Caution with regard to exposure of ataxia telangiectasia patients and heterozygous carriers to ionising radiation

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Ataxia Telangiectasia (A-T) is a rare, recessive neurodegenerative, inherited disease (affecting 1 in 100,000 individuals) caused by mutations of the ATM gene located on chromosome 11 (1,2). The ATM protein is essential in the normal signalling and repair of DNA and chromosome breaks (3,4).

Homozygous patients suffer from ataxia telangiectasia syndrome with variable phenotype. A-T is also the genetic syndrome with the highest sensitivity to ionising radiation in humans and one of the highest predispositions to lymphomas (3 to 10 times higher than normal) (5,6). In the 1970s, total body irradiation of A-T patients systematically led to death after the first irradiation session (7).

Individuals carrying heterozygous mutations (approximately 1% of the general population) do not suffer from Ataxia Telangiectasia syndrome but a high predisposition to cancer (1 to 5 times higher than normal) (8). Although there have been no officially documented clinical cases of tissue radiosensitivity in heterozygous ATM mutation carriers, scientific literature would suggest the need for caution (9).

Recommendations for A-T homozygote patients

1- Radiotherapy: caution danger!

All exposure to therapeutic ionising radiation (radiotherapy) must be avoided. A recent fatal reaction was reported in the USA after a patient suffering from a hyper-IgM syndrome with a Wilms tumour died after radiotherapy. The autopsy revealed a homozygous mutation of the ATM gene (10).

2- Diagnostic radiology: caution!

One of the most popular beliefs is that because lower X-ray doses and energy levels are delivered during diagnostic radiology examinations than radiotherapy, patients carrying mutations of the ATM gene are at no risk during X-rays, mammograms and CT scans. However, the latest scientific research points to a nonlinear phenomenon of low-dose hyper-radiosensitivity, generally observed from 1 mGy to 500 mGy, where deleterious effects are aggravated for X-ray energies below 100 kV (levels used in radiology). A-T patients are specifically sensitive to this phenomenon (11,12). The high predisposition of A-T patients to cancers, and especially to radio-induced lymphomas means caution is also required to prevent them from developing. Non-radiating medical imaging techniques must be used (ultrasound, magnetic resonance imaging – MRI) and radiology examinations must be avoided as first-line diagnostic tools. However, if the patient’s life is at stake and radiodiagnostic methods are required, A-T specialists must be consulted during the decision-making process.
Recommendations for A-T heterozygote patients

Scientific literature is also extremely clear about the exposure of a large majority of heterozygous ATM mutation carriers to ionising radiation (8,9). Therefore exposure to ionising radiation for diagnostic purposes must also be justified and limited for heterozygous carriers.

In any case, it is strongly advised that physicians specialised in this often poorly understood disease be contacted before any decisions are made. Fatal errors have been made, often due to a lack of scientific information (10). Finally, please recall that during the 2009 International Conference organised by the French Nuclear Safety Authority (ASN), consideration of individual radiosensitivity to any exposure to ionising radiation was presented as a priority (13).

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References