Primary intracranial extraosseous Ewing's sarcoma of the skull base in an elderly adult: illustrative case

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BACKGROUND Primary extraosseous intracranial Ewing's sarcoma, also known as a peripheral primitive neuroectodermal tumor or "small round blue cell tumor," is an extremely rare entity with limited representation in the literature beyond the pediatric population.

OBSERVATIONS A 67-year-old male suffering occipital headache, nausea, and gait disturbance was found to have a large, avidly contrast-enhancing cerebellopontine angle mass extending into the cervical spinal canal with associated mass effect on medulla, cerebellum, fourth ventricle, and cervical spinal cord. This mass was not present on the imaging from 8 years prior. He underwent surgical debulking and pathology results demonstrated a malignant small round cell tumor showing diffuse immunopositivity for cytokeratins, CD99 and NKX2.2 with EWRS1-FLI1 rearrangement in 84% of the nuclei confirmatory of Ewing's sarcoma. After 14 cycles of chemotherapy and 6 weeks of radiotherapy, 22 months after discovery, the patient remains in clinical and radiographic remission with complete return to his baseline functioning.

LESSONS Primary skull base extraosseous Ewing's sarcoma should be considered in the differential diagnosis even in the elderly population when imaging studies demonstrate aggressive tumor growth patterns. Tumor debulking to establish a diagnosis followed by adjuvant chemoradiation therapy can result in clinical improvement with remission.

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KEYWORDS Ewing's sarcoma; primary Ewing's sarcoma; skull base; sarcoma; peripheral primitive neuroectodermal tumor
progressed, and he also began experiencing progressive dysphagia, slurred speech, and subjective decrease in hearing. His dysphagia was treated preoperatively with nasogastric tube placement and the general surgery team was consulted for placement of percutaneous gastrostomy (PEG) tube in the same surgical setting as the patient’s surgical debulking.

**Initial Clinical Investigation**

Initial brain MRI with and without contrast (Fig. 1A–E) revealed a 4 × 3 × 9.5 cm lobulated extraaxial mass in the right CPA extending into the spinal canal to the C3–4 level. There was also extension to the clivus, into the prevertebral and paraspinal soft tissue, and through bilateral cervical neural foramina. There was resulting mass effect on the brainstem, cerebellum, and cervical spinal cord. The right vertebral artery from C2 through its intracranial course appeared encased within the mass. The lesion demonstrated heterogeneous contrast enhancement and was hypointense on T1 and hyperintense on T2/FLAIR sequences with mild associated diffusion restriction. The patient’s case was reviewed in multidisciplinary institutional tumor board and differential diagnoses included, in addition to the more common CPA tumors such as schwannoma and meningioma, malignant peripheral nerve sheath tumor among others. Contrast-enhanced computed tomography (CT) scan of the chest, abdomen, and pelvis did not reveal any metastatic or primary lesions. Catheter angiogram was also performed to evaluate the blood supply of the mass and to perform possible preoperative embolization. The tumor appeared to be fed primarily by small branches from the right ascending pharyngeal artery and right vertebral artery that were deemed unsuitable for embolization (Fig. 1E and F). Preoperative audiogram demonstrated bilateral sensorineural hearing loss.

