On the Origins of Pituitary Apoplexy

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Key Words

Pituitary apoplexy · Pituitary adenoma · Haemorrhagic necrosis · Meningism

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.

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Between 1912 and 1938, Harvey Cushing (1869–1939) [1] published 5 books about his unrivalled study and treatment of 2023 brain tumours. Approximately 70 years before his seminal monograph, *The functions of the pituitary body* [2], and his account of its surgery (fig. 1 and 2) [3], the German embryologist Martin Heinrich Rathke (1793–1860) gave one of the earliest descriptions of the pituitary gland [4]. He described the embryonic structure, known as Rathke's pouch, from which the anterior lobe of the pituitary gland develops. But its functions and histological pathology were not known until basophilic, eosinophilic and chromophobe adenomas were demarcated in the late 19th century [5–7].

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-

Fig. 1. The pituitary body and its disorders.

amples in the literature and at least 2 other clinically suggestive 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 replaced by a mass of orange-coloured, amorphous material 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 rectus muscles and a drowsiness which quickly progressed to coma and, 2 days later, death. At autopsy, a gross haemorrhage in a 'fetal adenoma' of the pituitary gland was found. The haemorrhage had enlarged the tumour and

Fig. 2. The pituitary and its dyscrasias.

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 chromophobe adenoma with both old and large, fresh haemorrhages.

In 1938, Voss described a 38-year-old man who presented in a lethargic state with complete right ophthalmoplegia, a dilated, fixed left pupil, stiff neck and xanthochromic 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 haemorrhage was found in an eosinophilic adenoma. In this case, the CSF was clear and acellular, but the total protein content 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 pituitary apoplexy can be asymptomatic, since 14–26% of

PEARCE BAILEY

Fig. 3. Pearce Bailey (1865–1922) from Wikimedia commons. This image (or other media file) is in the public domain because its copyright has expired.

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

Fig. 4. Schematic diagram, portal circulation of anterior pituitary.

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].

Disclosure Statement

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References

- 1 Pearce JMS: Harvey Williams Cushing (1869–1939). *J Neurol* 2000;226:1–2.
- 2 Cushing H: The functions of the pituitary body. *Amer J Med Sci* 1910;139:473–484.
- 3 Cushing H: *The Pituitary Body and Its Disorders*. Philadelphia, Lippincott, 1912.
- 4 Rathke MH: Ueber die Entstehung der Glandula Pituitaria. *Berlin, Archiv fur Anatomie, Physiologie und Wissenschaftliche Medicin*, 1838, pp 482–485.
- 5 Dott NM, Bailey P: A consideration of the hypophysial adenomata. *Br J Surg* 1925;13:314–366.
- 6 Sibal L, Ball SG, Connolly V, James RA, Kane P, Kelly WF, Kendall-Taylor P, et al: Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. *Pituitary* 2004;7:157–163.
- 7 Collin R: *La Neurocrinie Hypophysaire. Etude Histophysiologique du Complexe Tubéro-Infundibulo-Pituitaire*. Paris, Gaston Doin et Cie, 1928, pp 1–102.
- 8 Pearce JM: Pituitary tumours and acromegaly (Pierre Marie's disease). *J Neurol Neurosurg Psychiatry* 2002;73:394.
- 9 Wier J: *Medicarum observationum; in Virgo Gygentea ex Quartana Reddita*. Basel, Switzerland, Oporinus, 1567, pp 7–10. Cited by Chahal et al. *Neurosci J Hist Neurosci* 2006;15:269–275.
- 10 Pierre M: Sur deux cas d'acromegalie. Hypertrophie singuliere no congénitale des extrémités supérieures, inférieures et cephalique. *Révue Médicale Française* 1886;6:297–333.
- 11 Pearce JM: Nicolas Saucerotte: acromegaly before Pierre Marie. *J Hist Neurosci* 2006;15:269–275.
- 12 Brigidi V: *Studii Anatomopatologica Sopra un Uomo Divenuto Stranamente Deforme per Chronica Infirmata. Societe Medico-Fisica Fiorentina*, 1877.
- 13 De Herder WW: Familial gigantism. *Clinics (Sao Paulo)* 2012;67(suppl 1):29–32.
- 14 Chahal HS, Stals K, Unterländer M, Balding DJ, Thomas MG, Kumar AV, et al: AIP mutation in pituitary adenomas in the 18th century and today. *N Engl J Med* 2011;364:43–50.
- 15 Bailey P: Pathological report of a case of acromegaly, with special reference to the lesions in the hypophysis cerebri and in the thyroid gland; and a case of haemorrhage into the pituitary. *Philadelphia Med J* 1898;1:789–792.
- 16 Brougham M, Heusner AP, Adams RD: Acute degenerative changes in adenomas of the pituitary body: with special reference to pituitary apoplexy. *J Neurosurg* 1950;7:421–439.
- 17 Bleibtreu L: Ein fall von akromegalie (zerstörung der hypophysis durch blutung). *Munch Med Wochenschr* 1905;52:2079–2080. Cited by Brougham et al. [16].
- 18 Kux E: Über ein bösesartiges pinealom und ein bösesartiges fötales adenom der hypophyse. *Beitrag Path Anat* 1931;87:59–70. Cited by Brougham et al. [16].
- 19 Voss O: Beitrag zur Hirnblutung an der Schädelbasis: intrakranielle basale Blutungen. *Deutsch Z Chir* 1938;250:727–735.
- 20 Coxon RV: A case of haemorrhage into a pituitary tumour simulating rupture of an intracranial aneurysm. *Guy's Hosp Rep* 1943;92:89–93.
- 21 Shimon I: *Clinical Features of Pituitary Apoplexy*. Springer Berlin Heidelberg, 2014, pp 49–54.
- 22 Mohr G, Hardy J: Haemorrhage, necrosis and apoplexy in pituitary adenomas. *Surg Neurol* 1982;18:181–189.
- 23 Turgut DM, Mahapatra AK, Powell M, Muthukumar N (eds): *Pituitary Apoplexy*. Springer-Verlag Berlin Heidelberg, 2014.
- 24 Riedla M, Clodia M, Kotzmanna H, Hainfellner JA, Schimac W, et al: Apoplexy of a pituitary macroadenoma with reversible third, fourth and sixth cranial nerve palsies following administration of hypothalamic releasing hormones: MR features. *Eur J Radiol* 2000;36:1–4.
- 25 List CF, Williams JR, Balyeart GW: Vascular lesions in pituitary adenomas. *J Neurosurg* 1952;9:177–187.
- 26 Valente M, Marroni M, Stagni G, Floridi P, et al: Acute sterile meningitis as a primary manifestation of pituitary apoplexy. *J Neurosurg* 1984;14:363–373.
- 27 Randeve HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA: Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinol (Oxf)* 1999;51:181–188.
- 28 Rajasekaran S, Markey A, Plant G, Powell M, Sinha S, Wass J, et al: UK guidelines for the management of pituitary apoplexy. *Clin Endocrinol (Oxf)* 2011;74:9–20.