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Diagnostic value of the dried blood drop test in cancer. (Bolen's test)

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Early diagnosis of cancer and pre-cancerous conditions may in many cases decide the outcome of the disease treatment. However to the present day not a single method of investigations, if isolated, can be used for early diagnosis or even diagnosis at its later stages of cancer development.

A good diagnostic method for cancer diagnosis is taken as that, which shows more than 90% of tumours and produces no more than 5% of false negative results. (I.F. Greh). In this light Bolen's investigations of dried blood drop, taken from a patient's finger, is of particular interest.

From the test author's data, in a drop of blood taken from a healthy patient, one can see a darker spot in the middle and a lighter circle peripherally (picture 1.a attached). Microscopically, the dried drop consists of a dense net of fibrin molecules enveloping erythrocytes arranged in neat coin stacks (picture 1.b attached) – the negative Bolen's test.

If the blood is taken from a patient suffering from malignant cancer, there is an absence of the dark spot in the middle of a drop. Blood is less dense, more grainy (pic. 2.a attached). There is an absence of the coin stack erythrocytic arrangement. Erythrocytes are agglutinated, localised in piles with absence of the fibrin net or its remnants. There is also vacuole field formation (pic. 2.b attached) – positive Bolen's test.

Bolen explains the difference in blood drop structure by considerable decrease in fibrin concentration and increase coagulability of erythrocytes in patients with a malignancy.

His data shows positive investigation results in 96.5% of patients with malignancies and 100% negative results in healthy individuals, benign tumours and other conditions of non-carcinogenic nature. He therefore suggested this test as a mandatory investigation in early diagnosis of cancer.

There are only singular works on this topic in the literature. The majority of authors (Giron, Norman and Slicker etc) showed high diagnostic value of the Bolen's test and produced positive results of 90.4-97% cases of patients with malignant neoplasms.

O.S.Sergel et al recommend this simple investigation for widespread use and underline its diagnostic value, especially in the peripheral form of lung cancer.

Only White et al, have produced data showing 68.4% of positive predictive value and nil diagnostic value of the test.

Even though the method has produced such strongly promising results that are statistically significantly higher than any other more accurate and proven diagnostic methods, Bolen's test has not been used widely in everyday practical applications. This has stimulated us to perform the present work with an aim to investigate the value of Bolen's test in diagnosis of malignant cancers.

The blood for the test was obtained through a finger-prick. Then a dry, clean glass slide was coated with 5-6 drops of blood and dried. Only clear drops were subjected to examination macroscopically and microscopically with magnification 40x8. A number of authors (Bolen; Giron etc) suggest there are only positive and negative result values of the test. However since there are a number of transitional states between the two, we have accepted the following scale: strongly positive, positive, weakly positive, negative and non-specific (O.S.Sergel et al).

There were 237 patients under our observation (156 men and 81 women) ages 17 to 72. Disease characteristics and the results of the testing are included in the table.

Diagnosis of lung cancer, cancer of the stomach and other organs was confirmed by clinical investigations and imaging and confirmed histologically in 55 cases. 11 patients were at stage I, 23 – at stage II, 23 at stage III and 14 at stage IV.

All patients with acute appendicitis and 4 patients with acute cholecystitis were subjected to surgical treatment. Histological examination of the removed tissue in all cases showed acute inflammation, phlegmon or gangrene.

All benign tumour were also confirmed histologically.

All healthy individuals had a negative Bolen's test. This is in agreement with results produced by other researches (Bolen, Giron, O.S.Sergel et al).

In patients with malignant conditions 87.3% had a positive Bolen's test, 4.2% had a negative result and 8.5% - non-specific.

We have investigated into blood drop changes with cancer stage. 3 patients with stage I had a weakly positive result, 3 – positive, 2 – negative and 3 – non-specific. There were no strongly positive results in this group.

There were no negative results in patient with stage II cancer. 3 patients had a weakly positive result, 17 – positive and 3 – strongly positive.

In patients with stages III and IV, 25 patients had a strongly positive result and 8 had a positive result. One patient with stage III cancer had a negative test and 3 had a non-specific result. However is it worth mentioning that the latter 3 patients, 1 on whom had oesophageal cancer, 1 – central lung cancer and 1 – breast cancer, blood drop investigations were performed after a full course of preoperative radiotherapy, that might have influenced the results in some ways.

As can bee seen, in most cases there is a direct relationship between the blood drop breakdown and the cancer stage.

We have been unable, however to establish any influence or trend on blood drop structure in relation to the tumour location. There has also been no difference in test results between central and peripheral forms of lung cancer that has been implied by O.S.Sergel et al.

The group of patients with non-cancerous diseases had a positive Bolen's test in 50.7%, negative in 28.7% and non-specific in 20.6% of cases. Results have been predominantly negative in benign formations – 13 out of 20 patients. Negative results were obtained for 4 patients with stomach and colon polyps, 4 patients with breast fibroadenoma and 5 patients with lipomas.