**Surgical Debulking**

Extensive discussions were held with the patient and his family reviewing management options. Ultimately, recommendation was made to undergo surgery to establish a tissue diagnosis and to pursue maximal safe resection. Right transtemporal craniotomy for tumor resection followed by PEG placement was planned. Once the patient was intubated and necessary lines and monitors had been placed, neuromonitoring for lower cranial nerves, motor and somatosensory evoked potentials was established with good baseline readings. The patient was positioned in left lateral decubitus position. A right postauricular sigmoid incision extending inferiorly to the midline of lower cervical spine was marked and surgical area was prepped and draped in standard sterile fashion. After making the incision and performing soft tissue dissection, biopsies of grossly abnormal appearing paraspinal musculature were taken. However, intraoperative consultation with pathologist regarding these specimens was inconclusive. Therefore, a right transtemporal craniotomy with partial mastoidectomy and partial occipital condylectomy was performed. A curvilinear dural opening was made followed by the opening of cisterna magna to achieve brain relaxation. The intracranial component of the tumor was clearly visualized. Cranial nerves (CNs) IX and X were visualized partially encased in and partially spayed over the tumor. The tumor capsule was stimulated to localize a safe area to resect, which was then sent for frozen pathology. Intraoperative consultation with pathology revealed that though lymphoma was an unlikely diagnosis, the tumor specimen demonstrated features of malignant small round cells. Cautious tumor debulking was continued within the tumor capsule. Rootlets of the lower cranial nerves were found to be encased by tumor, which was a mix of soft and fibrotic areas. The resection was then carried down through the foramen magnum and up to the level of C1 where the tumor was partially resected off the C1 rootlets and a segment of the right vertebral artery. At the cervicomedullary junction, the tumor appeared to be invading into the medulla. The tumor was, however, easily dissectible from the upper cervical spinal cord. Cautious additional debulking was performed. However, it was evident that extensive resection of the malignant mass would likely result in potentially significant neurological and vascular injury due to the adherent and invasive nature of the tumor to the surrounding neurovascular structures. Therefore, decision was made to achieve

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**FIG. 1.** Preoperative imaging studies. Sagittal (A), coronal (B), and axial (C–E) contrast MRI sequences demonstrating a heterogeneous, lobulated, avidly contrast-enhancing mass centered at the right inferior posterior fossa/foramen magnum, with compression of the medulla and substantial mass effect on the adjacent cerebellum. Within the skull base, the mass involves the right hypoglossal canal, extends to the jugular bulb, as well as further anteriorly with involvement of the atlantoaxial joint anterior prevertebral soft tissues and downward to the level of C3–C4 with involvement of the neural foramina and a complete encasement of the vertebral artery on the right side. Preoperative digital subtraction angiograms, right vertebral artery (F) and right common carotid artery (G) injections, demonstrated small, hypervascular branches from the right vertebral artery and anterior laryngeal artery supplying the tumor mass (arrows).
hemostasis and close the surgical site in a standard multilayer fashion. Motor and somatosensory potentials remained stable throughout the case. The general surgery team then resumed the patient’s care and performed placement of PEG in the same anesthesia setting. Postoperatively, the patient required reintubation after an extubation trial due to his respiratory status and was transferred to the surgical intensive care unit. Postoperative head CT within 24 hours postsurgery revealed residual mass now measuring $3 \times 2.7 \times 3.4$ cm in the right posterior fossa extending through the foramen magnum into the cervical canal with slightly decreased mass effect on the brainstem, cerebellum, and cervical spinal cord with small amount of hemorrhage at the surgical site. The patient was successfully extubated on postoperative day (POD) 4 and remained neurologically stable.

Pathological Studies
Tumor specimen sections demonstrated monomorphic, round cells with minimal palely eosinophilic to clear cytoplasm and predominantly nested growth pattern. Tumor cells stained diffusely positive for cytokeratin (Cam5.2), CD99, and NKX2.2, and negative for markers of neural, myogenic, lymphoid, and germ cell differentiation (Fig. 2). NKX2.2 is homeodomain-containing transcriptional factor that plays a critical role in neuroendocrine/glial differentiation. The NKX2.2 gene is a target of EWS-FLI-1 the fusion protein specific to Ewing’s sarcoma. These findings were most consistent with Ewing’s sarcoma, which has been reported to exhibit diffuse cytokeratin staining in as many as 20% of cases. Cytogenic analysis of the specimen revealed EWRS1-FLI1 rearrangement in 84% of the nuclei confirmatory of Ewing’s sarcoma.

Chemotherapy and Radiotherapy
The patient was treated with an adjuvant chemotherapy regimen of 14 cycles of cyclophosphamide, doxorubicin, and vincristine alternating with ifosfamide and etoposide. Brain MRI with and without contrast after the fourth chemotherapy cycle demonstrated reduction in tumor size from $3.5 \times 2.8 \times 4.0$ cm to $2.7 \times 0.9 \times 3.4$ cm. Adjuvant radiotherapy was planned to start at week 13 along with the ongoing chemotherapy to be delivered daily over 6 weeks. While undergoing chemotherapy, the patient developed complications of neutropenic fever, pancytopenia and pleural empyema that were successfully treated. Brain MRI with and without contrast performed approximately 7 months after completion of 14 cycles of chemotherapy and 6 weeks of radiotherapy demonstrated complete remission of the tumor suggesting a potential cure given the fast-growing nature of Ewing’s sarcoma.

