Observational Study

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# Spinal paragangliomas

## Surgical treatment and follow-up outcomes in eight cases

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**Abstract**

Paragangliomas are neuro-endocrine tumors originating from the adrenal gland. They are usually benign and nonfunctioning, rarely seen in central nervous system. More than 90% of central nervous system paragangliomas are manifested as carotid and glomus jugulare tumors. Spinal paragangliomas are quite rare.

The study was conducted through retrospective analysis of the files of the patients who had undergone surgery with pre-diagnosis of spinal intradural tumor between 2011 and 2017 and diagnosed with paraganglioma.

A total of 8 patients (4 females and 4 males) were included in the study. Mean age of the patients was 51.1 years (28–64). Time to admission was mean 6.5 months (3 weeks–24 months). Recurrence was not observed in 7 patients, 1 patient is being followed up due to residual tumor.

Treatment may be achieved through recognizing malignant transformation in patients who were not diagnosed histopathologically. We consider that quality of life of the patients may be improved through this way.

**Abbreviations:** CT = computed tomography, SP = spinal paragangliomas.

**Keywords:** paragangliomas, spinal intradural tumor

### 1. Introduction

Paragangliomas are neuroendocrine tumors, usually originating from the adrenal gland. They are usually benign and nonfunctioning[1–3] and rarely observed in the central nervous system. More than 90% of central nervous system paragangliomas manifest as carotid and glomus jugulare tumors. Spinal paragangliomas (SPs) are quite rare[1–5] and were first defined by Miller and Torack[5] and Lerman et al.[6] Clinical findings of SPs generally include nonspecific spinal cord pressure findings. The diagnosis of an SP is based on histopathological findings due to the absence of specific clinical and radiological findings.[3,7]

Herein, we describe surgical treatment and follow-up outcomes of 8 patients with a prediagnosis of a spinal intradural mass lesion who underwent surgery between 2011 and 2017. All the patients were diagnosed with a paraganglioma histopathologically.

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### 2. Material and methods

This study is a retrospective analysis of the files of patients with a prediagnosis of a spinal intradural tumor who underwent surgery between 2011 and 2017. All the patients were subsequently diagnosed with a paraganglioma. Patients whose files were incomplete were excluded from the study. Patients were evaluated with regard to age, sex, tumor location, complaints on admission, neurological examination findings (Frankel classification),[3] spinal computed tomography (CT) findings, spinal magnetic resonance imaging findings, duration of follow-up, and recurrence (Table 1).

### 3. Results

In total, 8 patients (4 females, 4 males) were included in the study. The mean age of the patients was 51.1 years (28–64 years). The mean duration to admission was 6.5 months (3 weeks to 24 months). The main complaints were lumbar pain, lower back pain, and leg pain. Some patients also had hypoesthesia, neurogenic claudication, and motor deficits.

When the patients' files were evaluated, it was determined that radiographic diagnosis could not be performed as part of the preliminary diagnosis process. With the exception of 1 subject diagnosed with recurrent paraganglioma, surgeries were conducted on the basis of a prediagnosis of schwannoma, meningioma, and ependymoma. It was determined that the radiologic diagnosis could not be made in the preliminary diagnosis of all patients, when evaluated on the basis of the patients' files. Apart from a patient diagnosed with recurrent paraganglioma, others were operated on based on the presumption of schwannoma, meningioma, and ependymoma. The patients underwent general anesthesia and neuromonitoring with microsurgical techniques. Pathological results revealed spinal intradural extramedullary paraganglioma. Vanil-mandelic acid was negative in the patients' urine, and their abdominal ultrasonography and CT of the whole abdomen and thorax were

