GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

ESMO SUMMIT RUSSIA 2019

Clinical case.

Difficulties in treatment of patient with primary multiple malignancies with BRAF mutation

Polyanskaya Elizaveta
N.N. Blokhin Russian Cancer Research Center
Department of Clinical pharmacology and Chemotherapy

CONFLICT OF INTEREST DISCLOSURE

No conflict of interest

CLINICAL DATA

Male, 64 years old

ECOG 1

No clinically significant comorbidities.

Anamnesis of life: married, non smoker. No history of tumours in family.

November, 2018. Grade 1 pain in epigastric area, changes in stool behaviour.

Colonoscopy: stenotic tumor of the hepatic flexure of the ascending colon

Upper endoscopy: in the antrum of the gastric along its greater curvature is the tumor size 4.0 x 2.5 cm. Tumor is bumpy, rocky density, with foci of necrosis under fibrin

CT: tumor of hepatic flexure of the colon with regional lymphadenopathy. Single hepatic metastases 2.5cm in S3-4.

CEA 28.65 ng/ml, CA 19-9 108.50 u/ml. No laboratory abnormalities.

Histological examination

(gastric): low-grade adenocarcinoma. Her2/neu 1+;

(colon): moderately differentiated mucinous adenocarcinoma. **BRAF V600E mut**, MSS phenotype;

(liver mets): mucinous adenocarcinoma intestinal-type.

Diagnosis:

Primary multiple malignancies

1) Gastric cancer. cT3NxM0.

2) Cancer of the hepatic flexure of the colon. cT3N+M1. BRAF V600E mut, MSS phenotype. Single liver metastases.

What to do?

1) Surgery up-front (hemicolectomy, gastrectomy or both?)

2) Chemotherapy up-front (FOLFOX, FLOT, FOLFOXIRI?)

TREATMENT

11.12.2018 was urgently operated due to ileus.

Laparotomy: no signs of dissemination in abdomen. Right-sided hemicolectomy performed.

Histological examination: Moderately differentiated mucinous adenocarcinoma.

The tumor penetrate the intestinal wall and the serous membrane, grows into the omentum. No perineural invasion detected.

In 1 of 11 lymph nodes metastasis. In omentum tumor deposit (mucinous adenocarcinoma). **pT4bN1M1(liver).**

TREATMENT AND EFFECT

1 months later (January, 2019)

Patient completely recovered from the surgery. ECOG1.

No signs of disease progression on CT (2.5x2.0cm in S3-4).

Treatment plan

4 cycles FOLFOXIRI → gastrectomy + liver resection → up to 8 cycles FOLFOX

Treatment (January – March, 2019)

2 cycles FOLFOXIRI - poor tolerability (prolonged neutropenia and diarrhea gr.3) and

2 cycles FOLFOX (no significant toxicity).

CHEMOTHERAPY EFFICACY

Objective evaluation (March-April 2019)

Decrease of tumor markers CEA 13.22 ng/ml, CA 19-9 49.72 U/ml

MRI identifies **two** metastases in the liver:

