

Anti-mycobacterium treatment reverses cerebral radiation necrosis

Submission date 20/03/2013	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 18/04/2013	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 22/01/2019	Condition category Cancer	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Radiotherapy is used to treat a wide variety of head and neck tumors that arise in and around the skull base. Radiation-induced injury may occur when exposure of adjacent normal nervous system tissue to radiation is unavoidable. Acute injury is usually mild and transient, but the delayed radiation injury (DRI) of normal brain can be a devastating complication and generally occurs months to years after the initiation of therapy. DRI is generally progressive and irreversible, and have a tremendous negative impact on a patients quality of life. The mechanism of DRI is not well understood . DRI can occur even when the most stringent measures are taken to avoid exposing healthy tissue to harmful levels of radiation. To date, the treatment of DRI has typically been management of symptoms.

Nasopharyngeal carcinoma (NPC) is one of the most common malignant tumors that affects the southern Chinese population. Temporal lobe necrosis (TLN) is one of the most dreaded DRI complications in NPC after external radiation. Evaluation of the temporal lobes in patients previously treated for NPC can provide a better understanding of DRI in the brain unaffected by the underlying tumor outside of the planned field of radiation.

In 2008, we used anti-mycobacterium therapy (AMT) to treat a symptomatic TLN patient suffering headache and dysphasia, accompanied with pulmonary tuberculosis as evidenced by positive chest X-ray test. The AMT provided an unexpected symptom relief to TLN. Based on this experience, we have developed a trial protocol to evaluate whether AMT can reverse the disease in both symptoms and MRI abnormality.

Who can participate?

The study involves NPC patients who had undergone radiation therapy, suffering bilateral temporal lobe necrosis. The age ranges from 18 to 65 years old.

What does the study involve?

Participants belong to one of two groups: active treatment group or control group. In the AMT active treatment group, all former treatments with corticosteroids were discontinued for patients prior to AMT initiation.

In the control group, treatments were conducted with routine practices.

What are the possible benefits and risks of participating?

The main risks of treatment group are injuries to liver function and stomach. The treatment is carried out under extensive observation.

Where is the study run from?

The study is conducted at the First Affiliated Hospital of Sun Yat-sen University, Guangzhou (China)

When is the study starting and how long is it expected to run for?

January 2009 to June 2014.

Who is funding the study?

Grants from the Guangdong Natural Science Foundation (China).

Who is the main contact?

Prof. Yanqing Feng

fyqgz@vip.sina.com

Contact information

Type(s)

Scientific

Contact name

Prof Weixi Zhang

Contact details

58, Zhongshan 2 Road

Guangzhou

China

510080

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weixizhang@qq.com

Additional identifiers

Study information

Scientific Title

Effects of anti-mycobacterium treatment on temporal lobe necrosis following radiotherapy for nasopharyngeal carcinoma: a prospective, controlled study

Study objectives

The mechanisms of radiation-induced delayed brain injuries (DRI) remains poorly understood, and treatment with corticosteroids, surgery, and antioxidants is often ineffective. The aim of this study is to investigate whether temporal lobe necrosis, a severe type of DRI, can be reversed by anti-mycobacterium therapy (AMT).

Ethics approval required

Old ethics approval format

Ethics approval(s)

The SUN Yat-sen university ethics committee approved the study. The approval number is 2012 (06). The date of approval is 18-Dec-2012. All patients were informed of the potential short- and long-term drug complications of AMT. Written informed consent was obtained from patients who agreed to participate in the study.

Primary study design

Interventional

Study design

Prospective non-randomized controlled single-center study

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Delayed brain radiation injury/temporal lobe necrosis/oncology

Interventions

In the AMT active treatment group, all former treatments with corticosteroids were discontinued for patients prior to AMT initiation. Our initial treatment protocols (Treatment First Phase) comprised amikacin (600 mg/day) and mannitol 125 ml (bid) for 2 weeks, together with a three-drug AMT regimen (per day: isoniazid 8 mg/kg, rifampicin 10 mg/kg, pyrazinamide 25 mg/kg). Followed by treatment with a three-drug AMT regimen for nine months (Treatment Second Phase). And then by treatment with a combination of isoniazid and rifampicin with the same dosages that ceased after 24 months (Treatment Third Phase).

In the control group, treatments were conducted with routine practices including steroids, IVIG, Hyperbaric oxygen (HBO), nerve growth factor, and mannitol alone or combination during the observational period.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

The Activities of daily living (ADL) were adopted to assess subjects neurological status. ADL were assessed by the Barthel Index (BI) (0100 scale, with lower scores denoting less independence in activities of daily living)

Key secondary outcome(s)

Evaluation by MRI tests

Completion date

30/12/2014

Eligibility

Key inclusion criteria

Patients who fulfilled the following eligibility criteria were recruited in this study:

1. Aged 18 to 65 years
2. Histopathologically proven cases of NPC who had undergone radiation therapy, with negative brain MR before RT
3. Patients must have received cranial irradiation $\geq$ 6 months prior to study entry
4. MRI evidence of bilateral temporal lobe edema and/or necrosis with or without foci of contrast enhancement on MRI
5. Evidence of progressive neurologic signs or symptoms related with TLN

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria

Patients were excluded if they had:

1. Significant hepatic or renal insufficiency
2. Evidence of brain metastasis, brain abscess, any intracranial tumor, cerebral infarction, demyelinating disease
3. Clinical manifestations such as fever, meningeal irritation signs indicating meningitis

Date of first enrolment

01/01/2009

Date of final enrolment

30/12/2014

Locations**Countries of recruitment**

China

Study participating centre

58, Zhongshan 2 Road

Guangzhou

China

510080

Sponsor information

Organisation

Sun Yat-sen University (China)

ROR

<https://ror.org/0064kty71>

Funder(s)

Funder type

Research organisation

Funder Name

Guangdong Natural Science Foundation (Grant nos.2012B03180067), China

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2014	22/01/2019	Yes	No