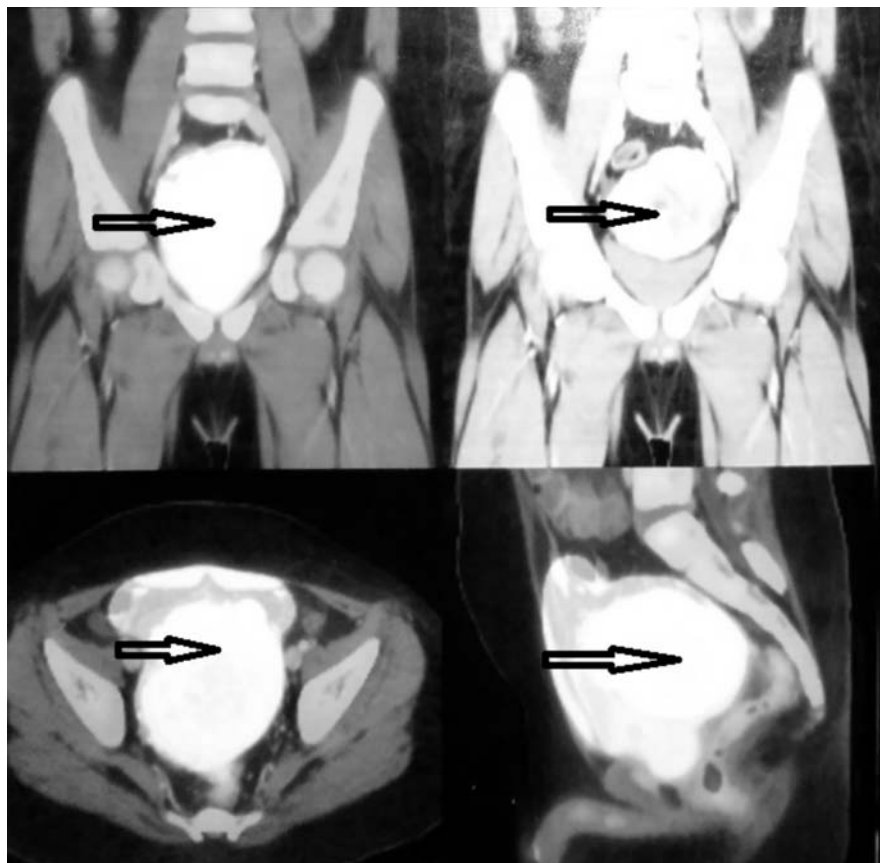
Epstein barr virus (EBV) VCA IgM, and parvo virus IgM were negative. Antinuclear antibody (ANA) was not raised. Chest X-ray, USG whole abdomen with color doppler of abdominal vessels and echocardiography were normal. Bone marrow aspiration and biopsy were also within normal limit.

Considering high levels of acute phase reactants, a whole body Positron emission tomographic scan (PET scan) was planned to find out any hot spot, especially to look for any occult malignancy. PET CT scan revealed a large lobulated mass (87 mm X 75 mm X 59 mm) in the rectovesical pouch with intense heterogeneous enhancement, increased fluorodeoxyglucose (FDG) uptake with central area of necrosis, preserved perilesional fat planes and without evidence of any distal metastasis (**Fig. 1**). Fine needle aspiration cytology (FNAC) showed interlacing spindle cells against a backdrop of dense chronic inflammatory infiltrate suggestive of an inflammatory myofibroblastic tumor and excision biopsy was planned.

Histopathology of the excision biopsy specimen showed interlacing fascicles of spindle cells and extensive storiform fibrosis associated with dense inflammatory cell infiltrate comprising of lymphocytes and many plasma cells, which were more around the blood vessels. Myofibroblastic cell proliferation and obliterative phlebitis were noted. IgG4 immuno-staining showed increase in IgG4 positive plasma cells (30-40/HPF). There was no nuclear atypia or increase in mitosis or atypical mitosis. Immuno-stain for CD34, beta catenin and anaplastic lymphoma kinase (ALK) were negative. The overall morphology was consistent with IgG4-related disease. Serum total IgG was 2270 mg/dL (cut off <1600 mg/dL) and IgG4 was 469 mg/dL (cut-off <135 mg/dL).

The fever subsided within 5 days of the complete surgical excision of the mass and he remains asymptomatic after 12 months follow-up.

IgG4-related disease is a spectrum of disorders previously appreciated as separate entities sharing



**FIG. 1.** PET-CT scan in coronal and sagittal plane shows a large lobulated necrotic mass (87 mm × 75 mm × 59 mm) at rectovesical pouch with increased FDG uptake.

particular pathologic, serologic and clinical features [1]. It should be suspected when there is an infiltrating mass involving one or more organs with signs and symptoms of inflammation, particularly when serum IgG level is very high and possibility of malignancy has been excluded. Pathogenesis of the disease is poorly understood. It is thought that both autoimmune and allergic mechanisms are central to the disease pathophysiology. Mainly Th2 cytokines like IL10 and TGF beta play a major role in the disease pathogenesis. Major presentation of this condition, which often affects more than one organ include: (i) autoimmune pancreatitis; (ii) sclerosing cholangitis; (iii) salivary and lacrimal gland enlargement; (iv) retroperitoneal fibrosis and related disorders; (v) thyroid diseases including Riedel's thyroiditis; (vi) lung and pleural diseases; and (vii) renal involvement causing tubulointerstitial nephritis [2]. Diagnosis is based upon characteristic biopsy findings with positive IgG4 staining. Serum IgG4 concentration and blood plasmablast concentration are other biomarkers for diagnosis.

Inflammatory myofibroblastic tumor, an uncommon benign tumor seen in children and young adults, usually is made up of myofibroblastic spindle cells. Common organs involved are lung, orbit, peritoneum and mesentery [3]. Diagnosis is based on the histology of the spindle cells and plasma cells rich in background that specifically stains with anaplastic lymphoma kinase-1 (ALK-1) [4]. Though some overlapping features of both the conditions with respect to clinical presentations, location of the lesions and gross histology confused the treating physicians initially, special staining with elevated serum IgG4 level finally helped in clinching the diagnosis.

All patients with symptomatic IgG4-related disease requires treatment and glucocorticoids are the first line agents. Immunosuppressives like rituximab, azathioprine and mycophenolate mofetil are used in steroid-resistant cases [5]. Surgery and radiotherapy are other modalities

of treatment. Prognosis has not been well defined. Majority responds well with standard treatment but most of them relapse subsequently. Some studies suggest an increased risk of malignancy but the issue remains controversial [6].

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