

CASE REPORT

Characteristics of ischemic stroke secondary to radiation-induced arteriopathy: a single-centre brief report

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ABSTRACT

Objectives: This paper aims to assess lesion distribution and the role of other factors in the development of radiation-induced arteriopathy, in relation to the established consensus.

Methods: We retrospectively evaluated 15 patients with cervical arterial stenosis and prior head or neck radiotherapy admitted for suspected cerebrovascular ischemia or acute neurological symptoms. Data collected included demographics, cardiovascular risk factors, and vascular imaging.

Results: The cohort consisted of predominantly older males, with 86.7% presenting at least one cardiovascular risk factor. Latency to ischemia ranged widely from 10 months to 26 years. Hemodynamically significant lesions and severe stenoses were most pronounced at the carotid artery bifurcation, with relative sparing of the vertebral arteries. Notably, all 7 patients with documented neoplasm laterality experienced more severe carotid artery stenosis contralaterally, resulting in ischemia contralateral to the primary malignancy in 6 patients.

Conclusions: Radiation-induced arteriopathy exhibits pronounced vulnerability at the carotid bifurcation and highly variable latency, suggesting the absence of a clearly defined safe temporal window post-radiotherapy. These findings, alongside the high burden of traditional cardiovascular risk factors, support the need for long-term carotid surveillance in head and neck cancer survivors.

Keywords: radiation-induced arteriopathy, ischemic stroke, head and neck cancer, carotid stenosis, radiotherapy

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Introduction

While advancements in radiotherapy technology have significantly improved survival rates of head and neck cancer (HNC) patients, extended survival has increased the window for vascular complications to manifest. The literature shows a significant association between radiation-induced carotid artery stenosis (CAS) and the subsequent risk of ischemic cerebrovascular events (ICVE) [1]. Traditionally, radiation-induced CAS manifests after a latency of 5-10 years, with relative sparing of the vertebral arteries [2]. Some authors further suggest that standalone radiotherapy poses greater risk of vasculopathy compared to post-surgery radiotherapy [3]. This paper aims to assess lesion distribution and the role of other factors in the development of radiation-induced arteriopathy (RIA), in relation to the established consensus.

Methods

For this single-centre retrospective observational study, 15 patients were selected from the archives of the „Neurology I” clinic of the Emergency Clinical County Hospital of Târgu Mureș. The criteria for inclusion were: patients with cervical arterial stenosis and history of radiotherapy for HNC, admitted for acute treatment or re-evaluation of

suspected ICVE, namely ischemic stroke (IS) or transient ischemic attack (TIA), or acute neurological symptoms of suspected vascular origin, between November 2022 and October 2025, with complete medical history and documentation of vascular lesions. Exclusion criteria were incomplete or absent documentation of oncological history or vascular lesions.

With the approval of the hospital's ethics committee, the following data were collected:

- Demographics: sex and age
- Risk factors: cardiovascular, metabolic and habitual
- Oncological history: neoplasm type and location, treatment modalities
- Vascular assessment: standard computed tomography angiography and cervical Doppler ultrasound protocols

Given the limited number of patients, only descriptive statistics were performed using Microsoft Excel.

Results

Our group consists predominantly of older male patients. While 86.7% of the group presents at least one cardiovascular risk factor, only 13.3% suffered prior myocardial infarction [Table I]. Conversely, prevalence of metabolic risk factors was lower, present in 53.3% of patients, with only 13.3% displaying increased serum lipids at the time of admission [Table I]. Regarding prior therapy, 73.3% of

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patients were already under at least one class of cardiovascular medication at the time of ICVE [Table I]. Notably, 60% associated history of cerebral vascular pathology at the time of admission [Table I].

The numbers and percentages presented in each category of the tables below will be calculated from the total of 15 patients, unless otherwise specified in areas where specific data was missing from some patients' files.

Of 15 patients, 10 had documented histology of the primary HNC, all 10 being classified as carcinomas [Ta-

ble II]. Of 10 carcinomas, 7 were specified as squamous cell carcinomas and 1 as epidermoid [Table II]. While only 7 patients had neoplasm laterality documented, left-sided neoplasms were slightly predominant [Table II]. All patients in our group received multimodal therapy for HNC, the most prevalent adjacent to radiotherapy having been surgical treatment, performed on 73.3% of patients [Table II]. Only 1 patient in our group was still receiving immunotherapy for HNC at the time of admission for ICVE [Table II].

