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INTESTINAL LYMPHANGIECTASIA IN CHILDREN (ILC)

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ABSTRACT

BACKGROUND: Primary Intestinal Lymphangiectasia (PIL) is a rare cause of protein losing enteropathy in children. To evaluate incidence, clinical and investigational profile and treatment outcome of PIL in children, the following study was conducted in a tertiary care center of North India.

METHOD: The children who attended pediatric gastroenterology OPD of PGIMER, Chandigarh from July 1993 to June 2003, with features of PIL, have adjusted. History, clinical examination, investigations (complete blood count, LFT, Lipid profile, USG whole abdomen, UGI Endoscopy, colonoscopy, immunoglobulins etc.) were reported. Secondary cause are carefully executed by echocardiography, wmc examination, CT are done depending upon causes. The patients were given low fat, high protein diet, MCT oil, octreotide, TPN etc. the patients were followed up till improvement of clinical figure and symptoms.

RESULTS: Five children (age 1 – 3 years) were admitted in pediatric gastroenterology ward of PGIMER from July 1993 to June 2003 with clinical feature of PIL. Bilateral pedal pitting edema of feet was present in all cases. USG whole abdomen showed thickened small bowel wall with dilating of loops in all cases. Central abdominal swelling, ascites was present in 4 cases. Severe mesenteric edema was present in 3 cases. Endoscopic abnormalities were scattered white plaques a presence of chyle like substances covering mucosa in all 5 cases. All 5 cases had located lesions in duodenum, upper jejunum. CT imaging should defuse modular small bowel wall thickening and edema, small bowel wall dilatation, "halo sign" lesions were patchy and restricted to duodenum and upper jejunum. Scintigraphy was not done. All 5 patients were gone diet modification, MCT oil, both enteral and praenteral nutrition. All responded very well to conservative management. Nobody needed surgery, lymphocytes, immunoglobulin, seen albumin which were care initially were restored to normal volume often treatment.

CONCLUSION: Primary intestinal lymphangiectasia (PIL) is rare but potential came of protein losing enteropathy. After careful exclusion of secondary cases PIL showed be properly investigated and management so that long term outcome becomes good.

KEYWORDS :

INTRODUCTION :

Intestinal lymphangiectasia (IL) is characterized by dilatation of intestinal lymphatics. It may be primary or secondary according to etiology. The clinical manifestations of IL are pitting edema, chylous ascites, pleural effusion, diarrhea, intestinal obstruction, lymphocytopenia, malabsorption, acute apendicytis etc. it is diagnosed by intestinal endoscopic biopsy. Dietary modification is mainstay of treatment. It is a rare benign disease. (1)

IL is characterized by focal or diffuse dilation of mucosal, subs mucosal and subserosal lumphatics. (2)

IL is an important cause of protein losing enteropathy. (3)

IL is also an important cause of extra intestinal lymphatic abnormalities. (4)

Primary IL is a congenital disorder of mesenteric lyphatics. (5)

IL can be secondary to diseases like constrictive pericarditis, lymphoma, sarcoidosis, scleroderma etc., (1)

A secondary cause must be ruled out by testing for proteinurio, rhenmatic, neoplastic or parasitic infection. (5)

Primary intestinal lymphangiectasia with typical endoscopic and pathological findings but without clinical symptoms has been reported. (5)

The clinical features of intestinal lymphangiectasia are pitting edema, diarrhea, lymphocytopenia, malabsorption intestinal obstruction, pleural effusion, chylous ascites, acute appendicitis etc. (6)

The most effective palliative treatment is lifelong dietary modification. (3)

Dietary fat intake limitation reduces chyle flow and protein loss. (1)
When enteric protein loss is stopped and protein level is brought within normal range, total parenteral nutrition with medium chain triglyceride is started. (1)

In case of secondary IL, treatment of underlying causes are curative. (2)

Lymphangiectasia is commonly seen in head, neck, axilla it rarely involves intestine.

