|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 diagnosisCraniotomy | 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 | CraniotomyBilateral 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 1Ketoconazole | 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 4Bilateral adrenalectomy after TSR x 1 | Alive at 2 year follow upACTH elevated |
| Pernicone [14] | 37M |  |  | 17 |  |  |  | Yes (twice) | -Spine-Liver | CraniotomySurgical resection of PC | Deceased after 12 months |
| Pernicone [14] | 48F |  |  | 18 |  |  |  | Yes (twice) | -Bone |  | Deceased after 6 months |
| Pernicone [14] | 65F |  |  | 5 |  |  |  | Yes | -Spine | CraniotomySurgical resection of Spine lesion | Deceased after 1.5 years |
| Pernicone [14] | 69F |  |  | 11 |  |  |  | Yes (twice) | -Cerebral-Spine | CraniotomySurgical 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 | AdrenalectomySupra-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 x2Ketoconazole 4monthNeck dissectionBilateral 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 2Bilateral adrenalectomySpinal 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 KetoconazoleBilateral adrenalectomy 2005 | Deceased 1 month |
| Bode [24] | 45F |  | 2004 | 6 |  | n/a |  | Yes | -Cerebral-Spinal  | Bilateral adrenalectomyMedical therapyTemazolomidePasireotide 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 1Craniotomy x2temazolomide | Alive at 17th months |
| Moshkin [26] | 38M | Macro | 1990 | 18 |  |  |  | Yes | -Spinal | TSR x 5Craniotomy x 2Temazolomide 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 1Metyrapone / ketoconazoleTemazolomideBilateral 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 2Spinal surgery x2Temazolomide 12 mth | Alive at 12 months follow up |
| Cornell [29] | 40 M | Macro | 1997 | 14 | Asymptomatic  | 5-7 %  | 80% | YEs | -CerebralLiver -Leptomeningeal | TSR x4Temazolomide CabergolineCisplatin/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 8Yttrium-DOTATOC treatmentBilateral adrenalectomy | Deceased after 12 months |
| Miller [31] | 37 F | Macro |  | 11 | -Headache-Vision loss |  |  | Yes  | -Cerebralspinal | TSR x 1Craniotomy x 3Temazolomide  | Deceased after 3 years |
| Shastri [32] | 27F | Macro |  | 8 | -Amenorrhoea-Weight gain-Hirsutism | 4%  | 9% | Yes | -Cerebral | TSR x 3Right craniotomy x 2ketoconazole | Deceased after 4 years |
| Mendola [33] | 58 M | Macro | 2008 | 6 |  | 10%  |  | Yes | -Liver-Vertebral-Meningeal | Multiple surgeryKetoconazole / DA (ineffective) Bilateral adrenalectomyTemazolomide (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 4Ketoconazole  | Deceased 1 month |
| Wang [36] | 26 M |  | 1992 | 16 | n/a |   | 4% | No | -Spinal-Cerebral | TSR x 1 initialSpinal metastasis resection x 2Craniotomy x 1 | Alive at 17 months follow up |
| Bengtsson [37] | 51 M |  |  | 1.3 |  |  | 80 | Yes | -Liver | Operations x 3AdrenalectomyCapecitabineTemozolomide | Deceased 8 months after starting Temozolomide |
| Bengtsson [37] | 62 M |  |  | 5.1 |  |  | 10 | Yes | -Intraspinal-Bone-Liver | Operations x 3AdrenalectomyDopamine agonist | Alive at 14 months follow-up |
| Bengtsson [37] | 70 M |  |  | 1.2 |  |  | 70 | Yes | -Bone-Liver | Operation x 1Ketoconazole | Deceased |
| Amy [38] | 52F | Macro | 2013 | 2 | -T2DM-Visual disturbance-Headache | 4% | 20% | YEs | -Liver-Cerebral | TSR x 2PasireotidemifepristoneLiver metastases resectionTemozolomide/capecitabine | Alive at 2 years |
| Bengtsson [39] | 53 M | Macro | 2015 | 1.5 | -Cushingnoid feature | 40% |  | Yes | -Liver-Bone | TSR x 2Ketoconazole/metyraponeBilateral adrenalectomyTemozolomide/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 adenomaTemazolomide | Alive at 3 months |
| Lin [43] | 35F | Macro  | 2011 | 5 | -Right 3rd nerve palsy-Weight gain-Hirsutism  |  | 50% | Yes | -Liver | TSR x 4Pasireotide/ ketoconazole/ cabergolineTemazolomide/capecitabine Mifepristone/metyraponeBilateral adrenalectomyIpilimumab/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 2Left neck dissectionBilateral adrenalectomyTemozolomide (TMZ) x 6 cycle of 5 day course | Recurrence of liver metastasis on PET scanConsideration 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 2Somatostatin receptor analogue |  |
| Alshaikh [45] | 49F | Micro  |  | 11 |  | 10% |  | YEs | -Liver-Spine-Bone | TSR x 3Bilateral adrenalectomyTemazolomideEverolimus/sunitinib / bevacizumab | Deceased after 7 years |
| Flores [46] | 45 F | Macro | 2013 | 4 |  | 8-12%  |  | Yes (3 times) | -Liver -Bone-Left adrenal | TSR x 2PasireotideRFA liver lesion | Alive at 14 months |
| Rotman [47] | 51M | Macro  | 1996 | 14 | -Cushingnoid feature | 15% |  | Yes (twice) | -Cerebral | TSR x 1KetoconazoleCraniotomyTemozolomide (12 months) Bevacizumab (2 years) | Alive at 8 yearshypopituitarism |
| Majd [48] | 35M | Macro |  | 4.5 | -Cushingnoid feature |  |  | Yes | -Liver-right orbit-Cerebral | Surgeries x3Temozolamide Capecitabine Bilateral adrenalectomyFGFR-targeted treatmentPembrolizumab | Alive at 118 months  |
| Majd [48] | 20s F | Macro |  | 3.8 |  |  |  | Yes | -Cerebral-Bone-Lung-Liver | Surgeries x 2Bilateral adrenalectomyTemozolamideCapecitabinePembrolizumab | Alive at 30 months |

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