Table I. Patient characteristics

Variable category	Variable	Number	Percentage of patients/ (Range)
Demographics	Mean age $\pm$ SD (range)	69.1 $\pm$ 6.1 years	(58-81 years)
	Male	11 patients	73.3%
	Female	4 patients	26.7%
Cardiovascular risk factors	Hypertension	11	73.3%
	Ischemic Heart Disease	12	80%
	Congestive Heart Failure	5	33.3%
	Prior Myocardial Infarction	2	13.3%
	Valvulopathies	7	46.7%
	Atrial Fibrillation	5	33.3%
	Other arrhythmias	2	13.3%
	Peripheral vasculopathy	3	20%
	Diabetes Mellitus	5	33.3%
Metabolic risk factors	Impaired Fasting Glucose	1	6.7%
	Obesity	3	20%
	Dyslipidaemia ^a	2	13.3%
	Smoker ^b	2	13.3%
Neurological history	Cerebral small vessels disease	7	46.7%
	Cerebral atherosclerosis	2	13.3%
	Non-vascular cerebral pathology	6	40%
Cardiovascular medication	Antiaggregant	5	33.3%
	Anticoagulants	3	20%
	Statins	4	26.7%
	Antihypertensives	7	46.7%

^a Includes hypertriglyceridemia, ^b Includes active and former smokers

Table II. Characteristics of neoplasm

Variable Category	Variable	Number	Percentage/ (Range)
Histological type (of 10 documented)	Carcinoma of unspecified type	2	20%
	Squamous Cell Carcinoma (SCC)	3	30%
	Keratinized SCC	3	30%
	Infiltrative SCC	1	10%
	Keratinized epidermoid carcinoma	1	10%
Location	Oral cavity ^a	2	13.3%
	Oropharynx ^b	4	26.7%
	Nasopharynx	1	6.7%
	Hypopharynx and Larynx	5	33.3%
	Cutaneous (Facial)	3	20%
Laterality (of 7 documented)	Right	3	42.9%
	Left	4	57.1%
Additional oncological treatment	Chemotherapy	7	46.7%
	Surgery	11	73.3%
	Immunotherapy	1	6.7%
	Mean latency $\pm$ SD (range)	11.4 $\pm$ 2.5 years	(0.83-26)years

a – Tongue, Floor of mouth, b – Oropharynx, Tonsils, Palate

Of our 15 patients, 10 experienced IS, 4 experienced TIA and 1 experienced recurring loss of consciousness [Table III]. The latter does not have documented location of ischemia [Table III]. For the remaining 14, the most frequently incriminated cause for ICVE was ischemia in the territory of the middle cerebral artery, followed by the

carotid and posterior-inferior cerebellar artery [Table III]. Right-sided ischemia is slightly predominant at 57.1%, as opposed to 42.9% left-sided ischemia [Table III]. Regarding therapy, 40% of patients received some form of acute revascularization therapy, with 20% receiving delayed stenting/ endarterectomy and 40% being managed

conservatively [Table III]. Notably, of 7 patients with documented laterality of the primary neoplasm, 6 suffered ICVE contralateral to the HNC, while the seventh suffered recurring loss of consciousness, with no documented location of the ischemia [Table III].

The distribution of stenosis severity highlights pronounced vulnerability of the carotid artery (CA) bifurcation [Table IV]. This segment suffered most hemodynamically significant lesions, namely all documented total occlusions and the highest number of severe (70-94%) stenoses [Table IV]. Conversely, the vertebral arteries (VA) demonstrated relative sparing, presenting almost exclusively non-stenosing or mild disease, while no external carotid artery (ECA) lesion was documented [Table IV]. Notably, all 7 patients with documented laterality of the primary

HNC demonstrated more severe CAS contralaterally. Table IV highlights the identified lesion distribution and severity, as well as the number and percentage of patients that presented each lesion.

Ultrasound vascular assessment reveals predominantly fibrotic and calcified lesions rather than typical lipid-driven atherosclerosis [Table V]. The plaques are predominantly mixed or hyperechogenic, most present in the internal carotid arteries (ICA) and the left common carotid artery (CCA) [Table V]. Unstable, purely hypoechogenic plaques were notably rare across all assessed vessels [Table V]. Of the 3 patients with complete carotid occlusion, 1 exhibited hyperechogenic plaque, while the other 2 presented mixed plaque [Table IV].

