|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference**  **Supplementary Table: Clinical characteristics and treatment outcomes of all published case reports of ACTH-secreting pituitary carcinoma between 1947-2020 (Shen A, Yates CJ, Colman P. Table summarising the currently published case reports of ACTH secreting pituitary carcinoma. doi:10.26188/13311962 (2020).)** | **Age / Sex** | **Tumour size at Dx** | **Year of diagnosis** | **Latency**  **(year)** | **Clinical feature** | **Ki67 in PA** | **Ki 67 in PC** | **Radiotherapy** | **Site of Metastases** | **Treatment** | **Outcome** |
| Forbes [1] | 43 F |  | 1947 |  |  |  |  | Yes | -Liver | Surgery | Deceased after 2 years |
| Feiring [2] | 48 F | Macro | 1942 | 3 | -Headache  -Vision disturbance  -Amenorrhoea | n/a |  | Yes (3 times) | -Large frontal lobe metastases  -Corpus collosum  -Pons | Craniotomy x 2 | Deceased 3 years later |
| Feiring [2] | 32 F | Macro | 1943 | 2 | -Cushingnoid features  -Weight gain (15kg)  -Amenorrhoea | n/a |  | Yes (4 times) | Multiple cerebral masses on post mortem autopsy | Craniotomy x 2 | Deceased 4 years after PC - mycotic aneurysm of abdominal aorta |
| Feiring [2] | 25 M | Macro | 1949 | 1.5 | -Lethargy  -Hypogonadism with erectile dysfunction  -Right eye diplopia and ptosis | n/a |  | Yes (3 times) | -Cerebral hemispheres (post mortem autopsy)  -Pons | Right trans-frontal Craniotomy | Deceased 9 months post PC diagnosis |
| Sheldon [3] | 26 F | Micro | 1949 | 1 | -Headache  -Weight gain,  -Infection,  -Hypertension  -Osteoporosis | n/a |  | No | -Liver (post mortem) | No | Deceased after 1 month |
| Salassa [4] | 42 M | Macro | 1951 | 2 | -Visual field deficit  -Cushingnoid features | n/a |  | Yes | -Spinal cord (post mortem)  -Liver (post mortem) | Bilateral adrenalectomy at diagnosis  Craniotomy | Deceased 2 years later |
| Moore[5] | 21 M |  | 1976 | 9 |  |  |  | Yes | -Cerebral cortex  -Spinal cord  -Liver (autopsy) | Adrenalectomy | Deceased 3 years after |
| Kaiser [6] | 17F | Macro | 1974 | 5 | n/a | n/a |  | Yes | -Liver  -Lung  -Bone | Craniotomy  Bilateral adrenalectomy (initially)  -Chemotherapy with cyclophosphamide, 5-FU, adriamycin | Alive with metastases at 6 year follow up |
| Zafar [7] | 60 M |  | 1984 |  |  | n/a |  | Yes | -Pons  -Spinal cord (post mortem) |  | 60 M |
| Gabrilove [8] | 37 M | Macro | 1967 | 5 | -Cushingnoid feature  -Proximal myopathy  -Osteoporosis,  -Hypertension | n/a |  | No | -Frontal lobe  -Spinal cord  -Cardiac  -Liver  -Pancreas | Bilateral adrenalectomy (initial) | Deceased after 10 months |
| Nawata [9] | 53 M | Macro | 1978 | 2 | -Bitemporal hemianopia | n/a |  | Yes | -Liver  -Lung | Craniotomy | Deceased after 4 months |
| Tonner [10] | 52 F | Macro | 1985 | 3 | -Cushingnoid feature,  -Hypertension | n/a |  | Yes | -Left cerebellum  -Anterior fossa (post mortem autopsy) | TSR x 1  Ketoconazole | Deceased 9 months post PC diagnosis |