Bolen's test was found to be weakly positive in 2 patients with fibroadenoma of the breast on the background of fibrocystic mastopathy. Histologic investigations revealed pronounced effects of stromal inflammation.

5 patients had non-specific results. 2 of those had ?fibroid breast disease and 3 had breast fibroadenoma on the background of fibrocystic changes.

It seems that patients with benign tumours there are more non-specific and weakly positive results in patients with benign breast changes. It could also be pointed out that amongst patients with benign breast tumours non-specific and weakly positive results were obtained from patients with fibrocystic mastopathy.

Patients with inflammatory processes of various localities had positive Bolen's test in 62.6%, negative in 19.6% and non-specific in 17.8% of cases.

It is interesting to compare the degree of blood drop change with the character of end organ inflammation. Gangrenous and phlegmonous appendicitis produced 2 times more positive results than weakly positive with overall positive results 2 times higher than negative. In catarrhal forms of acute appendicitis however, the number of negative results was higher than that of positive with domination of weakly positive results.

In patients with chronic pneumonia with abscess formation and bronchiectasis, the number of positive results was 3 times higher than negative. Presence in 6 cases of a positive and in 2 – strongly positive result was associated with acute on chronic exacerbations of the phlegmonous process. Out of 4 patients in remission, 1 had a weakly positive, 2 – negative and 1 – non specific Bolen's test.

For the illustrative purposes, the following is an exempt from a patient's history:

Patient G., 38 years old. Clinical diagnosis: chronic interstitial pneumonia with bronchiectasis of left lower lobe with disease duration of 3 months. On admission – productive cough with up to 100 ml sputum in 24 hours, L-sided chest pain, fever. Blood analysis showed leucocytosis 10800 with left shift. Neutrophils with toxic granulation. On CXR – cirrhosis of the left lower lobe with saccular and cylindrical bronchiectases with peripheral inflammation. Bolen's test positive (pic. 3.a attached). Patient has had a complex of therapeutic interventions, following which blood analysis and temperature returned to normal ranges, sputum production decreased and peripheral lung inflammation disappeared. Bolen's test after intervention – negative (pic. 3.b attached).

In patients with chronic interstitial pneumonia without suppuration 3 patients had a negative and 3 – non-specific results during remission. 2 patients had positive test results during exacerbation stages.

Therefore, the results of investigations show a common association between the degree of change in the blood drop and characteristics of the inflammatory process. The highest degree of blood drop destruction was seen in tissue destruction with no influence of localisation of the inflammatory centre. Even in patients with soft tissue ulceration Bolen's test was strongly positive.

In comparison of Bolen's test in inflammatory and cancerous diseases, we have got 24.7% more positive results in the second group. The number of strongly positive and positive results in patients with inflammatory diseases was 1.9 times that of weakly positive, and in patients with malignant tumours that number rises to 9.3%. Strongly positive results were encountered 4.7 times more often in cancer patients than in patients with inflammatory diseases.

Overall, Bolen's test is non-specific in patients with cancer. Positive Bolen's test could point to a presence of an inflammatory change but without any specifics. However in combination of other investigations of patients with cancer this test could potentially be used to better the diagnosis.

Conclusion:

1. Bolen's test produces negative results in practically all healthy individuals but also negative and non-specific results in patients with benign tumours.
2. Bolen's test is more pronounced in patiens with later cancer stages and destructive inflammatory conditions.

3. Dried blood drop change is non-specific for cancer. However in combination with other investigation modalities Bolen's test could be used in patients with malignancies for the purpose of confirming the diagnosis.

Blood characteristics	Healthy	Disease																Total
		Non-cancerous diseases										Malignant conditions						
		Acute appendicitis			Cholecystitis (acute, acute on chronic)	Chronic non-specific Lung diseases				Ulcers	Benign tumours	Lung cancer		Stomach	Breast	Colon	Oesophagus	
		Catarrhal appendicitis	Phlegmonous appendicitis	Gangrenous appendicitis		Chronic pneumonia with abscess formation and bronchiectasis	Interstitial pneumonia without pyogenesis	Spontaneous pneumothorax	Bronchial asthma, pneumo-sclerosis, emphysema			Central form	Peripheral form					
strongly positive	-	-	1	-	3	2	-	-	-	-	-	11	5	6	2	4	-	34
positive	-	3	12	7	7	6	2	-	3	-	-	12	6	7	1	2	-	68
weakly positive	-	6	7	3	3	1	-	-	1	-	2	2	2	1	1	-	-	29
negative	30	7	6	-	2	2	3	4	1	1	13	1	1	-	1	-	-	72
non-specific	-	4	6	2	3	1	3	2	-	2	5	1	1	1	2	-	1	34
Total	30	20	32	12	18	12	8	6	5	3	20	27	15	15	7	6	1	237

Table: Bolen's test results for patients with different forms of disease.