**Table 1**

**Demographic characteristics of the patients.**

| Patient no | Age, y | Gender | Duration of symptoms | Location | Complaint on admission | Frankelscale preop/postop | Duration of followed | Recurrence | Addition |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 64 | F | 14 mo | L3 | Lower back, leg pain | D/E | 65 mo | No | |
| 2 | 28 | F | 3 wk | L2 | Lower back, leg pain in both legs | E/E | 8 mo | No | |
| 3 | 54 | M | 5 mo | L3 | Pain reflecting to both thighs from back | E/E | 11 mo | No | |
| 4 | 54 | F | 2 y | L2-3-4 | Leg pain, numbness | D/E | 55 mo | No | |
| 5 | 46 | F | 2 mo | L2-3 | Pain reflecting to leg from the left thigh | E/E | 80 mo | No | |
| 6 | 62 | M | 1 mo | L2 | Lower back, leg pain in both legs | E/E | 79 mo | No | |
| 7 | 40 | M | 3 mo | L2-3 | Operation in 2005 residual tumor/recurence? Lower back pain, difficulty to walk | D/D | 37 mo | Residual (+) | First op. in 2005, re-operation in 2014 due to recurence |
| 8 | 61 | M | 2 mo | L2-3 | Wide spread pain in lower back and legs | E/E | 33 mo | No | |

F = female, L = lomber spine vertebrae, M = male.

considered normal. No multiple paragangliomas were found by clinical investigation.

Total surgery was performed in 7 patients. One patient had undergone subtotal resection at another center in 2005 but underwent surgery again in 2014 due to recurrence of complaints. However, residue was left due to common nerve adhesion.

The neurological examination was evaluated according to the Frankel classification system. During the postoperative period, a 1-stage improvement was observed in 2 patients. No differences were observed in the other 6 patients (as 5 patients did not have deficits, and postoperative deterioration was not observed).

The mean duration of follow-up was 46 months (8–80 months). Recurrence did not occur in 7 patients. One patient with a residual tumor continues to be followed (Table 1 and Figs. 1–3).

Tumors usually had a well-circumscribed nodular appearance. For example, the macroscopic examination of case 4 showed a well-circumscribed tumor with nodular appearance (size: $5.5 \times 2.5 \times 1.5$ cm). Microscopic examination revealed an invasive

