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Table of Contents

Original Articles

Study of Ethylenediaminetetraacetic acid (EDTA) - Dependent
Pseudothrombocytopenia

Nikita Subhash Oza, Narayan S. Ingole, Nitin M. Gangane

01-05

Coping strategies used by Mothers' of children with Leukemia in Pune, India

Dhanya Nair

06-08

Case Reports

Rehabilitation of long standing ankylosis of temporo-mandibular joint in a 65 year old
lady: A management quandary

*Abhay Taranath Kamath, Manish Bhagania, Deepika Pai, Satpal Singh, Dr Amit,
Ambika Pradeep*

09-10

Mucoepidermoid Carcinoma Of Thyroid Gland: A Rare Case Report

Bharath C., Priyanka Chadha

11-12

Original Article

Study of Ethylenediaminetetraacetic acid (EDTA) - Dependent Pseudothrombocytopenia

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Ethylenediaminetetraacetic acid (EDTA);
CPT (trisodium citrate, pyridoxal 5'-phosphate and Tris);
Pseudothrombocytopenia (PTCP);
Platelet count

Abstract

Objectives: To evaluate and compare the cases of EDTA-PTCP with actual platelet counts at different time intervals with new anticoagulant.

Methods: This cross-sectional study was carried out in rural tertiary centre in central India. Blood samples were collected in K3-EDTA and CPT vials separately and subjected for peripheral smear examination and manual platelet counts. Comparison of platelet counts obtained by automated cell counter at 30 minutes, 3-4 hours and at 24 hours of blood collection from both anticoagulants and with manual counts was done.

Results: The platelet counts in EDTA anticoagulated blood on suspicion of thrombocytopenia, as well as even after collection of fresh blood sample from same patient in EDTA and the counts at different time intervals showed significantly lower counts than that observed in CPT anticoagulated blood at the parallel time intervals and than that in the manual platelet counts.

Conclusions: Unrecognized PTCP may result in unnecessary laboratory testing, bone marrow aspiration and unwarranted transfusions and will prevent needless evaluations of thrombocytopenia and related therapeutic decisions.

1. Introduction

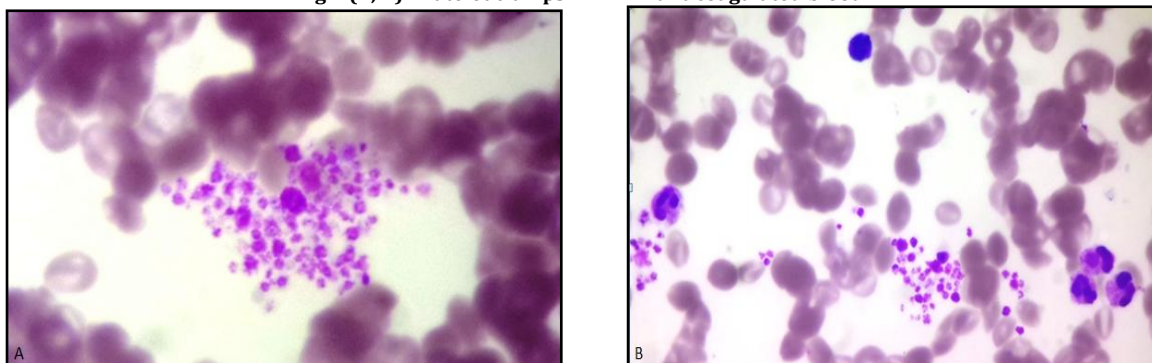
Spurious thrombocytopenia, also called Pseudo-thrombocytopenia (PTCP), results from low platelet counts due to *in vitro* platelet clumping [1-7]. Platelet clumping in PTCP results in inaccurate platelet concentration, which leads to misdiagnosis of thrombocytopenia when analyzed with hematology analyser [7-8].

Frequency of 0.3% and 1.2% respectively was reported by Mant *et al* [9] and Manthorpe *et al* [10], which referred however to a small case series. This type of alteration is now familiar to the clinical pathologist; and consequently it has been evaluated more accurately, and at present its frequency is considered to be within range of 0.09 – 0.11% [11]. Although PTCP is an infrequent condition, it accounts for a sizable fraction of all the cases of "thrombocytopenia" that are referred to for further evaluation [12].