Follow-Up and Outcome
Brain MRI with and without contrast at 2 weeks after tumor debulking (Fig. 3) revealed the T2 hyperintense, contrast enhancing mass that was stable in size as compared to the immediate postoperative CT. Part of the mass extending into the spinal canal now appeared to be peripherally enhancing with central blood products measuring $1.0 \times 0.8 \times 3.0$ cm, extending to the right-sided C1–C2 neural foramen, and abutting the right C2–C3 neural foramen. The slightly enlarged ventricles appeared stable in size. No new lesions, infarcts or hemorrhages were detected. After postoperative recovery

**FIG. 2.** Morphology of the tumor and immunohistochemical stains for the diagnosis of Ewing’s sarcoma. Hematoxylin and eosin staining of tumor (A), immunohistochemical stains positive for cytokeratin Cam 5.2 (B), focal positive staining for epithelial membrane antigen (C), strong and diffusely positive for CD99 (D), and high proliferative index for Ki-67 (E). Positive immunostaining for NKX2.2 was also demonstrated by an outside institution; photomicrographs are not available. Original magnification $\times 200$ (A–E).

**FIG. 3.** Postoperative contrast MRI at 2 weeks after craniotomy and debulking. Sagittal (A), coronal (B) and axial (C–E) projections show slight decrease in the size of the heterogeneous, lobulated enhancing skull base mass with cervical spinal extension now demonstrating more peripheral contrast enhancement with central blood products. There is persistent mass effect on the medulla and right cerebellar hemisphere.
in the intensive care unit, the patient was transferred to a surgical intermediate care unit on POD 6. By POD 7 the patient had recovered up to the point that he was able to tolerate tube feeds at goal, ambulated with assistance and his pain was well controlled, he was discharged to an acute rehabilitation center on a slow dexamethasone taper regimen. Nine months postoperatively, the patient was doing well neurologically without any new deficits, ambulating without assistance, enjoying his hobbies such as golfing, and tolerating a regular diet without the need for a feeding tube. Approximately 16 months after the initial discovery of the lesion, brain MRI with and without contrast (Fig. 4) revealed minimal residual asymmetrical dural enhancement along the right side of the clivus just anterior to the medulla. There was no mass effect on neural elements and there was no evidence of recurrence.

Discussion

Observations

Ewing’s sarcoma or peripheral primitive neuroectodermal tumor (pPNET) is the second most common primary bone malignancy in children typically involving long bones, ribs, vertebrae, or pelvic bones. Only 1%–2% of reported Ewing’s sarcomas are intracranial and are commonly referred to as the tumors belonging to the “small round blue cell” central nervous system tumor group. Less than 80 cases of intracranial Ewing’s sarcoma have been reported to date. Intracranial Ewing’s sarcomas may be intra- or extraxial with or without bone involvement and are typically dura-based. The most common sites of intracranial involvement are convexity, parafalcine, falcine, skull base, and tentorium with nearly 80% of the tumors being supratentorial leaving the posterior fossa as an uncommon location of this malignancy.

Ewing’s sarcoma has a reported peak incidence in men between the ages of 5 and 13 years, with one database query finding only 6.3% of tumors discovered in patients over the age of 50. Older age has been demonstrated as a poor prognostic factor for Ewing’s sarcoma due to the larger, more advanced and invasive tumor characteristics upon presentation. This makes the current patient’s good functional outcome at the age of 67 extremely unusual despite rapid progression of his symptoms and the invasive nature of the tumor encasing neurovascular structures and extending into the soft tissue.

