

Ionizing radiation in Crohn's disease

Patients with Crohn's disease (CD) necessarily require assessment using imaging techniques. This is mainly due to the fact that the clinical indices used to monitor CD, which incorporate clinical data and biological parameters, as is for instance the case with the Crohn's Disease Activity Index (CDAI), may underestimate true disease activity particularly in patients with penetrating forms. Furthermore, clinical activity indices do not correlate with endoscopic findings or serum markers, and inflammatory activity is commonly present in the bowel mucosa of patients with no symptoms (1). In addition, endoscopic images, usually considered the gold standard in the diagnosis of CD, identify neither transmural inflammation, a typical feature of CD, nor the presence of penetrating complications (fistula, abscess, fibrous tract), particularly when the mucosa has a normal appearance.

Not only are imaging techniques necessary at initial CD diagnosis, they are also routinely employed for clinical follow-up and complication assessment. Therefore, multiple imaging studies will be carried out in patients during the natural history of CD—abdomen X-rays, computerized tomography (CT), magnetic resonance imaging (MRI), ultrasounds, and fluoroscopic exams including gastrointestinal follow-through (GIFT) and opaque enema (2). All these studies, except MRI and ultrasonography, will expose patients with inflammatory bowel disease to ionizing radiation.

Exposure to ionizing radiation damages DNA, which is in turn associated with gene and chromosome mutations. Hence, the route through which ionizing radiation will favor the development of solid neoplasms does not differ from what is seen in the development of spontaneous tumors or tumors associated with exposure to other carcinogens (3).

Exposure to ionizing radiation in high doses has been shown to have significant consequences to human beings, including tumor induction. However, it must be remembered that long-term exposure to a given dose of radiation entails a lower risk *versus* sudden exposure. Up to 2% of tumors worldwide are thought to be associated with diagnostic radiation in the medical setting (4). When we also consider that inflammatory bowel disease both in itself and when combined with immunosuppressive agents induces a higher risk for solid tumors, the role of diagnostic radiation may have a greater impact than predicted on the possibility of neoplastic condition development in these patients.

As discussed in the paper reported in this issue of the present journal (5), a dose equal to or higher than 50 millisieverts (mSv) is thought to be associated with tumor development in the colon and urogenital tract (6). This dose is attained rather easily should we bear in mind that GIFT and abdominal CT release approximately 9 mSv per procedure. In a recent metaanalysis around 10% of patients with inflammatory bowel disease are believed to be exposed to doses equal to or higher than 50 mSv

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from diagnostic imaging techniques. As expected, risk is higher for patients with CD (around 11%) as compared to patients with ulcerative colitis (2%). In the paper reported by Ana Ciáurriz et al. (5) over 20% of patients had exposures above 50 mSv. Such data possibly derive from the inclusion of patients with very long-standing disease in this retrospective study -the cohort was started back in 1972, when new technologies such as ultrasounds and MRI played no role in the routine management of CD, and no problem awareness was in place to try and avoid ionizing radiation in these patients. However, I would like to underscore the fact that these results possibly reflect a situation most common in our setting.

When looking for risk factors associated with a higher exposure to ionizing radiation the need for corticoids as a marker for inflammatory activity and need for surgery stands out, which may be associated with to the presence of a higher number of complications and therefore more diagnostic testing both pre- and post-operatively (7).

Another factor that is worthy of note for tumor development is the delay between radiation exposure and tumor onset; evidence available indicates that fewer than 5 years may elapse between radiation exposure and tumor development, although 10 to 20 years is more common. In the present issue of the journal (5) similar risk factors are reported.

Ana Ciáurriz et al. (5) highlight a specific group of patients, namely those where CD started during childhood (less than 16 years of age). This subgroup of patients will not only have more severe forms for a longer term but also are more sensitive to the potential carcinogenic effects of ionizing radiation, being particularly prone to develop solid tumors as described in studies on pediatric populations (8,9).

Interestingly, while immunomodulators have been related to a higher risk for tumors, their use has also been associated with a lower risk of exposure to high-dose radiation, which leads to acknowledge that patients with better controlled disease need fewer diagnostic tests in order to measure disease activity and have fewer complications (7).

The best way to protect patients against potential radiation effects is to decrease exposure time. Thus, major guidelines published on CD management suggest that the classical GIFT approach be replaced by enteric MRI (2,10) given its higher diagnostic precision, which in addition to providing information on the intestinal lumen also reveals extraluminal involvement and CD complications, allowing for repeat follow-up testing in the absence of ionizing radiation. The development of ultrasonography and contrast-enhanced ultrasonography allows the use of these studies to monitor CD progression also in the absence of radiation. Another important goal in CD management today is limiting the use of CT scans, which represent around 10% of all radiation-emitting studies and two thirds of the whole radiation dose received by patients with CD (3). Therefore, whenever possible, CT should be substituted for by ultrasounds and enteric MRI; also, should CT be absolutely indispensable, methods to reduce radiation amounts, including novel low-radiation CT protocols (where milliamperes or kilovolts in the X-ray tube are decreased) should be used, which considerably reduce exposure while maintaining diagnostic accuracy (3). A notable fact that renders reduced exposure to radiation difficult is that up to 35% of CT scans for CD are estimated to take place in emergency rooms, where MRI is not available and ultrasounds are not enough to reach a definite diagnosis in patients with complicated CD. Repeat abdominal X-rays and radiographic studies for extraintestinal CD complications (arthropathy, nephrolithiasis, fractures, etc.) should also be taken into account.

In summary, we must bear in mind that besides clinical, serological and endoscopic data, repeat imaging studies are necessary to appropriately assess CD. Both clinicians

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and radiologists should expose patients with CD to the least amount possible of ionizing radiation, particularly those with more severe disease and earlier onset. The use of ultrasounds with or without a contrast medium, and of enteric MRI, must be incorporated into the routine management of this condition.

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