

SUCCINATE DEHYDROGENASE DEFICIENT GIST: CASE SERIES AND REVIEW OF LITERATURE FROM A TERTIARY CARE CENTRE IN INDIA

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Background

- Around 5 to 10% of GIST lack driver mutations (KIT, PDGFR α) and are deficient in succinate dehydrogenase.
- Succinate dehydrogenase deficient GISTs are unique in the fact that they occur predominantly in the younger population, are multifocal and generally resistant to imatinib.
- Surgery is the mainstay, but recurrence is common.
- Data regarding SDH deficient GIST from Indian subcontinent is very sparse.

Methods

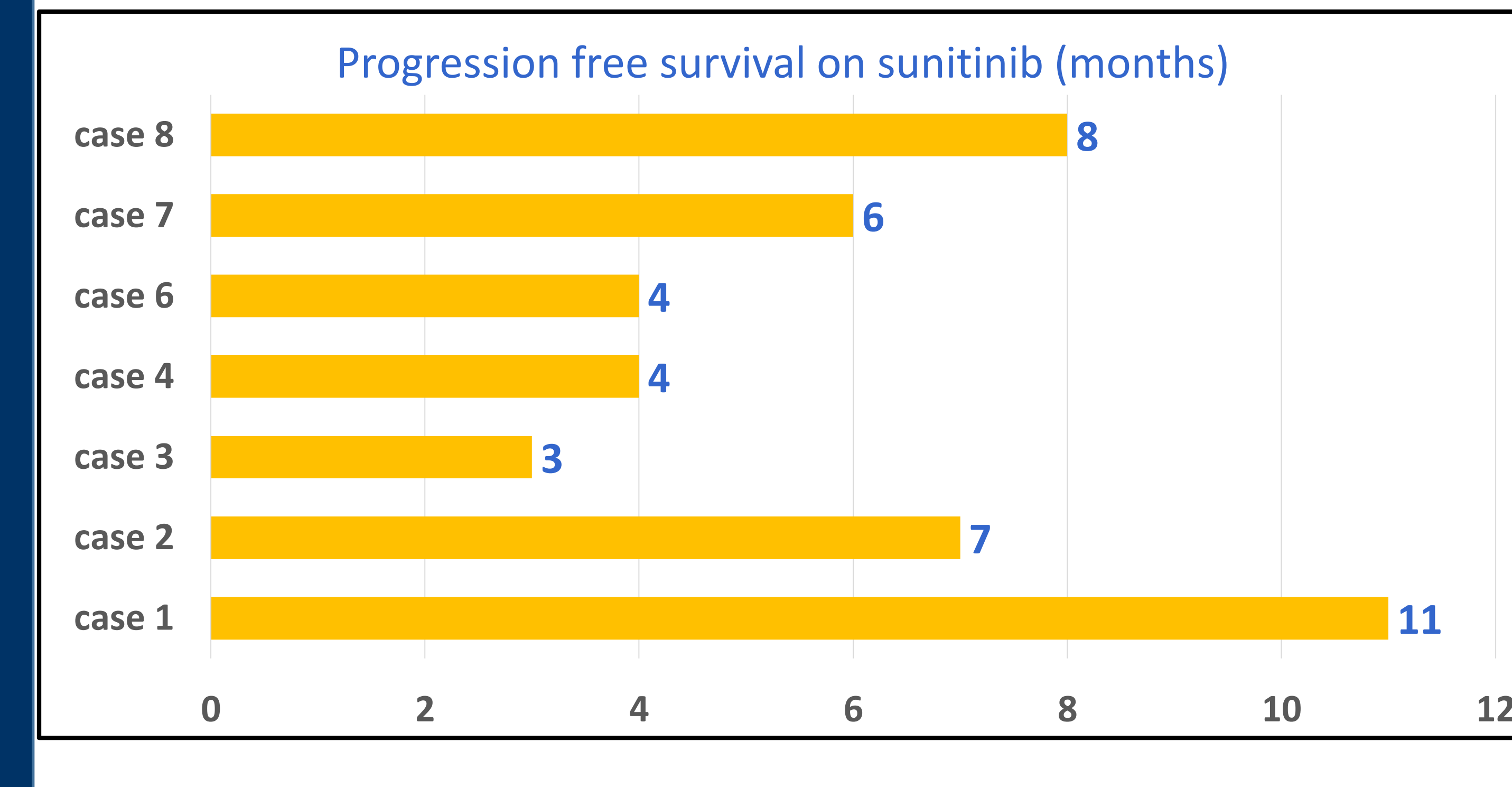
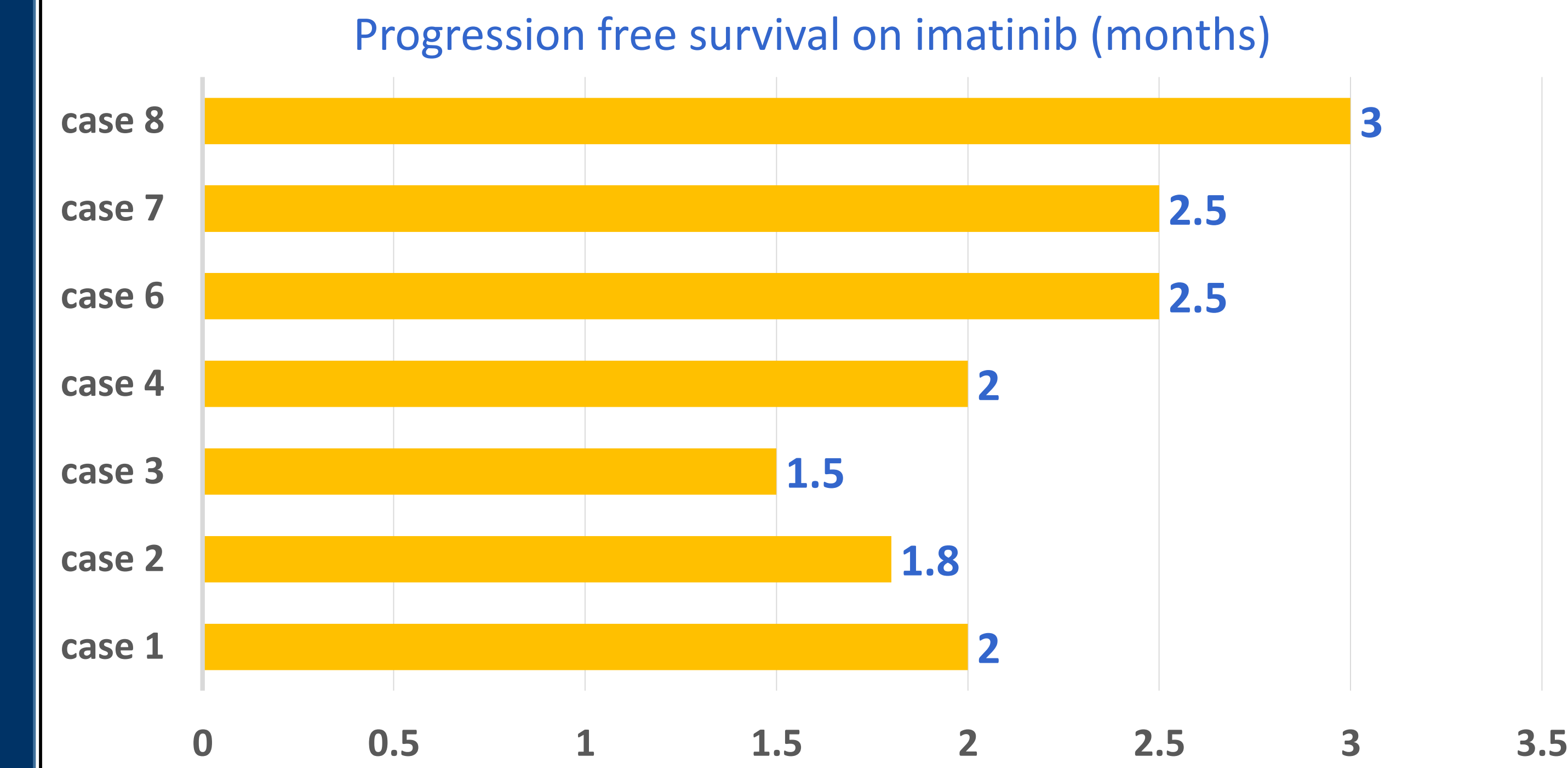
- This is a retrospective study of patients with SDH deficient GIST who presented to the GIST clinic in AIIMS, New Delhi, India from 2016 to 2022.
- 9 out of 120 GIST patients (7.5%) were SDH deficient.
- All patients were discussed in GIST tumor board and pathologies were re-reviewed by dedicated GIST pathologists.
- Data was collected retrospectively from prospectively maintained database.