Exact cause of primary IL is ****** some studies have shown that there are genetic mutations are found in IL in mice. Certain genetic mutations are related to lymphatic dysfunction. Certain genes are related to lymphatic system development. These are VEGFR3 (Vascular endothelial growth factor receptor 3), PROX I (Prospero related homebox transcriptional factor) and FOXC2 (forkhead transcriptional factor). (7)

In IL, there is obstruction and subsequent dilation of lymphatic vessels in submucosa of small bowel. (8)

Dilated lymph vessels may leak chyle into small bowel lumen and sometimes in peritoneal/pleural space causing chylous ascites or pleural effusion. (8)

Educative enteropathy causes lymphopenia, hypoalbuminemia, and low oncotic pressure producing pitting edema. (9)

Inability to absorb fat and fat soluble vitamins results in hypocalcemia.(1)

The worldwide incidence of intestinal lymphangiectasia is still unknown. It affects male and female equally. (1)

Primary IL usually presents in children and adolescents. (8)

But it can be present even in 30-40 yr of age. (3)

Episodic abdominal pain, steatorrhea, peripheral edema, ascites are common symptoms of primary intestinallymphangiectasia. (4)

Initially peripheral edema is intermittent. Later on it becomes permanent. (8)

Sometimes macular edema is seen in some patients. It can cause reversible blindness. (1)

Rarely lymphedema is seen in intestinallymphangiectasia. (9)

Lymphedema is less pitting than edema due to hypoproteinemia. Lymphedema is limited to lower limbs and bilateral. (9)

METHOD

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(complete blood count, LFT, Lipid profile, USG whole abdomen, UGI Endoscopy, colonoscopy, immunoglobulins etc.) were reported. Secondary cause are carefully executed by echocardiography, wmc examination, CT are done depending upon causes. The patients were given low fat, high protein diet, MCT oil, octreotide, TPN etc. the patients were followed up till improvement of clinical figure and symptoms.

RESULTS

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Severe mesenteric edema was present in 3 cases.

Endoscopic abnormalities were scattered white plaques a presence of chyle like substances covering mucosa in all 5 cases. All 5 cases had located lesions in duodenum, upper jejunum.

CT imaging should defuse modular small bowel wall thickening and edema, small bowel wall dilatation, "halo sign" lesions were patchy and restricted to duodenum and upper jejunum. Scintigraphy was not done. All 5 patients were gone diet modification, MCT oil, both enteral and praenteral nutrition. All responded very well to conservative management. Nobody needed surgery, lymphocytes, immunoglobulin, seen albumin which were care initially were restored to normal volume often treatment.

DISCUSSIONS:

Some studies have shown that intestinallymphangiectasia improved with Total parenteral nutrition (TPN) and medium chain triglyceride (MCT). (2)

Intestinal obstruction in IL is rare. Sometimes IL is diagnosed after examination of resected segment. (4)

Some patients of IL develop respiratory symptoms like cough, respiratory distress. It can be explained by pulmonary lymphangiectasia associated with IL. (10)

USG or CT scan of abdomen reveals halo or target sign which indicates thickened intestinal wall and ascetic fluid. (8) (9)

Small bowel barium study shows nodular mucosa and mild to moderate loop dilatation in more than 75% cases of intestinally mphangiectasia. (8)

Low serum Ig is seen in intestinallymphangiectasia. (9)

The diagnosis of pediatrics intestinallymphangiectasia is confirmed by endoscopic biopsy. (9)

Double balloon enteroscopy, multi-dot biopsy, pathological examination of small intestine showing dialated mucosal and submucosal lymphatic channels are helpful to diagnose intestinally mphangiectasia. (4)

Histopathology is hall mark of diagnosis of IL. It is identical in both primary and secondary forms. (2)

The dilated intestinal lymphatics may be seen in many villi or it may be seen in only few. (3) (9)