Table III. Characteristics of ICVE

Variable Category	Variable	Number of patients	Percentage
Location (of 14 documented)	Middle Cerebral Artery	10	71.4%
	Carotid Artery	3	21.4%
	PICA	1	7.1%
Laterality (of 14 documented)	Right	8	57.1%
	Left	6	42.9%
Relation to neoplasm (of 7 documented)	Contralateral	6	85.7%
	Ipsilateral	0	0%
Type of ICVE	Ischemic Stroke	10	66.7%
	Transient Ischemic Attack	4	26.7%
	Syncope	1	6.7%
Therapeutic management	Conservative	6	40%
	Thrombolysis	5	33.3%
	Thrombectomy	4	26.7%
	Acute Stenting	3	20%
	Delayed Stenting	2	13.3%
	Endarterectomy (delayed)	1	6.7%

PICA – Posterior-Inferior Cerebellar Artery

Table IV. Severity of Stenosis in Assessed Vessels

Severity of Stenosis	Laterality	CCA	ICA	CA Bifurcation	ECA	VA
Non-stenosing lesion	Right	1 (6.7%)	0	3 (20%)	0	0
	Left	2 (13.3%)	0	1 (6.7%)	0	0
Mild (<50%)	Right	2 (13.3%)	1 (6.7%)	2 (13.3%)	0	0
	Left	2 (13.3%)	0	3 (20%)	0	0
Moderate (50-69%)	Right	0	1 (6.7%)	2 (13.3%)	0	0
	Left	1 (6.7%)	1 (6.7%)	2 (13.3%)	0	0
Severe (70-94%)	Right	1 (6.7%)	0	5 (33.3%)	0	1 (6.7%)
	Left	0	0	3 (20%)	0	1 (6.7%)
Near-occlusion (95-99%)	Right	0	0	0	0	0
	Left	1 (6.7%)	0	1 (6.7%)	0	0
Occlusion	Right	0	0	1 (6.7%)	0	0
	Left	0	0	2 (13.3%)	0	0
Stenosis of unspecified severity	Right	0	0	0	0	1 (6.7%)
	Left	0	0	0	0	1 (6.7%)

CCA – Common Carotid Artery, ICA – Internal Carotid Artery, CA- Carotid Artery, ECA – External Carotid Artery, VA – Vertebral Artery

Table V. Ultrasound Morphology of Vascular Lesions

Type of lesion	Laterality	CCA	ICA	CA Bifurcation	VA
Increased IMT	Diffuse	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)
Hypoechogenic plaque	Right	1 (6.7%)	1 (6.7%)	0	0
	Left	2 (13.3%)	1 (6.7%)	0	0
Hyperechogenic plaque	Right	2 (13.3%)	4 (26.7%)	1 (6.7%)	1 (6.7%)
	Left	0	1 (6.7%)	0	1 (6.7%)
Mixed plaque	Right	1 (6.7%)	5 (33.3%)	2 (13.3%)	0
	Left	4 (26.7%)	5 (33.3%)	0	0

IMT – Intima-Media Thickness, CCA – Common Carotid Artery, ICA – Internal Carotid Artery, CA- Carotid Artery, VA – Vertebral Artery

Discussions

There is no clear consensus as of yet regarding latency windows from radiotherapy for HNC to RIA, as some authors claim 5 to 10 years, while others report latency exceeding 6 years post-treatment [2, 4]. No maximal latency threshold, beyond which vessels are free of the effects of previous radiation, has been proven. However, recent studies have begun to show there is no hard minimum latency limit either, describing detectable vasculopathy 1 year post-radiotherapy, with one paper reporting vessel wall alterations one month post-treatment [4, 5]. Regarding latency from radiotherapy to ICVE, sources report similar findings; some quote ranges of 6 months to 20 years, while other studies report 0.3-78.3 months [6, 7]. Our findings are consistent with recent reports, the group's latency ranging from 10 months to 26 years.

Regarding lesion distribution, reports suggest that the CCA and ICA are most frequently affected, followed by the ECA and VA [5, 8]. Our findings correspond, as the most affected region in our group was the bifurcation of the CA, the bordering territory between the CCA and ICA, and the least affected was the ECA, which had no detectable lesions or stenosis in any patient from our group.