Intracranial Ewing’s sarcoma typically presents with nonspecific symptoms such as nausea, headaches, cranial nerve palsies, vision changes and imbalance secondary to increased intracranial pressure or mass effect of the tumor on surrounding structures. The illustrative patient’s chief complaint of nausea was likely secondary to increasing mass effect from the tumor and development of obstructive hydrocephalus. In cases of skull involvement, an externally visible scalp swelling, or irregularity might be present. Given the nonspecific presentation, initial differential diagnosis can be wide including a variety of primary or secondary intracranial tumors such as meningioma, chordoma, lymphoma, eosinophilic granuloma, neuroblastoma or metastasis. While imaging findings help narrow the differential diagnoses, molecular confirmation of EWS gene rearrangement is required for confirmation of peripheral primitive neuroectodermal tumor (pPNET) as opposed to central primitive neuroectodermal tumor (PNET; e.g. medulloblastoma, pinealoblastoma and supratentorial PNET) that can also present with similar morphological findings.

Our English MEDLINE online literature review identified only 13 cases of primary intracranial Ewing’s sarcoma in patients of age 50 years or older (Table 1). The mean (standard deviation) age of these patients was 59.2 (8.2) years. Male to female ratio was 8:5 (61.6%:38.4%). Of these patients, only 3 (23%) were of age similar to or older than our patient. Of these 3 patients, 2 died during follow-up at 13 and 15 months while 1 was alive at the latest follow-up of 12 months. Seven (58%) of the 12 reported cases with follow-up resulted in death upon mean (standard deviation) follow-up time of 14.9 (13.7) months either from progression of the tumor or complications of treatment. Bone involvement was reported in only 3 (23%) cases with majority of cases amenable to only partial resection or biopsy of the tumor with adjuvant chemotherapy and/or radiation therapy. Only 3 (23%) of these cases involved skull base and/or posterior fossa. Additionally, no extensive soft tissue and cervical spinal involvement observed in the current patient was reported for any of these cases from the literature.

In the large database analysis by Martin et al., including 80 Ewing’s sarcoma cases, the median size of the tumor was found to be 4.5 cm at greatest length/width ranging from 4 to 6 cm. At the initial time of discovery, the current patient already had developed a lesion measuring approximately 9 cm at its largest diameter, without any evidence of intracranial lesion on imaging from 8 years prior. The current patient’s age and the tumor size, therefore, boded very poorly for his expected outcome. However, as is common standard of care, after surgical debulking, the patient completed adjuvant chemotherapy of 14 cycles of alternating regimens. His continued clinical remission now 22 months after tumor discovery count against the predicted poor survival and the trend of the limited data on elderly primary intracranial Ewing’s sarcoma patients currently available in the literature.

Lessons

Primary skull base Ewing’s sarcomas, while already exceptionally rare in pediatric patients, should not be excluded from the initial
differential diagnoses in older patients given the tendency to achieve larger size and more advanced stage upon diagnosis. The atypical presentation that these tumors may pose in this atypical demographic, needs further investigation to discern whether a different investigative and subsequent treatment approaches can lead to earlier diagnosis. Additionally, given the predominance of cases with similar demographics suffering poor outcomes, there may be hesitation in interdisciplinary discussion to offer and encourage surgical intervention if prognosticated recovery is misaligned with the patient’s goals of care. This may lead to fewer biopsies/resections of primary skull base Ewing’s sarcomas, furthering the insufficiency of data on how these tumors progress when approached with aggressive primary and adjuvant therapy and lost potential opportunities of treatment and survival with good quality of life.

References
1. Cherif El Asri A, Benzagmout M, Chakour K, et al. Primary intracranial pPNET/Ewing sarcoma: diagnosis, management, and