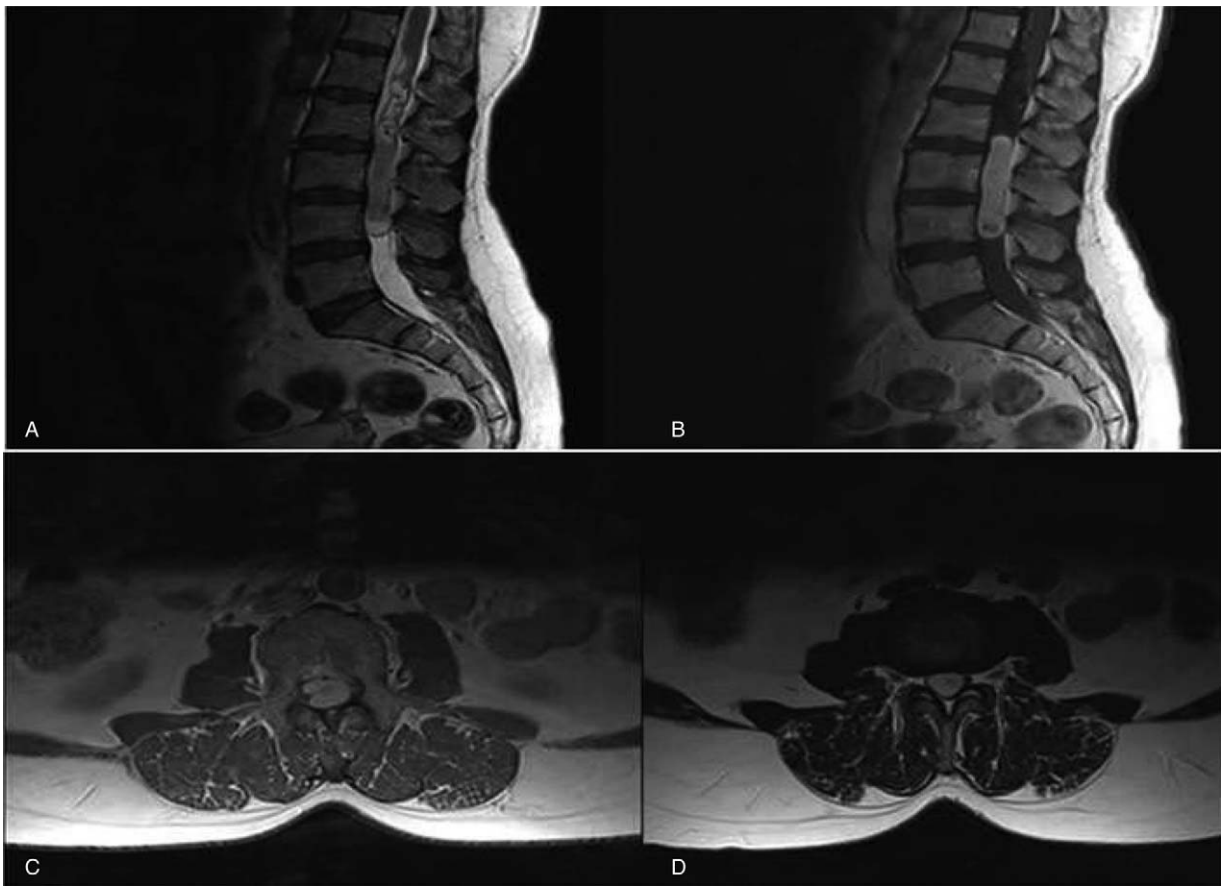


**Figure 1.** (A–D) Preoperative spinal magnetic resonance imaging (MRI) images of the patient 4 in Table 1.

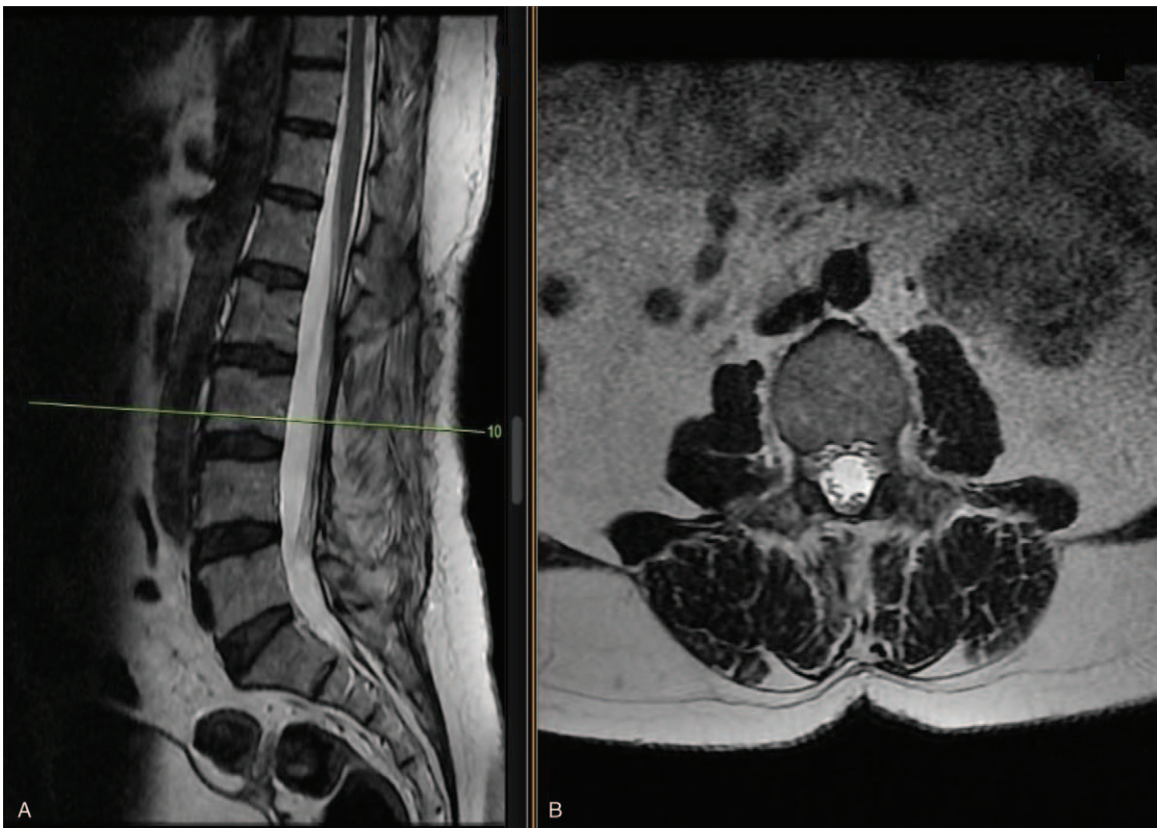


**Figure 2.** Postoperative spinal magnetic resonance imaging (MRI) images of the patient 4 in Table 1.

tumoral lesion with local zellballen nests across a large section and with solid pattern. Tumor cells displayed hyperchromatic nuclei showing small round pleomorphisms with eosinophilic cytoplasm locally. Diffuse positive staining was observed in tumor cells with cluster differentiation 56 and chromogranin (neuroendocrine differentiation markers). No staining was observed with epithelial membrane antigen. Sustentacular cells were stained with S100 (Fig. 4).