Regarding laterality, literature suggests that, even in unilateral radiotherapy, contralateral vessels receive residual scatter radiation, causing RIA [9, 10]. Radiation also potentially causes cytokine-induced systemic inflammation, which accelerates atherosclerosis and fibrosis [11]. Of 7 patients with documented HNC laterality, all experienced more severe CAS contralaterally, with 6 developing subsequent ICVE on the side with the greater CAS. Of these patients, 1 had suffered oral cavity carcinoma, 3 oropharyngeal and 3 facial. Although radiotherapy protocols were not documented, oral cavity and oropharyngeal carcinomas typically receive bilateral radiation, while cutaneous facial carcinomas traditionally require unilateral, localized radiotherapy. Thus, we hypothesize that the contralateral RIA of the former 4 patients may be the result of bilateral radiation fields, while scatter radiation and systemic endothelial inflammatory injury may be the cause of the contralateral RIA present in the latter 3. The systemic vascular injury caused by radiation may also potentially explain the association of peripheral vasculopathy in 3 out of the total 15 patients.

Regarding traditional cardiovascular risk factors, literature suggests age over 65, cardiovascular disease, dyslipidaemia and smoking play significant roles in radiation-induced CAS [7]. Our findings are consistent for the most part; thirteen patients present cardiovascular risk factors and ten are over 65, only one is an active smoker and two had dyslipidaemia at presentation.

Although previous reports suggest that upfront surgery reduces stroke risk by 23%, seven of ten stroke patients in our series (70%) underwent resection [12]. Our findings do not seem to support a protective effect of surgery in this small group; however, conclusions are limited by sample

size.

Regarding the ultrasonographic characteristics of RIA, recent literature describes increased intima-media thickness (IMT) as a specific feature of RIA and identifies hypoechogenic plaque as the primary predictor of carotid occlusion [13,14]. Conversely, another study reports that the main consequence of RIA is accelerated carotid plaque formation and stenosis, with minimal alteration of other flow-dependent hemodynamic parameters [15]. Regarding plaque echogenicity, one study suggests that RIA-associated plaques tend to be more calcified and hyperechoic than those of conventional atherosclerosis, which are predominantly lipid-rich and hypoechoic [16]. Our findings are only partially consistent with these reports: of 15 patients, only one showed increased IMT, while the majority presented mixed or hyperechoic plaques. Moreover, none of the 3 patients with complete carotid occlusion had hypoechoic plaque, which does not support the predictive role proposed in [13,14]. Again, these conclusions are limited by the small sample size.

Notably, one patient's history of radiotherapy for HNC, recurring syncope, tachycardia-bradycardia syndrome and hypertension may suggest radiation-induced afferent baroreflex failure (RABF). RABF represents an autonomic complication caused by radiation damage to the carotid sinus mechanoreceptors and glossopharyngeal fibres, resulting in pronounced hemodynamic volatility [17]. The patient has no documented autonomic function tests at time of investigation to confirm the suspicion.

Limitations

- This study is constrained by its retrospective observational design.
- The sample size is small, consisting of only 15 patients from a single clinical centre.
- There was no control group available.
- Statistical analysis was limited to descriptive statistics, due to the limited number of patients.
- Incomplete medical documentation hindered a comprehensive analysis, mainly:
 - Primary neoplasm laterality was only available for 7 of the 15 patients.
 - Specific radiotherapy fields, doses and treatment protocols were not documented.
- The clinical suspicion of radiation-induced afferent baroreflex failure in one patient could not be confirmed. This limitation was due to a lack of documented autonomic function tests at the time of investigation.

Conclusions

In this patient group, radiation-induced arteriopathy was most pronounced at the carotid bifurcation, with relative sparing of the vertebral arteries. Latency to ischemic cerebrovascular events was highly variable, ranging from under one year to more than two decades, underscoring the absence of a safe temporal window after radiotherapy.

Contralateral ischemic events predominated in patients with documented neoplasm laterality, though this observation is limited by the small sample size. The high burden of traditional cardiovascular risk factors suggests that radiation may act synergistically with pre-existing vascular vulnerability.

These findings support long-term carotid surveillance in patients treated with radiotherapy for head and neck cancer and warrant further investigation in larger prospective cohorts.

Authors' contributions

SC (Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing – original draft; Writing – review & editing)

ZB (Conceptualization; Supervision; Resources; Writing – review & editing)

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