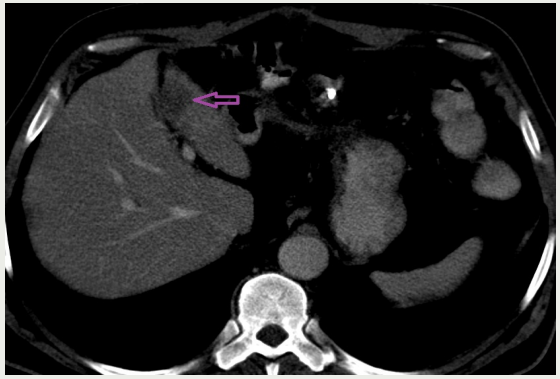
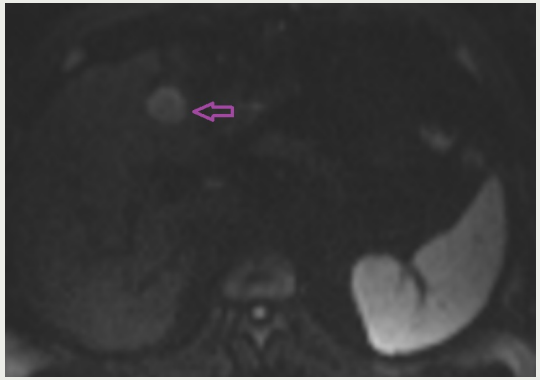
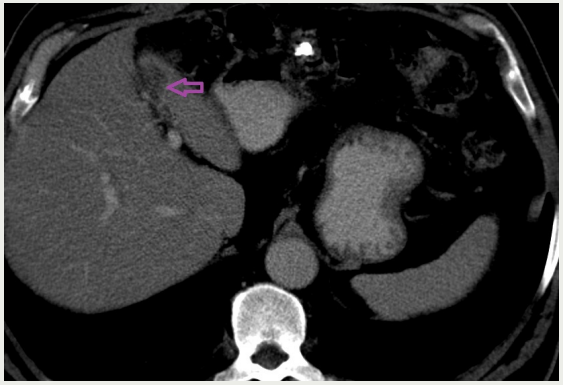
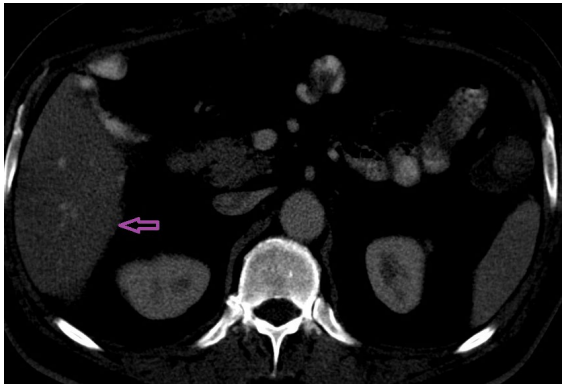
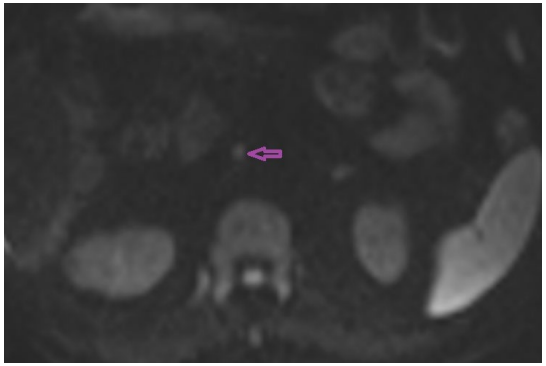
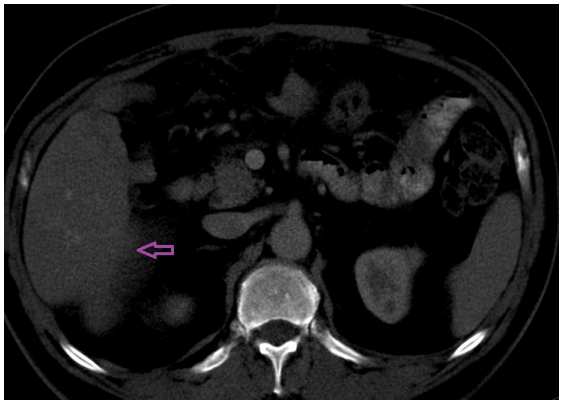
In S3-4 - 2.5 cm in diameter

In S6 1x0.8 cm - *was not determined by CT before chemotherapy. Highly likely metastases.*

CT-scan (comparing with January): no changes in S3-4, growth in S6 from 0.5 to 1cm.

Upper endoscopy: stabilization.

DYNAMICS BY CT AND MRI

	January 2019 CT	March 2019 MRI	April 2019 CT
SIII			
SVI			

CHEMOTHERAPY EFFICACY

Objective evaluation (March-April 2019)

Decrease of tumor markers CEA 13.22 ng/ml, CA 19-9 49.72 U/ml

MRI identifies **two** metastases in the liver:

In S3-4 - 2.5 cm in diameter

In S6 1x0.8 cm - *was not determined by CT before chemotherapy. Highly likely metastases.*

CT-scan (comparing with January): no changes in S3-4, growth in S6 from 0.5 to 1cm.

Upper endoscopy: stabilization.

What to do?

1) **Surgery up-front** (gastrectomy + hepatic resection)

2) **2-nd line therapy** (poorly tolerated and progressed (?) on irinotecan).

- Irinotecan or FOLFIRI - for gastric,
- IRI + BRAF TKI + anti-EGFR mAB – for mutBRAF colorectal mets)

ONGOING

24.04.2019 explorative laparotomy was performed.

- extensive peritoneal carcinomatosis

Histological examination - moderately differentiated adenocarcinoma. BRAF V600E mut

Second-line chemotherapy was recommended:

irinotecan 150 mg/m2 every 2 weeks

cetuximab 500 mg/m2 (or panitumumab 6 mg/kg) every 2 weeks

vemurafenib 960 mg BID continuously.