Results

- There were a total of 9 patients with median age of 48 years (range 15-63), of which there were 5 males (n=5, 55.5%).
- Median follow up duration was 15 months. 8 patients (n=8, 88.8%) had primary in stomach, 1 had duodenal GIST.
- In stomach, body was the most common location (n=6, 75%).
- 3 out of 9 patients (n=3, 33.3%) had multifocal disease. 8 out of 9 (88.8%) had metastasis at presentation.
- Most common site of metastasis was liver (7 out of 8, 87.5%) Lymph node involvement was present in 4 out of 9 patients (44.4%).
- One patient had classical Carneys triad at presentation. 8 out of 9 (n=8, 88.8%) had epithelioid morphology and 1 (n=1, 11.1%) had mixed epithelioid-spindle picture.
- 5 out of 9 (55.5%) patients had germline SDH mutations.

- KIT and PDGFR mutations were negative in all patients.
- Out of 9 patients, 1 patient was kept on observation post surgery and therapy was given for 8 patients (n=8, 88.8%).
- None of the 8 patients responded to imatinib, 3 out of 5 patients (60%) had response with sunitinib (2 partial response, 1 stable disease), 3 were started on regorafenib out of which 1 had partial response.
- Median overall survival was NR (not reached) (95% CI 12.96-NR). 1 patient who progressed on sunitinib achieved partial response with Temozolomide.

Case	Age (years) sex	Primary site	Localized/metastatic	Histology	IHC	Mutation NA: (not available)	Follow up duration (months)	Response to TKI PFS in brackets (months)
Case 1	49/M	Stomach (antrum) multifocal	Carneys triad Metastatic Pulmonary chondromas + adrenal adenoma	epithelioid	SDH B deficient	SDH A	24	PR on sunitinib
Case 2	63/M	Stomach (body) unifocal	Metastatic-liver, peritoneum	epithelioid	SDH B deficient	SDH A	17	PD on imatinib, avapritinib, ripretinib. SD on sunitinib
Case 3	25/F	Stomach (body) unifocal	Metastatic-liver	epithelioid	SDH B deficient	SDH A	15	PD on sunitinib, PR on Temozolamide
Case 4	48/F	Stomach (body) unifocal	Metastatic liver	epithelioid	SDH B deficient	SDH A	36	PD on imatinib, sunitinib PR on regorafenib
Case 5	52/M	Stomach (body) multifocal	Localized	mixed-epithelioid-spindle	SDH B deficient	NA	24	observation
Case 6	63/F	Stomach (unifocal) body	Metastatic: Liver, abdominal lymph nodes	epithelioid	SDH B deficient	SDH B mutation	14	PD on imatinib PD on sunitinib
Case 7	31/F	Stomach (body) multifocal	Metastatic-liver, pararenal, peri-splenic and ascending colon deposits	epithelioid	SDH B deficient	NA	13	Sunitinib (ongoing)
Case 8	20/M	Duodenum	Metastatic: liver	epithelioid	SDH B deficient	NA	12	PR on sunitinib
Case 9	15/M	Stomach (antropyloric) unifocal	Metastatic-liver, mesenteric and RP nodes	epithelioid	SDH B Deficient	NA	7	Sunitinib (ongoing)



Conclusion

Majority of our patients with SDH deficient GIST had advanced disease and most of them were in stomach and had epithelioid morphology. We had male preponderance as compared to literature and higher age. Also, there was poor response to imatinib. Based upon this data we have incorporated SDH IHC upfront in all cases similar to CAP guidelines

Conflict of interest: none

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