Lifelong dietary modification with low fat, high proteins, vitamin supplements, MCT oil is mainstay of treatment for primary intestinallymphangiectasia (PIL). (3) (4)

Enteral nutrition and TPN is useful for management of PIL. (8)

After normalization of serum proteins, enteral nutrition is to be maintained to prevent relapse. (1)

If dietary regimen is neglected, frequent relapses of chemical signs and symptoms are bound to occur. (6) Lifelong dietary modification is recommended. (1) (3) (6)

In a comparative study, one group who received MCT therapy in extreme feeding has 63% more improvement than those who did not take MCT. (5)

In a study, intermittent TPN was used with gradual tapering along with long term dietary control and regular monitoring. It was found that there was great improvement in both chemical and laboratory parameters. (6)

MCT oil has some problems. It has a strong odour. It is expensive, extremely flammable and it has tendency to smoke. (5)

If patient does not improve with diet modification, MCT therapy, then octreotide, a somatostatin analogue is considered. (3)

Long term octreotide therapy improves endoscopic and histological findings in primary intestinallymphangiectasia. (3)

The exact mechanism of action in intestinal lymphangiectasia is unknown. However, it is expensive. It requires parenteral administration. (3)

Fat soluble vitamin deficiencies are common in PIL. Oral fat soluble vitamin supplementation is an important part of management. (3)

For segmental lesions of IL, surgery is very useful. Local resection has been recognized as successful treatment. In our study all five cases responded to conservative medical treatment. (6)

For secondary type of intestinal lymphangiectasia, treatment of underlying causes are important. (2)

Intestinal lymphangiectasia is a form of secondary immunodeficiency. In case of recurrent infections, gamma globulin infusion is considered. (3)

Intestinal lymphangiectasia may be associated with wide spread viral wart, lymphoma which is presumed to be due to immune deficiency. It is not clearwhether IL can cause malignancy or not. When lymphone, pleural or pericardial effusion occur, prognosis is poor. (9)

Intestinal lymphangiectasia is a rare cause of protein losing enteropathy characterized by dilatation of Intestinal lymphatics and loss of lymph fluid into GI tract leading to hypoproteinemia, edema, lymphocytopenia, hypogamme Ilobulinemia, immunologic anomalies.

In primary Intestinal lymphangiectasia, protein losing enteropathy is due to mucosal damage leading to increased permeability to protein (usually not involving mucosal ulcerations).

Secondary cause of Intestinal lymphangiectasia are due to mucosal erotions or ulcers or secondary to mechanical lymphatic obstructions. (11)

Primary Intestinal lymphangiectasia (PIL) also called Waldman's disease is a rare disorder diagnosed before 3 yrs of age or adulthood presenting with protein losing enterpathy, hypoproteinemia, edema. It is thought to be congenital disorder with abnormal lymphatic drainage of small bowel lymphatic hypoplasia is thought to be cause of obstruction of lymph flow in intestinal. (12)

Itistopathological findings are characterized by presence of lacteal juice, dilated mucosal and sub-mucosal lymphatic vessels shown also in serosa. (9)

In our study all cases responded well to conservative therapy. Nobody needed surgery. several genes like VEGFR3, SOX18, Foxc2, CcBE I are responsible for lymphogenesis. Mutations of these genes are thought to be cause of lymphangiectasia. (9)

Secondary causes of Intestinal lymphangiectasia are cardiac conditions, lymphone mesenteric tuberculosis etc or associated conditions describes in literature (noonan, turner, kippel – Trenannay, Hennckam, non reckling hausen syndrome etc). (13)

Abdominal pain, cystic abdominal mass, diarrhea, edema are common signs and symptoms of PIL. (14)

Endoscopic abnormalities like scattered white plaques or presence of clyle like substances covering mucosa are observed in PIL. (15)

Intestinal lymphangiectasia, a rare cause of protein losing enteropathy is caused by congenital malformation or obstruction of lymphatic drainage. (9)

