QUESTION 2

A 42yo man with acromegaly undergoes transphenoidal pituitary surgery for a growth hormone-secreting macroadenoma. Six months post-op he has an elevated insulin-like growth factor type I (IGF-I) concentration. A repeat MRI scan reveals a residual and inoperable tumour confined to the right cavernous sinus only.

Which of the following is the most appropriate management?

A. Expectant management  
B. Radiotherapy  
C. Bromocriptine  
D. Octreotide  
E. Cabergoline

GROWTH HORMONE

Reference: http://www.colorado.edu/kines/Class/IPHY3430-200/17endo1.html

Growth hormone:

- mobilises fatty acids from adipose tissue  
- opposes action of insulin on glucose metabolism  
- increases muscle growth
IGF-I:
- produced in liver
- promote DNA synthesis and cell multiplication

ACROMEGALY
- Almost always caused by somatotroph adenoma
- Associated with increased morbidity and mortality
- Almost all patients should be treated

Features:
- Overgrowth of cartilage and collagen-containing tissues
  - Frontal bossing
  - Deeply furrowed creases on face
  - Growth of lower jaw and laryngeal cartilage
  - Broad, thick hands
  - Thickened heel pads
  - Skin tags
  - Shiny, sweaty skin
- Symptoms
  - Headache
  - Sweating
  - Poor bite
  - Arthritis
  - Carpal tunnel
  - Symptoms of hypopituitarism
- Can develop
  - Cardiovascular disease, cardiomyopathy, hypertension
  - Respiratory disease, sleep apnoea
  - Arthropathy
  - Neuropathy
  - Malignancy, colonic polyps
  - Glucose intolerance or diabetes

Autonomous secretion of GH is demonstrated by lack of suppression by glucose

Treatment:
- Aim is to lower serum IGF-1 concentration to within the reference range for pt's age and gender and to lower serum GH concentration to < 1ng/mL (1mcg/L) as measure after glucose load
- If IGF-1 level normalised then life expectancy is close to normal
- Also aim to rid pt of symptoms without causing hypopituitarism
- GH cannot often be returned to completely normal
- Metabolic symptoms (s/a diabetes mellitus) often improve
- Bone and joint symptoms usually persist

Trasphenoidal Surgery
- Treatment of choice in pts with somatotrophs that are
Medical Therapy

Used when surgery alone has not reduced GH and IGF-1 to normal.

1) Somatostatin analogs
   - Octreotide, lanreotide
     - Analogs of growth-hormone-inhibitory hormone (somatostatin)
       - Inhibit GH secretion
     - Octreotide binds to specific receptors for somatostatin and its analogs
     - Octreotide has long acting forms (monthly IM injection) and short acting forms (tds s/c injection)
       - Both can be increased if initial response inadequate
     - Should lead to normalisation of IGF-1 and GH and reduced adenoma size and reduced soft tissue swelling and improved insulin sensitivity, LV function improves, sleep apnoea improves
     - Normalisation of bloods occurs in 40 to 75% of pts
     - Can consider combination with cabergoline if not effective alone
       - Side effects: nausea, abdo discomfort, bloating, diarrhoea, fat malabsorption – tends to resolve in few weeks
     - Octreotide reduces postprandial GB contractility and delays GB emptying so 25% of pts get asymptomatic cholesterol gallstones or sludge in 1st 18/12 of Rx

2) Dopamine agonists
   - Cabergoline (better than bromocriptine)
     - Inhibit GH secretion
     - Not as good as somatostatin analogues
     - Oral form
     - Reduced GH and IGF-1 to near normal in ~40% of pts
     - Not very effective at reducing adenoma size

3) GH receptor antagonist
   - Pegvisomant
     - Used if no response to other treatments
     - Blocks native GH from binding
     - Cannot use serum GH to monitor effectiveness of Rx
- Normalises IGF-1 in 97% of pts
- Potentially increases adenoma size due to increase GH concentration
- Side effects: elevated liver enzymes, avoid in pts w abnormal LFTs
- Combination w somatostatin analogue is good

4) XRT
- Used for pts who have failed surgical and medical Mx
- Stops adenoma growth
- Slow decline in GH secretion, slow clinical improvement
- Hormone deficiencies relatively common
- Other complications: cranial nerve palsies, loss of vision, memory deficits (all rare), increased incidence of other intracranial tumours

Long-term Monitoring

1) 3-4/12 GH and IGF-1 after glucose
2) Other pituitary hormones yearly
3) Adenoma size on MRI – yearly at first
4) Visual field assessments if close to chiasm
5) Colonoscopy every 3-4 yrs in pts > 50 (increased risk of polyps)
6) Regular cardiovascular check-up