Pseudothrombocytopenia (PTCP) is an immunologically mediated phenomenon caused by the presence of EDTA – dependent cold anti-platelet auto-antibodies in blood that cause *in vitro* platelet clumping as shown in figure 1 – A, B [5,7,13-15].

In automated electronic cell counting of blood samples anticoagulated with edetic acid, PTCP was observed due to *in vitro* platelet clumping induced by edetic acid. It is caused by activation of an abnormal protein identified as an immunoglobulin/ agglutinin [5, 7, and 16]. The mechanism of EDTA induced platelet clumping may be related to the physiological function of the platelet membrane, as EDTA modifies platelet and red blood cell membranes, in presence of reduced calcium concentration [17]. The phenomenon appears to involve a protein fraction with some relation to fibrinogen, which in some cases, is an IgM or IgG antibody against platelet antigens that is maximally reactive at low calcium concentrations [12, 16, 17].

Pseudothrombocytopenia may lead to the erroneous diagnosis of thrombocytopenia, with resultant unnecessary and costly additional laboratory testing, inappropriate treatment with delay of surgery and unwarranted exposure to transfusion-related complications; all being the potential outcomes for an individual with this form of *in vitro* artefact [15,18,19].

Fig.1 (A, B): Platelet clumps in EDTA-anticoagulated blood.

2. Methods

This Cross sectional study was carried out in the Hematology division of the Department of Pathology, over a period of 2 years from May 2011 to May 2013, in a medical institute in central India.

Subjects:

Inclusion criteria:

All the cases in which the automated counter report showed thrombocytopenia with platelet counts less than $130 \times 10^9/\text{litre}$ with peripheral blood film examination showing platelets in fair number, either diffusely distributed or in clumps or aggregates and appeared to be within normal limits; were considered as Pseudothrombocytopenia and included in the study.

Exclusion criteria:

- 1) The platelet counts between $130-150 \times 10^9/\text{litre}$ were excluded.
- 2) The cases with known cause for thrombocytopenia as obtained from history, clinical examination and medical records, were excluded.

Study methodology:

Blood samples were collected in K3-EDTA and CPT (trisodium citrate, pyridoxal 5'-phosphate and Tris) vials separately and examination of well prepared, air-dried, labeled peripheral smear stained with Leishman was done. Examination was done using light microscope under oil immersion (100x) with (10x objectives) for evaluation of platelet morphology, clumps, and counts. For EDTA-PTCP cases, the manual platelet count is considered 'gold standard' for this comparison as reported by Hyun-Sook Chi[15] and Lippi *et al*[17]. This method was performed using improved Neubauer's chamber. Convenient procedure is to count five groups of 16 small squares in the central area (0.02 μl).

$$\text{Platelet count per litre} = \frac{\text{Number of cells counted} \times \text{Dilution} \times 10^6}{\text{Volume counted } (\mu\text{l})}$$

To ensure a coefficient of variation of 8-10 %, the total number of platelet count should always exceed 200.

Using automated blood analyser, platelet counts were obtained at 30 minutes, 3-4 hours and at 24 hours of blood collection.

Thus, the platelet counts obtained by manual method; by automated counter at 30 minutes, 3-4 hours and at 24 hours of blood collection using two different anticoagulants were compared and these were also compared with the initial platelet counts on which pseudothrombocytopenia was suspected..

The data is recorded and findings were analyzed statistically using z-test and test statistics. The software used in the analysis is SPSS 17.0 version and graph pad prism 5.0. The p-value of less than 0.05 is considered as statistically significant.

3. Results

In the present study, we assessed the cases of suspected EDTA - dependent Pseudothrombocytopenia (showing thrombocytopenia on initial automated platelet counts from EDTA anticoagulated blood with adequate platelet count and presence of platelet clumps in the peripheral blood smear) for accurate platelet count with manual method and also using EDTA and CPT as anticoagulants with automated platelet counts at different time intervals.

Study included 43 males and 60 females with M: F ratio of 1:1.3. The patient's age varied from 3-85 years with the mean age of 36.78 ± 20.33 years. No significant association was found with respect age or distribution of cases. EDTA-PTCP cases were found to be associated both in health and disease state.

