On the Origins of Pituitary Apoplexy

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Abstract
This paper sketches the early history of pituitary apoplexy, a disorder later fully described in 1950 by Brougham, Heusner and Adams. Haemorrhage or necrosis in an adenoma causes a characteristic sudden drowsiness, stupor or coma, headache and stiff neck, ocular palsy, and impaired acuity with visual field loss owing to optic nerve or chiasmal compression. The associated endocrinopathy and management are described.

Clinical observations [8] of pituitary disorders were however published before this time though the endocrine symptoms were often unexplained. For example, in the 16th century, the Dutch surgeon, Johannes Wier (or Weyer) (1515–1588), recognized gigantism [9] and acromegaly (before Pierre Marie’s (1853–1940) classical account in 1886 [10]). Acromegaly is also plainly depicted in the 1801 work of Nicolas Saucerotte (1741–1814) [11]. Vincenzo Brigidi in 1877, reported early macroscopic and microscopic descriptions of pituitary tumours in acromegalic patients [12]. Pituitary gigantism was described in Irish giants, Cornelius Magrath (1736–1760), Patrick Cotter (1760–1806) and Charles Byrne (1761–1783) [13]; Byrne was later shown to harbour an aryl hydrocarbon-interacting protein gene (AIP) mutation [14].

A new and rare complication of haemorrhage into the gland producing dramatic symptoms was recorded by Pearce Bailey (1865–1922) (fig. 3) in 1898 in a man with acromegaly presenting with sudden headache, vomiting, fever, visual loss and ocular palsy. Postmortem showed bleeding into an intrasellar adenoma [15]. But only sparse case reports were subsequently published, until in 1950 Brougham, Heusner and Adams provided a meticulous, clinicopathological account of 5 patients. They coined the name 'pituitary apoplexy' [16], a term embracing both an acute clinical presentation and haemorrhage or necrosis with expansion of the gland. The growth rate of the neoplastic cells was thought to outstrip the vascular supply (fig. 4). They could find only 5 pathologically verified ex-
amples in the literature and at least 2 other clinically sug-

gestive cases [16].

Historically, after Pearce Bailey, Leopold Bleibtreu,
physiologist in Bonn, in 1905 recorded the postmortem
examination of a 21-year-old acromegalic patient in
whom he discovered that the pituitary gland had been re-
placed by a mass of orange-coloured, amorphous mate-
rial representing an old haemorrhage. Clinical details
were not given [17].

Kux reported in 1931 an eosinophilic adenoma with
acromegaly and headache. While under observation there
was a sudden amblyopia, palsy of one of the internal rec-
tus muscles and a drowsiness which quickly progressed
to coma and, 2 days later, death. At autopsy, a gross haem-
orrhage in a ‘fetal adenoma’ of the pituitary gland was
found. The haemorrhage had enlarged the tumour and
had compressed structures in the cavernous sinuses and
floor of the 3rd ventricle [18].

A similar case was reported by Dingley of a 37-year-old
clerk who died suddenly while climbing stairs on a bus. Autopsy showed a previously asymptomatic chromo-
phobe adenoma with both old and large, fresh haemor-
rhages.

In 1938, Voss described a 38-year-old man who pre-
sented in a lethargic state with complete right ophthal-
moplegia, a dilated, fixed left pupil, stiff neck and xan-thochromic CSF. Autopsy disclosed a fresh haemorrhage
into a chromophobe adenoma [19].

Coxon in 1943 reported a patient with a sudden onset
of severe headache followed 24 h later by diplopia and
drowsiness. He died 3 weeks later and a large haemor-
rhage was found in an eosinophilic adenoma. In this case,
the CSF was clear and acellular, but the total protein con-
tent was 170 mg/100 ml [20].

Many more instances have been recognized since CT
and MR imaging became available [21].

Pituitary apoplexy is uncommon. It occurred in 0.6 to
10% of pituitary adenomas [22]: two thirds are males,
with a mean age of 57 years. Perhaps surprisingly pitu-
itary apoplexy can be asymptomatic, since 14–26% of
patients with adenomas at surgery or imaging have signs of old haemorrhage or necrosis, without past symptoms. Further, at presentation about 60% have no previously recognized symptoms of an adenoma.

Although pituitary apoplexy [23] occurs spontaneously in pre-existing pituitary adenomas in most cases, hypertension pregnancy, bromocriptine, hypothalamic releasing hormones for preoperative testing [24], pituitary irradiation, and heart surgery have been identified as precipitating factors.

Haemorrhage or necrosis in an adenoma causes the sudden onset of a characteristic syndrome of drowsiness, stupor or coma, headache and stiff neck, ocular palsies (70%) and impaired acuity with visual field loss (75%) owing to optic nerve or chiasmal compression. Increased intracapsular pressure favours ischemia and thrombosis. Once infarction has occurred, the tumour may become haemorrhagic and swells rapidly like a soaked sponge [25].

At presentation, there is laboratory evidence of deficient gonadotrophin (76%), corticotrophin (60%), prolactin (40%), and thyrotrophin (57%); and at follow-up about 80% have evidence of hypopituitarism [5].

The cerebrospinal fluid is usually abnormal [16, 25] showing blood or xanthochromia. But a pleocytosis can occur if blood leaks into the suprasellar cisterns through the diaphragma sellae into the CSF and can simulate infective meningitis [26].

MRI and CT imaging techniques [27] and the debated indications for surgery [6] are described in the UK guidelines [28]. Most patients treated either surgically or conservatively recover their decreased visual acuity, visual fields and ocular palsy [5, 23]. However, patients with severely impaired visual acuity, severe or deteriorating visual field defects or deteriorating level of consciousness should be considered for trans-sphenoidal pituitary decompression, preferably within the first 8 days [27].

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References