| Authors & Year | Age (yrs)/Sex | Tumor Location/ Origin | Intra Axial/ Extra Axial | Bone Involvement | Op Type/ Extent | Pathology Characteristics | Chemo | RT (mos) | FU | Outcome |
|----------------|--------------|------------------------|-------------------------|-----------------|----------------|--------------------------|-------|---------|----|---------|
| VandenHeuvel et al., 2015 | 61/M | Frontal temporal dura-based convexity | Extraaxial | No | Biopsy | CD99+; t(11:22)+ | None | None | 5 | Failure to FU after op |
| Salunke et al., 2014 | 52/M | Dura-based torcular | Extraaxial | Yes | Near-total resection | CD99+, Vimentin+ | Yes | 50 Gy | 6 | Death at 6 mos |
| Inniss et al., 2014 | 51/F | Occipital parafalcine | Extraaxial | No | Total removal | CD99+, vimentin+; S100+; t(11:22)+ | 14 cycles of chemo | None | 24 | Disease free at 24 mos |
| Mellai et al., 2010 | 56/F | Temporal dura-based convexity | Extraaxial | No | Total removal | CD99+; t(11:22)+ | None | None | 18 | Disease free after 18 mos |
| D’Antonio et al., 2004 | 50/M | Temporal dura-based convexity | Extraaxial | No | Total removal | CD99+; t(11:22)+ | None | None | 12 | Alive at 1 yr |
| Simmons et al., 2001 | 67/F | Cerebellopontine angle/CN VIII | Intraaxial | No | Biopsy | CD99+ | Yes | Yes | 13 | Asymptomatic at 13 mos, followed by rapid decline & death |
| Asmoniene et al., 2011 | 51/F | Mesencephalic-pineal region w/ 3rd/4th ventricle extension | Intraaxial | No | Biopsy & partial resection | CD99-; S100+; dCDKN2A | None | 58 Gy | 36 | Death at 3 yrs & 8 mos postop |
| Gupta et al., 2018 | 74/F | Clivus | Extraaxial | Yes | Subtotal resection | CD99+ | None | None | 3 | Death of unknown cause at 3 mos |
| Haveman et al., 2020 | 53/M | Temporal | NS | No | Resection | S100+ | 6 cycles of VIDE; 7 cycles of VAC | Yes | 15 | Death after 15 mos |
| Haveman et al., 2020 | 69/M | Parieto-occipital | NS | No | Resection | CD99+, NSE+; vimentin+; t(11:22)+ | 6 cycles of VIDE; 7 cycles of VAC | Yes | 15 | Death after 15 mos |
| Jiang et al., 2020 | 55/M | Frontal | Extraaxial | No | Total removal | CD99+, vimentin+ | None | Yes | 18 | Asymptomatic w/o recurrence |
| Salunke et al., 2011 | 62/M | Occipital | NS | No | Resection | t(11:22)+ | Yes | Yes | 8 | Recurrence & death |
| Schartz et al., 2024 | 68/M | Petroclival | Extraaxial | Yes | Biopsy | CD99+, S100+ | 21 cycles of chemo | Yes | 12 | Living |