| Frost [11] | 33M |  | 1981 | 10 |  |  |  |  | -Spinal | Spinal surgery x 1 | Deceased 4 years |
| Garrao [12] | 47 F | Macro | 1981 | 14 | n/a | n/a |  | Yes | -Bone | Surgery x 2 | Deceased after 4 months |
| Lormeau [13] | 18 F | Macro | 1985 | 8 | -Amenorrhoea  -Hypokalemia | n/a |  | Yes (twice) | -Liver | TSR x 4  Bilateral adrenalectomy after TSR x 1 | Alive at 2 year follow up  ACTH elevated |
| Pernicone [14] | 37M |  |  | 17 |  |  |  | Yes (twice) | -Spine  -Liver | Craniotomy  Surgical resection of PC | Deceased after 12 months |
| Pernicone [14] | 48F |  |  | 18 |  |  |  | Yes (twice) | -Bone |  | Deceased after 6 months |
| Pernicone [14] | 65F |  |  | 5 |  |  |  | Yes | -Spine | Craniotomy  Surgical resection of Spine lesion | Deceased after 1.5 years |
| Pernicone [14] | 69F |  |  | 11 |  |  |  | Yes (twice) | -Cerebral  -Spine | Craniotomy  Surgical resection | Deceased after 3 months |
| Pernicone [14] | 70M |  |  | 8 |  |  |  | Yes | -Cerebral  -Spine | Craniotomy | Deceased after 1.5 years |
| Nose-Alberti [15] | 22F | Micro | 1998 | 0.3 |  |  |  |  | -Liver | TSR x 1 | Deceased after 4 months |
| Kemink [16] | 22 F |  | 1962 | 33 |  |  |  | Yes | -Cerebral (autopsy)  -leptomeningeal | Adrenalectomy  Supra-sphenoidal surgery x 2 | Deceased 12 month |
| Masuda [17] | 59 M | Macro | 1995 | 2 | -Headache  -Blindness | 30% | 25% | No | -Lung  -Spinal cord  -Liver (autopsy)  -Midbrain (autopsy) | TSR x 1 | Deceased 3 months |
| Zahedi [18] | 40 F | Macro | 2001 | 2 | -T2DM  -Amenorrhoea,  -Weight gain 15kg |  |  | Yes (twice) | -Cervical LN | TSR x2  Ketoconazole 4month  Neck dissection  Bilateral adrenalectomy | Alive at end of the study |
| Landman [19] | 14 F | Micro | 1979 | 13 | -weight gain  - emotional instability | n/a |  | Yes | -Cranial (frontal lobe and pons) | - craniotomy  - bilateral adrenalectomy | - Hypopituitarism (cortisol, thyroid, gonadal)  - Remission in 2002 (follow up period 21 years) |
| Suzuki [20] | 61yF | Macro | 1994 | 4 | -Bi-temporal hemianopia |  |  | Yes | -Liver | TSR x 1  metyrapone | Alive at 2 year follow up |
| Tysome [21] | 11 M | Macro |  | 16 | -Visual disturbance |  |  | Yes | -Craniospinal  -Liver | Craniotomy x 2  Bilateral adrenalectomy  Spinal metastases resection | Alive 12 month follow up |
| Sivan[22] | 45 F | Macro | 1993 | 9 | n/a | n/a |  | No | -Spinal  -Liver  -Breast | TSR x 4 | Deceased 1.5 years |
| Pinchot [23] | 59 F | Macro | 2003 | 2 | -Diplopia |  |  | Yes | -Liver | Endoscopic trans-nasal resection x2  Ketoconazole  Bilateral adrenalectomy 2005 | Deceased 1 month |
| Bode [24] | 45F |  | 2004 | 6 |  | n/a |  | Yes | -Cerebral  -Spinal | Bilateral adrenalectomy  Medical therapy  Temazolomide  Pasireotide  Cranial surgery x 2 | Alive at 9 months |