Factors causing elevated pressure of lymph drainage in intestinal wall can lead to dilatation and ever rupture of lymphatic vessels which may lead to leakage of lymphatic fluid. (16)

As lymphatic fluid contains lots of protein, fat and lymphocytes, leakage of lymph causes hypoproteinemia, lymphocytopenia and decreased serum levels of immunoglobulin. (17)

Primary Intestinal lymphangiectasia or Waldmann's disease was described for first time by Waldmann in 1961. (18)

Since then, less than 200 cases of primary Intestinal lymphangiectasia has been reported globally. (17)

In our study we got mesenteric edema in 3 cases. All five cases in our study had localized lesions in duodenum and jejunum.

Some researchers reported that 86% of diagnoses can be achieved by endoscopy alone and rest through other methods. Such as surgery, capsule endoscopy, double balloon enteroscopy rtc. (17)

Exclusion of long chain fatty acids prevents engorgement and rupture of malformed lymphatics while MCT has direct access to portal circulation. In case of poor response to treatment, total or partial parenteral nutrition, antiplasmin therapy, octreotide, corticosteroids, small bowel resection, albumin infusions, peritoneovenous (Levine) shunt and intestinal transplant. (6)

It is not clear whether malignancy, especially lymphoma is related to PIL. In a study it was found that 5% cases of PIL had malignant transformation of lymphoma after average duration of 31 yrs (from PIL onset to lymphoma mainly affects GI system (mainly stomach, small intestinal, ileum) but may affect retro peritoneum and mediastinum. (17)

Some observers noticed complete revision of signs and symptoms of IPL even withdrawing diet intervention. These patients tolerate full normal diet **** few years after diagnosis. (17)

Recurrent and opportunistic infections (e.g. streptococcus, Cryptococcus, CMV etc) can occur due to moderate or severe hypogammaglobulinemia and lymphopenia. (19)

Endoscopic biopsy of IPL shows dilated lymphatics in intestinal mucosa, lympho plasmacytic inflammation. Mild to moderate vilious injury with blunting and edema. Mild inflammation without lymphangiectasia can be seen in esophapeal, gastric, colonic biopsies. (20)

Recently CD55 deficiency with hyper activation of complement, angiopathic thrombosis and protein losing enteropathy (CHAPPLE syndrome) has been identified as monogenic form of PIL. (21)

99m technetium labeled human serum albumin (99m Tc – has) scintigraphy may show marked enhancement in bowel shows protein leakage in intestine in PIL.

The L-1 antitrypsin method has replaced 99m Tc – HsA scintigraphy which is costly, less readily available, potentially carrying infectious risk.

Ultrasonographic findings of PIL show dilatation of intestinal loops, regular and diffuse thickening of wall, plecal hypertrophy, severe mesenteric edema and in some case as cites.

CT images of PIL (both oral and IV contrast) show diffuse modular small bowel wall thickening and edema, small bowel wall dilatation, halo sign due to swelling and edema. CT is specially helpful to identify localized Intestinal lymphangiectasia.

At present lymphoscintigraphy (after subcutaneous injection of 99m Tc – antimony sulfide colloid) is not very useful methodology for PIL diagnosis because it has low sensitivity.

PIL patients have immunological abnormalities involving both B-cell and T-cell lineages of immune system. T-cell defect is characterized by lymphocytopenia, low CD4+ Tclhs, prolonged skin allograft rejection and impaired in vitro proliferative response to various stimulants (anti CD3, anti CD28). (9)

The differential diagnosis of PIL should be considered – these are constrictive pericarditis, intestinal lymphoma, lymphoenteric fistula, whipple's disease, ****** disease, sarcoidosis, intestinal tuberculosis, subtonic sclerosis, retroperitoneal fibrosis, HIV enteropathy. (15)

CONCLUSION:

Primary intestinal lymphangiectasia (PIL) is rare but potential came of protein losing enteropathy. After careful exclusion of secondary cases PIL showed be properly investigated and management so that long term outcome becomes good.

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