The present study compared the mean platelet counts in EDTA anticoagulated blood on initial suspicion of pseudothrombocytopenia and at different time intervals after collection of fresh blood sample from same patients in EDTA anticoagulant with parallel platelet counts in CPT anticoagulated blood and also with manual platelet counts.

The study observed the mean initial platelet counts in EDTA ($103.67 \pm 25.34 \times 10^9/\text{l}$) to be much lower than the mean manual platelet count ($222.63 \pm 85.22 \times 10^9/\text{l}$) and the difference was statistically significant. The mean platelet count in EDTA anticoagulated blood at 0-30 minutes and at 3-4 hours ($171.40 \pm 78.10 \times 10^9/\text{l}$) and (171.63 ± 81.16), though it was in the normal range, was also significantly lower than mean manual platelet count and the parallel automated platelet count in CPT anticoagulated blood ($226.63 \pm 93.25 \times 10^9/\text{l}$) and (230.25 ± 97.57) at 0-30 minutes and 3-4 hours respectively (Table 1).

Table 1: Showing comparison of initial platelet count suspicious of pseudothrombocytopenia with manual platelet count and platelet count in EDTA and CPT anticoagulated blood at 0-30 minutes and at 3-4 hours.

Number of cases	Mean initial platelet count ($\times 10^9/\text{l}$)	Mean manual platelet count ($\times 10^9/\text{l}$)	Mean automated platelet count ($\times 10^9/\text{l}$) at 0-30 minutes		Mean automated platelet count ($\times 10^9/\text{l}$) at 3-4 hours	
			EDTA	CPT	EDTA	CPT
103	103.67 ± 25.34	222.63 ± 85.22	171.40 ± 78.10	226.63 ± 93.25	171.63 ± 81.16	230.25 ± 97.57
Initial Platelet Count		p-value	0.000, S, $p < 0.05$	0.000, S, $p < 0.05$	0.000, S, $p < 0.05$	0.000, S, $p < 0.05$
Manual Platelet Count		p-value	0.000, S, $p < 0.05$	0.74, NS, $p > 0.05$	0.000, S, $p < 0.05$	0.55 NS, $p > 0.05$
Initial Vs Manual Platelet Count		p-value	0.000, S, $p < 0.05$		0.000, S, $p < 0.05$	

S: Significant; NS: Not significant

The present study also assessed the changes in the platelet counts in anticoagulated blood samples after preserving the blood samples at 3-4°C in a refrigerator for 24 hours, in total 74 cases. The mean platelet counts in EDTA and CPT anticoagulated blood were found

to be $183.70 \pm 100.21 \times 10^9/\text{l}$ and $266.04 \pm 103.51 \times 10^9/\text{l}$ respectively. In the same cases, the mean initial platelet count was $100.51 \pm 26.57 \times 10^9/\text{l}$ and the manual platelet count was $240.68 \pm 89.24 \times 10^9/\text{l}$, as shown in table 2.

Table 2: Showing comparison of initial platelet count suspicious of pseudothrombocytopenia with manual platelet count and platelet count in EDTA and CPT anticoagulated blood at 24 hours.

Number of cases	Mean initial platelet count ($\times 10^9/\text{l}$)	Mean manual platelet count ($\times 10^9/\text{l}$)	Mean automated platelet count ($\times 10^9/\text{l}$)	
			EDTA	CPT
74	100.51 ± 26.57	240.68 ± 89.24	183.70 ± 100.21	266.04 ± 103.51
Initial Platelet Count		z-value	6.90	13.32
		p-value	0.000, S, $p < 0.05$	0.000, S, $p < 0.05$
Manual Platelet Count		z-value	3.65	1.59
		p-value	0.000, S, $p < 0.05$	0.11 NS, $p > 0.05$
Initial Vs Manual Platelet Count		z-value	12.95	
		p-value	0.000, S, $p < 0.05$	

S: Significant; NS: Not significant

By using z-test, statistically significant difference was found between initial platelet count and platelet count in EDTA anticoagulated blood at 24 hours ($z = 6.90$; $p = 0.000$), and between initial platelet count

and platelet count in CPT anticoagulated blood at 24 hours ($z = 13.32$; $p = 0.000$).