| Curto [25] | 42 M | Macro | 2004 | 4 | -T2DM,  -Osteoporosis  -Weight gain  -Hypertension | 2% | 18% | Yes | -Cerebral  -Spinal | TSR x 1  Craniotomy x2  temazolomide | Alive at 17th months |
| Moshkin [26] | 38M | Macro | 1990 | 18 |  |  |  | Yes | -Spinal | TSR x 5  Craniotomy x 2  Temazolomide with no response  Bevacizumab | Alive at 16 months |
| Annamalai [27] | 65 F | Macro | 2006 | 2 | -Headache  -Bilateral 3rd nerve palsy | <1% | 5-15% | Yes | -Liver | TSR x 1  Metyrapone / ketoconazole  Temazolomide  Bilateral adrenalectomy | Alive at follow up 4 years |
| Arnold [28] | 48 F |  |  | 8 | -Headache  -Right 3rd nerve palsy  -Menstrual disturbance |  |  | Yes (3 times) | -Spinal (cauda equina)  -Neck | TSR x 2  Spinal surgery x2  Temazolomide 12 mth | Alive at 12 months follow up |
| Cornell [29] | 40 M | Macro | 1997 | 14 | Asymptomatic | 5-7 % | 80% | YEs | -Cerebral  Liver  -Leptomeningeal | TSR x4  Temazolomide  Cabergoline  Cisplatin/etoposide | Deceased within 12 months |
| Kovacs [30] | 16 F | Macro | 1993 | 13 | -Amenorrhoea  -Weight gain (30kg)  - Bi-temporal hemianopia | 5-10 % | 15-20% | Yes (3 times) | -Periparotid  -Adrenal  -Liver | TSR x 8  Yttrium-DOTATOC treatment  Bilateral adrenalectomy | Deceased after 12 months |
| Miller [31] | 37 F | Macro |  | 11 | -Headache  -Vision loss |  |  | Yes | -Cerebral  spinal | TSR x 1  Craniotomy x 3  Temazolomide | Deceased after 3 years |
| Shastri [32] | 27F | Macro |  | 8 | -Amenorrhoea  -Weight gain  -Hirsutism | 4% | 9% | Yes | -Cerebral | TSR x 3  Right craniotomy x 2  ketoconazole | Deceased after 4 years |
| Mendola [33] | 58 M | Macro | 2008 | 6 |  | 10% |  | Yes | -Liver  -Vertebral  -Meningeal | Multiple surgery  Ketoconazole / DA (ineffective)  Bilateral adrenalectomy  Temazolomide (result in haemorrhage) | Deceased within 12 months of follow up |
| Takeuchi [34] | 47M |  | 1998 | 9 |  |  |  | Yes | -Spinal (cauda equina) | Transnasal surgery (multi for initial tumour)  Spinal surgery | Alive at 2 year follow up |
| Borba [35] | 55F | Macro | 2008 | 2 |  | < 5% | 5-10% | Yes | -Liver | TSR (initial tumour) x 4  Ketoconazole | Deceased 1 month |
| Wang [36] | 26 M |  | 1992 | 16 | n/a |  | 4% | No | -Spinal  -Cerebral | TSR x 1 initial  Spinal metastasis resection x 2  Craniotomy x 1 | Alive at 17 months follow up |
| Bengtsson [37] | 51 M |  |  | 1.3 |  |  | 80 | Yes | -Liver | Operations x 3  Adrenalectomy  Capecitabine  Temozolomide | Deceased 8 months after starting Temozolomide |
| Bengtsson [37] | 62 M |  |  | 5.1 |  |  | 10 | Yes | -Intraspinal  -Bone  -Liver | Operations x 3  Adrenalectomy  Dopamine agonist | Alive at 14 months follow-up |
| Bengtsson [37] | 70 M |  |  | 1.2 |  |  | 70 | Yes | -Bone  -Liver | Operation x 1  Ketoconazole | Deceased |
