Colorectal cancer in patients with X-linked agammaglobulinaemia

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Primary immunodeficiency disorders can predispose to certain malignancies but hitherto no such relation has been established for X-linked agammaglobulinaemia (XLA). We have diagnosed rapidly progressive colorectal cancer in 3 unrelated young adults with XLA. We could find no explanation for the tumours. Since the calculated incidence of rectosigmoid cancer is increased 30-fold in patients with XLA, we advise the screening of these individuals, and perhaps people with other agammaglobulinaemias, for colorectal cancer.


Gastrointestinal ailments are common in patients with primary agammaglobulinaemia. Intestinal infections with Gabilia lambia, Campylobacter jejuni, and Salmonella spp are frequent. Giardiasis may lead to malabsorption, while C jejuni infection may result in recurrent fever. In late-onset agammaglobulinaemia (LOA), lymphonodular hyperplasia is common; the aetiology and pathogenesis of this abnormality are not known. Antral gastritis with abnormal gastrin production capacity is also a common finding in people with LOA, whose risk of developing gastric cancer is some 47-fold greater than that of the normal population. Malignant lymphoma is also 30 times more common in people with LOA. An increased risk of developing cancer is less well established for the other common types of agammaglobulinaemia (X-linked [XLA] and early-onset agammaglobulinaemia). Here we describe 3 unrelated patients with XLA who developed colorectal cancer at an early age.

Patient A was born in 1959 and agammaglobulinaemia was diagnosed at an early age. Our diagnosis of XLA was based on family history, absence of B lymphocytes, and very low serum concentrations of immunoglobulins (IgG 0-6 g/L, IgA and IgM not detectable). 3 brothers with the same disorder had died of pulmonary complications, and an affected male cousin survives. There was no family history of colorectal or other cancers. The patient did well on intramuscular gammaglobulin until October, 1984, when he complained of abdominal distension, cramps, and diarrhoea. During the next few months he lost 16 kg and he was cachectic when admitted to hospital in March, 1985. He was pale with a pulse rate of 100/min, but there were no other abnormalities on physical examination. He had a haemoglobin concentration of 6-9 mmol/L, macrocytic red blood cells, serum iron concentration of 1 mmol/L, and thrombocytosis (760 x 109/L). Serum albumin and IgG were 30 g/L and 1.3 g/L, respectively. A jejunal biopsy revealed complete villus atrophy, but no G lobia infection. A biopsy revealed complete villus atrophy, but no G lambia infection. 2 weeks after admission an acute abdomen with hyperperistalsis developed. An abdominal mass was palpated on rectal examination. Subphrenic gas was seen on a chest radiograph. At laparotomy, a nonresectable rectal carcinoma was found together with a perforation and carcinomatous peritonitis. An adenocarcinoma was some 47-fold greater than that of the normal population.

Malignant lymphoma is also 30 times more common in people with LOA. An increased risk of developing cancer is less well established for the other common types of agammaglobulinaemia (X-linked [XLA] and early-onset agammaglobulinaemia). Here we describe 3 unrelated patients with XLA who developed colorectal cancer at an early age.
What pathogenetic mechanisms could underly the development of these cancers? Cellular immunity in XLA is normal, but the absence of a functional mucosal-humoral immune system may lead to alterations in intestinal microflora. Increased susceptibility to any pathogens present in the gut may lead to chronic inflammation and dysplasia. Multiple courses of antibiotics might further modify the microflora, especially those organisms producing potentially carcinogenic substances. Intimate contact between those substances and the bowel epithelium would be possible, owing to the deficiency in mucosal immunoglobulins. The patient reported by Adachi et al.\(^1\) had 20 adenomatous polyps and 9 adenocarcinomas in his colon. Histological examination of the resected bowel of patient B also showed multiple foci of adenomatosis. Therefore, there may be increased susceptibility to colorectal cancer. Long-term abdominal symptoms or irregular bowel movements should not be dismissed as the benign gastrointestinal ailments to which patients with XLA are prone. Infection with an enteric pathogen such as \textit{C jejuni} may not be wholly responsible, and a more extensive diagnostic approach (endoscopic examination or barium enema) is indicated.

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