Radiation optic neuropathy after external beam radiation therapy for acromegaly: report of two cases

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Abstract

For diagnosing radiation optic neuropathy (RON) ophthalmological and imaging data were evaluated from 63 acromegalic patients, irradiated between 1967 and 1998. Two patients developed RON: one patient in one optic nerve 10 years and another patient in both optic nerves 5 months after radiation therapy. RON is a rare complication after external beam radiation therapy for acromegaly, which can occur after a considerable latency period.

Keywords: Radiation optic neuropathy (RON); Acromegaly; Pituitary adenoma; Radiation therapy

1. Introduction

Acromegaly is an uncommon disease, mostly caused by a growth hormone (GH)-secreting pituitary adenoma. Surgery, drug therapy with somatostatin analogs and external beam radiation therapy are currently the available treatment options [8]. Postoperative radiation therapy is performed to reduce the time span of medical treatment, to normalise GH hypersecretion, and to prevent regrowth of residual tumour [10].

In the past decades, scattered reports on radiation optic neuropathy (RON) have appeared in the literature [4]. RON is usually defined as a sudden and profound irreversible vision loss due to damage of the optic nerves or damage of the chiasm caused by radiation therapy [7].

The aim of this retrospective study is to describe the occurrence of RON in a cohort of patients treated with radiation therapy for a GH-secreting pituitary adenoma.

2. Materials and methods

During the period 1967–1998, 80 patients with acromegaly were diagnosed at the University Hospital Groningen, The Netherlands. The diagnosis of acromegaly was based on the typical clinical features of acral enlargement and soft tissue swelling and was confirmed by appropriate laboratory tests. In all operated patients histological evaluation of the specimen confirmed the presence of a GH-producing pituitary adenoma.

In 1999 and 2000, a retrospective investigation was performed. The ophthalmological, surgical and radiation therapy data were reviewed. The time period 1967–1998 was chosen because data before 1967 were frequently incomplete. To be included in the present survey, time of follow-up had to be at least 18 months. The ophthalmological data obtained before treatment were available in all but two patients and after radiation therapy from all patients.

Of these 80 cases, 63 patients, who were treated with external beam radiation therapy, were included in our
survey. External radiation therapy was mostly performed at
the University Hospital Groningen ($n = 56$), but also in two
other regional institutions ($n = 7$), where equivalent
radiation therapy schedules were applied.

Before 1977 the neurosurgical procedures were cranio-
tomies only. Since 1978 the trans-sphenoidal approach was
the preferred method.

Visual acuity was measured with a Snellen acuity chart.
A visual acuity less than 0.8 was defined as impaired. Visual
fields were obtained with Goldmann kinetic perimetry. The
visual field data ($n = 1195$) of all patients at diagnosis, after
neurosurgery and/or radiation therapy were retrospectively
reviewed by one neuro-ophthalmologist.

We diagnosed RON using the criteria by Kline et al. and
Parsons et al. [7,9]:

Irreversible visual loss with visual field defects, indicating
optic nerve or chiasmal dysfunction.
Absence of visual pathway compression due to recurre-
rence or progression of tumour, radiation-induced
neoplasm, arachnoidal adhesions around the chiasm,
radiation retinopathy or any other apparent ophthalmo-
logical disease.
Absence of optic disc edema.
Optic atrophy within 6–8 weeks after onset of
symptoms.

Evaluation of RON was performed by review of visual
field, visual acuity and fundoscopic examinations in
combination with imaging of the sellar region.

The time span of follow-up was defined by the period
between the first day of radiation therapy and the last
ophthalmologic examination.

3. Results and discussion

Median age at the start of radiation therapy was 43 years
(range 19–64 years). Twenty-eight patients were males
(44%) and 35 patients were females (56%). Fourteen
patients were treated with radiation therapy alone. Forty-
ine patients were treated with a combination of radiation
therapy and surgery of whom 40 patients had one, five
patients had two and one patient had three operations before
radiation therapy. Two patients underwent surgery after
radiation therapy. One patient had radiation therapy in
between two pituitary operations. Median follow-up time in
the radiation therapy group was 84 months (range 18–250
months).

Total radiation therapy dose ranged from 45 to 55.5 Gy
(median dose 49.5 Gy). Median overall treatment time was
36 days (range 31–54 days). The daily fraction size varied
from 1.8 to 2.1 Gy in 55 patients (median dose 1.8 Gy). In
six patients the radiation therapy course was initiated with
gradually increasing doses between 1 and 2 Gy daily. From
two patients only the total dose was known, but we assume
that they were treated with an increasing daily dose as just
mentioned, which was standard between 1967 and 1974.
The most common dose and fractionation scheme used was
45 Gy in 1.8 Gy daily fractions ($n = 27$; 43%), mainly
performed in the time period 1985–1998. Fifty gray in 2 Gy
daily fractions, mainly performed in the time period 1974–
1984 was administered to 20 patients (32%). Eleven patients
received a total dose greater than 50 Gy; 10 of them had
been irradiated before 1981. In all patients all radiation
treatment fields were given every treatment day.