| Amy [38] | 52F | Macro | 2013 | 2 | -T2DM  -Visual disturbance  -Headache | 4% | 20% | YEs | -Liver  -Cerebral | TSR x 2  Pasireotide  mifepristone  Liver metastases resection  Temozolomide/capecitabine | Alive at 2 years |
| Bengtsson [39] | 53 M | Macro | 2015 | 1.5 | -Cushingnoid feature | 40% |  | Yes | -Liver  -Bone | TSR x 2  Ketoconazole/metyrapone  Bilateral adrenalectomy  Temozolomide/Capecitabine | Deceased after 6 months |
| Casar-Borota [40] | 35 M | Macro |  |  |  |  |  |  |  |  |  |
| Casar-Borota [40] | 39 F |  |  |  |  |  |  |  |  |  |  |
| Touma [41] | 63M | Macro |  | 0 | -Visual disturbance | 50% |  | No | -Lung | -TRS x 1  - Temozolomide  -Currently with bevacizumab | Alive at 5 years |
| Guo [42] | 55M | Macro |  | 5 | -Vision changes | < 1% | 80% | Yes | -Cerebral  -Lung | TRS x 2 for adenoma  Temazolomide | Alive at 3 months |
| Lin [43] | 35F | Macro | 2011 | 5 | -Right 3rd nerve palsy  -Weight gain  -Hirsutism |  | 50% | Yes | -Liver | TSR x 4  Pasireotide/ ketoconazole/ cabergoline  Temazolomide/capecitabine  Mifepristone/metyrapone  Bilateral adrenalectomy  Ipilimumab/nivolumab | Alive at 6 months follow up |
| Yoo [44] | 43 M | Macro |  | 4 | - T2DM (10 year)  - Right 3rd nerve palsy & visual disturbance (one week) | 5-10% | 15-20% |  | -Cervical LN (9/27)  - Liver | TSR x 2  Left neck dissection  Bilateral adrenalectomy  Temozolomide (TMZ) x 6 cycle of 5 day course | Recurrence of liver metastasis on PET scan  Consideration of immunotherapy |
| Yoo [44] | 67 F | Macro |  |  | -Headache | 15% | 20-25% | Yes | -Clivus & sphenoid sinus  -Right petrous apex & Meckel’s cave  -Left neck region (level II B and V) | - TSR x 3  - temazolomide 10 cycle | - Total follow up period 8 years  - Pan-hypopituitarism  - Trial with nivolimumab |
| Alshaikh [45] | 40F | Micro |  | 9 | -Cushingnoid feature | 5% |  | No | -Liver | TSR x 2  Somatostatin receptor analogue |  |
| Alshaikh [45] | 49F | Micro |  | 11 |  | 10% |  | YEs | -Liver  -Spine  -Bone | TSR x 3  Bilateral adrenalectomy  Temazolomide  Everolimus/sunitinib / bevacizumab | Deceased after 7 years |
| Flores [46] | 45 F | Macro | 2013 | 4 |  | 8-12% |  | Yes (3 times) | -Liver  -Bone  -Left adrenal | TSR x 2  Pasireotide  RFA liver lesion | Alive at 14 months |
| Rotman [47] | 51M | Macro | 1996 | 14 | -Cushingnoid feature | 15% |  | Yes (twice) | -Cerebral | TSR x 1  Ketoconazole  Craniotomy  Temozolomide (12 months)  Bevacizumab (2 years) | Alive at 8 years  hypopituitarism |
| Majd [48] | 35M | Macro |  | 4.5 | -Cushingnoid feature |  |  | Yes | -Liver  -right orbit  -Cerebral | Surgeries x3  Temozolamide  Capecitabine  Bilateral adrenalectomy  FGFR-targeted treatment  Pembrolizumab | Alive at 118 months |
| Majd [48] | 20s F | Macro |  | 3.8 |  |  |  | Yes | -Cerebral  -Bone  -Lung  -Liver | Surgeries x 2  Bilateral adrenalectomy  Temozolamide  Capecitabine  Pembrolizumab | Alive at 30 months |

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