Similarly, statistically significant difference was found between manual platelet count and platelet count in EDTA anticoagulated blood at 24 hours ($z = 3.65$; $p = 0.000$); but no significant difference was found between manual platelet count and platelet count in CPT anticoagulated blood at 24 hours ($z = 1.59$; $p = 0.11$) also.

Thus, the platelet counts in EDTA anticoagulated blood on suspicion of thrombocytopenia, as well as even after collection of fresh blood sample from same patient in EDTA and the counts at 0-30 minutes, 3-4 hours and after 24 hours showed significantly lower counts than that observed in CPT anticoagulated blood at the parallel time intervals and than that in the manual platelet counts. Thus, we found the difference of initial mean platelet count in EDTA with manual platelet count of 55% and the difference of mean platelet count in EDTA and CPT

anticoagulated blood of about 25% with counts at 0-30 minutes and at 3-4 hours, and of about 31% at 24 hours. Thus, low platelet counts were probably because of the effect of EDTA anticoagulant on platelets.

The mean automated platelet counts in CPT anticoagulated blood at 0-30 minutes and at 3-4 hours as well as at 24 hours after blood collection were found to be comparable with the mean manual platelet counts. Thus, the CPT anticoagulant was found to be a better anticoagulant for getting correct platelet counts in cases of EDTA-dependent pseudothrombocytopenia.

The present study also compared the initial platelet count in EDTA ($103.67 \pm 25.34 \times 10^9/l$) with that at 0-30 minutes ($171.40 \pm 78.10 \times 10^9/l$) and at 3-4 hours ($171.63 \pm 81.16 \times 10^9/l$) in the same anticoagulant. The statistical analysis is shown in table 3:

Table 3: Showing comparison of initial platelet count in EDTA anticoagulated blood with that at 0-30 minutes and 3-4 hours in same anticoagulant.
Descriptive Statistics:

EDTA	No. of cases	Mean platelet count $\times 10^9/l$	Standard Deviation	Standard Error Mean
Initial	103	103.67	25.34	2.49
0-30 min	103	171.40	78.10	7.69
3-4 hrs	103	171.63	81.16	7.99

Wilcoxon Signed Rank Test:

Wilcoxon signed Rank Test:								
Paired Differences					z	df	p-value	
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower				Upper
Initial & 0-30 min	67.72	80.45	7.92	52.00	83.45	8.54	102	0.000, S, p<0.05
Initial & 3-4 hrs	67.95	82.375	8.11	51.85	84.05	8.37	102	0.000, S, p<0.05
0-30 min & 3-4 hrs	0.22	28.45	2.80	5.33	5.783	0.08	102	0.937, NS, p>0.05

By using Wilcoxon signed rank test, significant difference was found between initial platelet count and that at 0-30 minutes ($z = 8.54$; $p = 0.000$); and between initial platelet count and that at 3-4 hours ($z = 8.37$; $p = 0.000$); but, no statistical change was found in platelet count from 0-30 minutes to 3-4 hours ($z = 0.08$; $p = 0.937$).

Similarly, the initial platelet count in EDTA was compared with the platelet count in CPT anticoagulated blood at 0-30 minutes and at 3-4 hours. The statistical analysis is shown in table 4:

Table 4: Showing comparison of initial platelet count in EDTA with platelet counts in CPT anticoagulated blood at 0-30 minutes and at 3-4 hours.
Descriptive Statistics:

CPT	No. of cases	Mean platelet count $\times 10^9/l$	Std. Deviation	Std. Error Mean
Initial	103	103.67	25.34	2.49
0-30 min	103	226.63	93.25	9.18
3-4 hrs	103	230.25	97.57	9.61

Wilcoxon Signed Rank Test:

Paired Differences							z	df	p-value
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference					
				Lower	Upper				
Initial & 0-30 min	122.95	96.16	9.47	104.15	141.74	12.97	102	0.000, S, p<0.05	
Initial & 3-4 hrs	126.57	100.48	9.90	106.93	146.21	12.78	102	0.000, S, p<0.05	
0-30 min & 3-4 hrs	3.62	18.82	1.85	0.05	7.299	1.95	102	0.054, N.S, p>0.05	

By using Wilcoxon signed rank test, statistically significant difference was found between initial platelet count in EDTA anticoagulated blood with platelet count in CPT anticoagulated blood at 0-30 minutes ($z = 12.97$; $p = 0.000$) and that at 3-4 hours ($z = 12.78$; $p = 0.000$); but no statistical change was found in platelet count from 0-30 minutes to 3-4 hours ($z = 1.95$; $p = 0.054$) in CPT anticoagulated blood.