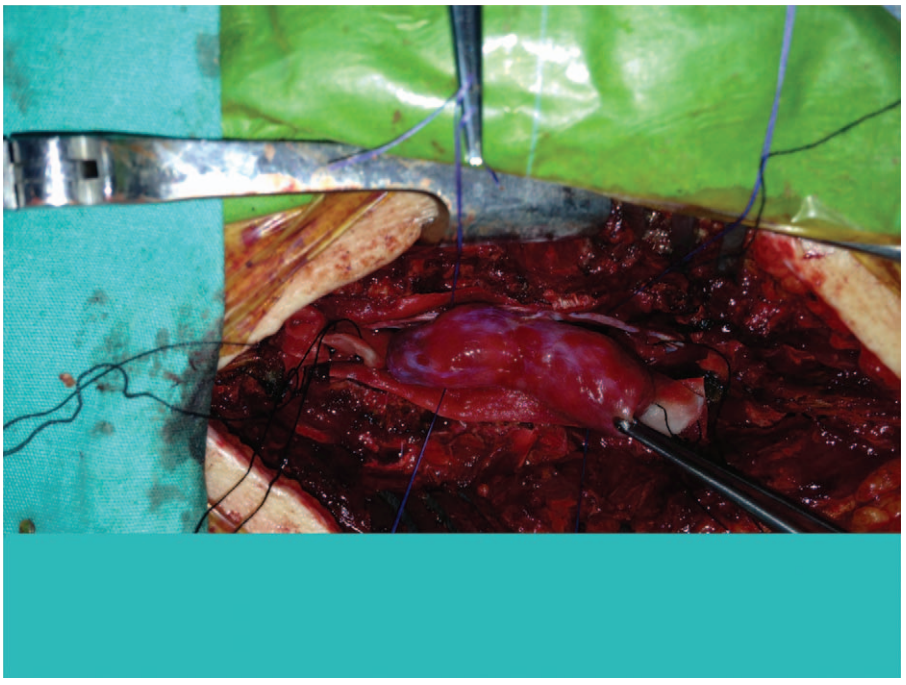

**Figure 3.** Peroperative images of the patient 4 in Table 1.

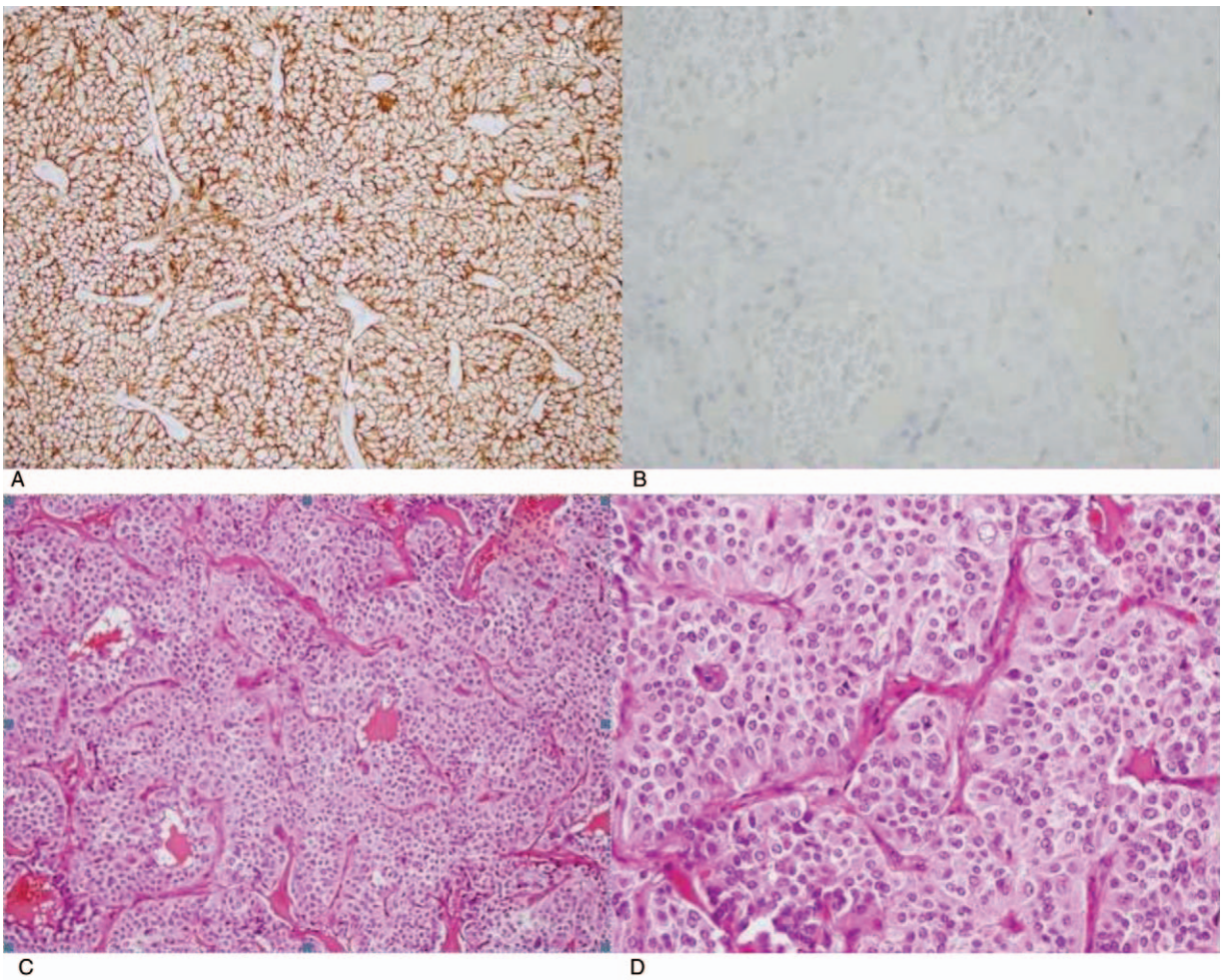


**Figure 4.** Histochemical pathology image of case 4 presented in Table 1. A. HEX200. B. HEX400 C. CD56 D. EMA.

## 4. Discussion

According to the World Health Organization (WHO) classification, paragangliomas are grade 1 tumors which develop from neural crest cells. They may be secretory, although the vast majority is nonsecretory. Although paragangliomas mainly originate from sympathetic system cells, 80% to 90% of paragangliomas are located in the carotid and glomus jugulare regions and are of parasympathetic system origin. Secretory paragangliomas usually do not lead to clinical findings, although they produce excessive amounts of catecholamines.[3,4,8,9] They are usually benign and grow slowly. The rate of malignant transformation was reported to be 2.4% to 14% in the literature.[3]

With regard to the demographic characteristics of patients, paragangliomas are generally seen in individuals aged 9 to 74 years, with a slight male predominance (male:female ratio of 1.4:1). The most common complaints upon admission include lower back pain and leg pain, sometimes with urinary incontinence and paraparesis.[4]

According to the literature, paragangliomas rarely occur in the orbits, larynx, vagal nerve, gastrointestinal tract, urinary tract, or thyroid gland. Intraspinal paragangliomas are quite rare.[3,4] The incidence of SPs is unknown. In the literature, SPs were reported to be mainly located in the lumbar and sacral regions.[5,10] In all of our cases, the lesion was located in the lumbar region.

Clinical manifestations of SPs are nonspecific. Patients are usually admitted with lower back pain, leg pain, hypoesthesia at various levels, neurogenic claudication, and incontinence due to cord pressure. Secretory-type paragangliomas may present with hypertension, palpitation, tremor, vomiting, and weight loss.[3,4] None of our patients had clinical findings of secretory-type paragangliomas.