d = deletion; FU = follow-up; NS = not specified; RT = radiotherapy; t = translocation; VAC = vincristine, actinomycin; VIDE = vincristine, ifosfamide, doxorubicin, and etoposide.
prognostic factors dilemma—a systematic review of the literature. World Neurosurg. 2018;115:346–356.
2. Gu M, Antonescu CR, Guinte G, Huvos AG, Ladanyi M, Zakowski MF. Cytokeratin immunoreactivity in Ewing’s sarcoma: prevalence in 50 cases confirmed by molecular diagnostic studies. Am J Surg Pathol. 2000;24(3):410–416.
3. Grier HE, Krailo MD, Tarbell NJ, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing’s sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med. 2003;348(8):694–701.
4. Sundaresan N, Rosen G, Boriani S. Primary malignant tumors of the spine. Orthop Clin North Am. 2009;40(1):21–36.
5. VandenHeuvel KA, Al-Rohil RN, Stevenson ME, et al. Primary intracranial Ewing’s sarcoma with unusual features. Int J Clin Exp Pathol. 2015;8(1):260–274.
6. Alvarez-Berdacia A, Schut L, Bruce DA. Localized primary intracranial Ewing’s sarcoma of the orbital roof. Case report. J Neurosurg. 1979;50(6):811–813.
7. Fitzer PM, Steffey WR. Brain and bone scans in primary Ewing’s sarcoma of the petrous bone. J Neurosurg. 1976;44(5):608–612.
8. Gupta S, Kumar A, Rangari KV, Mehrotra A, Pal L, Kumar R. Intracranial peripheral primitive neuroectodermal tumor arising from the clivus with intracranial metastasis in an elderly woman: case report and review of the literature. World Neurosurg. 2018;119:331–334.
9. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021;23(8):1231–1251.
10. Jiang Y, Zhao L, Wang Y, Liu X, Wu X, Li Y. Primary intracranial Ewing’s sarcoma/peripheral primitive neuroectodermal tumor mimicking meningioma: a case report and literature review. Front Oncol. 2020;10:528073.
11. Steinbok P, Flodmark O, Norman MG, Chan KW, Fryer CJH. Primary Ewing’s sarcoma of the base of the skull. Neurosurgery. 1986;19(1):104–107.
12. Baccio G, Longhi A, Ferrari S, Mercuri M, Versari M, Bertoni F. Prognostic factors in non-metastatic Ewing’s sarcoma of bone: an analysis of 579 patients treated at a single institution with adjuvant or neoadjuvant chemotherapy between 1972 and 1998. Acta Oncol. 2006;45(4):469–475.
13. Rodriguez-Galindo C, Liu T, Krasin MJ, et al. Analysis of prognostic factors in Ewing sarcoma family of tumors: review of St. Jude Children’s Research Hospital studies. Cancer. 2007;110(2):375–384.
14. Balasubramaniam S, Nadkarni T, Menon R, Goel A, Rajashekaran P. Primary Ewing’s sarcoma of the petroclival bone. J Clin Neurosci. 2008;15(6):712–714.
15. Martin E, Senders JT, Ter Wengel PV, Smith TR, Broekman MLD. Treatment and survival of osteosarcoma and Ewing sarcoma of the skull: a SEER database analysis. Acta Neurochir (Wien). 2019;161(2):317–325.
16. Simmons MA, Luff DA, Banerjee SS, Ramsden RT. Peripheral primitive neuroectodermal tumour (pPNET) of the cerebellopontine angle presenting in adult life. J Laryngol Otol. 2001;115(10):848–852.
17. Mellai M, Caldera V, Comino A, Fortunato M, Bernucci C, Schiffer D. PNET/ESFT of the cranial vault: a case report. Clin Neuropathol. 2010;29(6):372–377.
18. Salunke PS, Gupta K, Malik V, et al. Primary Ewing’s sarcoma of cranial bones: analysis of ten patients. Acta Neurochir (Wien). 2011;153(7):1477–1485.
19. Salunke P, Sharma M, Gupta K. Ewing sarcoma of the occipital bone in an elderly patient. World Neurosurg. 2014;81(2):e10–e12.
20. Cole M, Parajuli S, Laske D, et al. Peripheral primitive neuroectodermal tumor of the dura in a 51-year-old woman following intensive treatment for breast cancer. Am J Case Rep. 2014;15:294–299.
21. Asmoniene V, Skirutė D, Gudinavičienė I, et al. A primary primitive neuroectodermal tumor of the central nervous system in a 51-year-old woman: a case report and literature review. Medicina (Kaunas). 2011;47(8):440–445.
22. D’Antonio A, Galea A, Garcia JF, Marsilia GM, De Dominicis G, Bosciano A. Primary peripheral PNET/Ewing’s sarcoma of the dura with FISH analysis. Histopathology. 2004;45(6):651–654.
23. Haveman LM, Ranft A, Berg HVD, et al. Primary and metastatic intracranial ewing sarcoma at diagnosis: retrospective international case series and systematic review. Cancers (Basel). 2020;12(6):1675.
24. Scharz D, Divakar P, Tafe L, Paydarfar J. Primary Ewing’s sarcoma of the petroclival bone: A case report and literature review. Surg Neurol Int. 2020:11:6.
25. Reed DR, Hayashi M, Wagner L, et al. Treatment pathway of bone sarcoma in children, adolescents, and young adults. Cancer. 2017;123(12):2206–2218.

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Author Contributions
Conception and design: Jha, Ravina, Windermere, Dyer. Acquisition of data: Jha, Ravina, Windermere, Zhao. Analysis and interpretation of data: Jha, Ravina, Zhao, Lerner, Upadhyay. Drafting the article: Jha, Windermere, Lerner, Dyer, Upadhyay. Critically revising the article: Jha, Ravina, Windermere, Lerner, Upadhyay. Reviewed submitted version of manuscript: Jha, Ravina, Windermere, Zhao, Lerner, Upadhyay. Approved the final version of the manuscript on behalf of all authors: Jha. Statistical analysis: Ravina. Administrative/technical/material support: Jha, Windermere, Upadhyay Study supervision: Jha.

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