Unusual tree bark like skin pigmentation over veins after 5-flourouracil infusion with spontaneous resolution

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ABSTRACT
5-Fluorouracil (5-FU) is a commonly used chemotherapeutic agent used alone or in combination to treat a variety of cancers particularly of gastrointestinal origin. Skin hyper pigmentation is a very rare adverse event occurring with 5-FU infusions occurring in 2 to 5% of cases. This has become even rare due to versatile use of peripherally inserted central catheters and chemo ports in patients requiring prolonged infusions. We are hereby reporting this rare tree bark like Serpigenous supravenous skin pigmentation in a patient receiving prolonged 5-flourouracil infusion who denied for chemo port insertion. It resolved spontaneously over a month in left upper limb veins, but appeared again in right side when these veins are used in next cycle of chemotherapy. No alteration in drug dose or discontinuation of chemotherapy is needed in this condition as underlying veins are patent unlike in thrombophlebitis.

Key words: 5 fluorouracil, Supra venous hyper pigmentation, Tree bark appearance, Serpigenous pigmentation

INTRODUCTION
5-flourouracil is one of the important and commonly used chemotherapeutic agents in various types of cancers particularly of gastrointestinal origin. It is commonly associated with hematological, gastrointestinal, cardiovascular, neurological side effects and mucositis. Cutaneous side effects are very rarely reported with this drug and includes facial and palmar hyper pigmentation and supravenous hyper pigmentation in about 2-5% of cases[1].

We are reporting a case of supravenous tree bark like serpentine hyperpigmentation in a patient who is receiving prolonged continuous infusion of 5-flourouracil. He is a diagnosed case of metastatic periampullary carcinoma who is receiving second line palliative FOLFOX-4 based chemotherapy in which 5-flourouracil is given over 22 hours infusion after bolus dose. Patient has been counseled about peripheral inserted central catheter and chemo port in view of prolonged infusion of chemotherapy, but he declined. After two cycles, he developed serpentine pigmentation of skin exactly over the veins of left for arm resembling tree bark. Patient was counseled again for central line but declined. Next cycle was started through cannulation on right upper limb. After two cycles, again he developed similar serpentine rash over left forearm veins. By this time over 1 month duration, the rash over left forearm disappeared spontaneously without any treatment.

DISCUSSION
The mechanism of 5-flourouracil induced supravenous hyper pigmentation with patent underlying veins is not clearly understood. Proposed hypothesis is that endothelial destabilization caused by 5-flourouracil causes it to seep into layers of dermis and its interaction with melanocytes without causing inflammation is the reason for pigmentation [2]. This is characteristically distinguished from thrombophlebitis by the presence of patent veins without any occlusion to the flow of blood or swelling at the local site. 5fluorouracil can cause thrombophlebitis in case of extravasation and is classified as irritant chemotherapy in extravasation guidelines [3]. But in this case, there is no extravasation noted. Other differences form previously reported case reports is that patient doesn’t have any pain or stinging sensation over the pigmented sites[4]. Contrary to the term PSSH (persistent serpentine supravenous

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hyperpigmentation), pigmentation in this case is temporary and resolved over one month. It is important for the clinicians to recognize this rare side effect as it does not require any dose modification or discontinuation of the treatment [5]. Change of site preferably central line will prevent this side effect. Flushing with normal saline is an important measure to decrease this side effect in case use of peripheral line is unavoidable.