According to the literature, SPs do not have specific radiological findings and do not lead to bone erosion and destruction. The lesion is observed as a mildly calcified homogenous mass, with an intense vasculature and foraminal enlargement on spinal CT.[9,11,12] They appear as hypo-isointense on T1W1 spinal magnetic resonance imaging images and as iso-hyperintense homogenously contrasting masses on T2W1 images.[9,10] SPs are difficult to distinguish from neuromas and ependymomas radiologically.[4] In the present series, the radiological images were consistent with those in the literature. However, they could not be distinguished from other tumors (Table 2).[13–17]

Histologically, paragangliomas are composed of balls of cells (zellballen), which are usually well encapsulated, very rich in vascular stroma, and supported by vascular sinusoids. Immunohistochemically, the main cells are stained with neuron specific enolase, chromogranin, and synaptofizin, and fusiform sustentacular cells are stained with S-100 protein and glial fibrillary

**Table 2**

**Differential diagnosis for spinal paraganglioma with radiological parameters.**

| | sCT | sMRI T1W1 | T2W1 | C+ (Gd) |
|---|---|---|---|---|
| Spinal paraganglioma[13–15] | Common contrast enhancement (due to rich capillary network). Rarely causes changes in the vertebral bone. | Isointense | Hyperintense, hemorrhage is common, leading to a hemosiderin cap sign | Intense enhancement is virtually always seen |
| Spinal meningioma[17] | Isodense or moderately hyperdense mass hyperostosis may be seen but is not as common as in the intracranial forms, calcification may be present. | Well circumscribed, isointense to slightly hypointense | Isointense to slightly hyperintense | Moderate homogeneous enhancement. Dural tail |
| Spinal ependymoma[16] | Ependymomas may expand the spinal canal, cause scalloping of the vertebral bodies and extend out of the neural exit foramina. | Usually isointense, hemorrhage and calcification can also lead to regions of hyper or hypointensity | Hyperintense, low intensity may be seen at the tumor margins because of hemorrhage. Calcification may also lead to regions of low T2 signal | Typically homogeneous |

Gd = gadolinium, sCT = spinal computed tomography, sMRI = spinal magnetic resonance imaging.

acidic protein.[3,4] It is difficult to discriminate between benign and malignant paragangliomas, as there is relatively little invasion of neighboring tissues.[18] Metastasis has been reported in 7% of malignant paragangliomas. Therefore, the histopathological assessment should include not only a microscopic examination.[19] In the present series, the histopathology results were benign in all cases.

Primary treatment of a paraganglioma involves total excision, as the tumor is well encapsulated. The prognosis following total surgical resection is very good in cases of benign paragangliomas.[3] In their review, Gelabert-Gonzales[20] reported a local recurrence rate of 2.2% in cases of total excision and 5.4% to 10.5% in cases of subtotal excision. In a study by Yin et al[4] of SPs in 18 patients, they observed recurrence in only one patient. Mishra et al[5] reported no recurrence in eight patients with SPs. The role of postoperative radiotherapy or chemotherapy in cases of paragangliomas is controversial. It is recommended for patients who do not undergo surgery.[3,4,21,22] In the present series, total excision was performed in seven patients. Adjuvant therapy was required and relapse occurred in no patients. Residual tissue was left in 1 patient due to widespread adhesions. This patient was re-operated on due to recurrence. This patient continues to be followed.

## 5. Conclusion

SPs are relatively rare and usually benign tumors. The prediagnoses include neuromas, schwannomas, and ependymomas due to the difficulty in making a diagnosis based on radiologic findings. Total resection is important at the time of surgery to prevent recurrence and ensure progression-free survival. Primary treatment includes total surgical resection. Chemotherapy and radiotherapy are supportive treatments, but their use is controversial. The current consensus is that they are not effective. The patient's prognosis depends on a correct diagnosis prior to surgery and total resection.

We consider that long-term follow-up is important in cases of paragangliomas. Early recognition of malignant transformation may improve the success of treatment in patients who are not diagnosed based on histopathological findings. Such early recognition can improve the quality of life of patients.

## Author contributions

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**Visualization:** Ayhan Kocak.
**Writing – original draft:** Can Yaldız, Okan Turk, Sebnem Batur.

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