In the time period 1969–1978 the betatron with energy
18 MV HVD 17 mm PB was used in 13 patients; a five-
or seven-field technique was used with standard field sizes of 4
by 4 cm. Three patients were treated with a cobalt source,
energy 1.25 MV HVD 11 mm PB, a four-field technique
was used twice and a combination of an opposed lateral field
technique followed by a three-field technique was used
once. Treatment fields varied between 4 and 5 cm in lateral
or cranio-caudal dimension. From 1979 onwards patients
were treated on linear accelerators with 4 MV photons
($n = 2$), 6 MV photons ($n = 20$), 8 MV photons ($n = 24$)
and 10 MV photons ($n = 1$). A two-field opposed lateral
technique was used in seven patients, a three-field technique
in 12 patients, a rotation technique in one patient, a five-field
technique in 11 patients, a six-field technique in one patient
and a combination of above mentioned techniques in 15
patients; most of the time a combination of opposed lateral
fields followed by a five-field ($n = 11$) or a three-field
technique ($n = 3$). In the time period 1979–1989 the
treatment plan was normalised on the encompassing isodose,
aftewards according to ICRU [11]. Treatment-field
dimensions varied between 3 and 6 cm.

RON was diagnosed in two of the 63 irradiated patients
(3.2, 95% CI: 0.3–11.2%). In one patient RON was
unilateral (case 1) and in the other patient RON was
bilateral (case 2).

3.1. Case 1

A female, aged 52 years, underwent pituitary irradiation
in 1969, with a total dose of 55.5 Gy given in 54 days, with
an assumed daily dose 1–2 Gy, with 18 MV betatron
photons and a seven-field technique for a GH-producing
pituitary adenoma. At diagnosis of acromegaly and within
the first 10 years after radiation therapy no visual deficits
were reported. In 1979 she suffered sudden visual loss in the
left eye decreasing to light perception only. On fundoscopy
of the left eye, the optic nerve was atrophic. Goldmann
kinetic perimetry showed a central scotoma; the visual
functions of the right eye were normal. A CT-scan of the
pituitary fossa showed a residual intrasellar pituitary mass
without suprasellar extension.

Subsequent CT scans also did not reveal suprasellar
mass; she declined to undergo an MRI.
3.2. Case 2

The second patient, a 42 year old female, underwent a frontal craniotomy in 1968 because of a suprasellar pituitary adenoma. The optic nerves and the optic chiasm were embedded in the tumour, but pre- and postoperatively the visual acuity of both eyes was normal and there were no visual field defects. Six months later radiation therapy was started, because of persistence of GH hypersecretion. The radiation schedule was 50 Gy in 2 Gy daily fractions in 42 days. Eight megavolt photons and a three-field technique were used. Five months later, she complained of progressive visual loss, occurring within a few weeks. At ophthalmological examination the visual acuity of the left eye was 0.1 and was accompanied by a temporal hemianopsia. The visual acuity of the right eye was 1.0 with an altitudinal visual field defect in the upper quadrant. On fundoscopy there was bilateral optic atrophy. The visual field defect of the left eye did not change, but the visual acuity deteriorated gradually in a time span of 2 years to 1/60. The visual field defects of the right eye worsened in 1983 and 1988. In this eye the visual acuity changed to 0.7 in 1992 and 0.5 in 1995.

A pneumoencephalogram made in 1979 showed limited suprasellar extension of the pituitary adenoma with the optic system well demarcated in the suprasellar air thus excluding tumour recurrence. This finding strongly suggests that the visual deterioration in the left eye was due to radiation treatment. We assume by reviewing of all ophthalmologic data and exclusion of other causes, that the gradually worsening of vision in the right eye is also due to RON.

In the present series, two out of 63 irradiated patients (3.2%) developed RON. A total radiation dose greater than 50 Gy and/or a radiation fraction size greater than 2 Gy are suggested to be risk factors for RON [1,9]. One of the presently reported cases had a total radiation dose of 50 Gy and a radiation fraction size of 2 Gy. This would suggest the presence of other risk factors, associated with the development of RON after radiation therapy in GH-secreting pituitary adenoma. Apart from the probable risk attributable to vascular compromise [6,9], GH-secreting pituitary adenoma as such may confer an increased risk for RON development as previously suggested [1–3,5]. In case 2 of the present series the optic nerves and optic chiasm were embedded in the tumour, which may have been contributed to the development of RON.

It is generally proposed that most cases of RON occur within 18 months after radiation therapy [7]. Case 1 of the present series well illustrates that late development of RON can occur, indicating that the clinician should remain alert of this complication, even many years after radiation therapy.

RON is a rare complication after external beam radiation therapy for acromegaly, which may occur after a considerable latency period.

References