4. Discussion

The present study entitled, "Ethylenediaminetetraacetic acid (EDTA) - Dependent Pseudothrombocytopenia", was carried out in the Department of Pathology in a medical institution in central India. Total of 103 cases of suspected EDTA-dependent Pseudothrombocytopenia (EDTA-PTCP) were assessed for its correctness using manual platelet count as the gold standard. The platelet counts in two different anticoagulants (EDTA and CPT) were compared at different times from the time of collection of blood sample.

Prevention of platelet aggregation in EDTA-PTCP cases using CPT anticoagulant (Citric acid tri-sodium salt dehydrate, Pyridoxal 5'-phosphate, Tris/ hydroxymethyl/ aminomethane) is opined by Lippi *et al* [17]; Lam *et al* [20]; Paparo *et al* [21] and Lippi and Faschinetti [22]. Most of the studies have tried different other anticoagulants to get correct platelet count in cases of EDTA-PTCP and have found CPT anticoagulant

as a better alternative for EDTA in cases of EDTA-PTCP [15,17,20] similar to the present findings. The present study used manual platelet count to be the gold standard for platelet count in EDTA-PTCP cases [15, 17].

The study included 103 cases, of which 9 cases were found to be incorrect. Incidence of thrombocytopenia in 1.5% cases was noted and that of EDTA-dependent Pseudothrombocytopenia in 0.07% cases of total haemograms and 4.9% of total thrombocytopenia was observed. The study was comparable with incidence of 0.03-1.9% as reported by Sakurai *et al* [23].

The study compared the mean platelet count obtained in EDTA and from CPT anticoagulated blood at different time intervals with that of manual platelet count and with initial platelet count on which suspicion of PTCP was based.

The mean initial platelet counts in EDTA ($103.67 \pm 25.34 \times 10^9/l$) were much lower than the mean manual platelet count ($226.63 \pm 85.22 \times 10^9/l$) and the difference was statistically significant. The mean platelet count in EDTA anticoagulated blood at 0-30 minutes and at 3-4 hours ($171.40 \pm 78.10 \times 10^9/l$) and ($171.63 \pm 81.16 \times 10^9/l$) respectively, though it was in the normal range, was also significantly lower than mean manual platelet count and the parallel automated platelet count in CPT anticoagulated blood ($226.63 \pm 93.25 \times 10^9/l$) and ($230.25 \pm 97.57 \times 10^9/l$) at 0-30 minutes and at 3-4 hours respectively (Table 1).

In 74 cases, the platelet counts were compared after 24 hours of preservation of blood sample. Even at this time, the mean platelet count in EDTA anticoagulated blood was significantly lower than that in CPT anticoagulated blood (Table 2). The present study observed the difference of mean initial platelet count in EDTA with manual platelet count of 55% and the difference of mean platelet count in EDTA and CPT anticoagulated blood of about 25% at 0-30 minutes and at 3-4 hours, and of 31% at 24 hours.

None of the studies reviewed have shown the comparison of the mean platelet counts in EDTA with manual platelet counts and with that in other anticoagulants, except for the study of Lippi *et al* [17] where they compared the automated platelet counts in EDTA and CPT anticoagulated blood in 4 different make cell counters with the mean manual platelet counts. The mean automated platelet counts in STKS coulter counter in EDTA and CPT anticoagulated blood were found to be $101.75 \pm 49.22 \times 10^9/l$ and $256.25 \pm 80.08 \times 10^9/l$ respectively, whereas, the mean manual platelet count was $255.31 \pm 82.82 \times 10^9/l$. These findings well correlate with that of the present study.

Different workers explained this phenomenon in different ways. The basic fact is there is *in vitro* binding of antibodies in the blood with some antigenic determinant on the platelet membrane in presence of EDTA which results in formation of platelet aggregates. The size of these platelet aggregates are beyond the upper limit of discrimination of platelet width of the automated cell counters and hence they are counted in the WBC channel and omitted from the platelet channel resulting in low platelet counts shown by automated blood cell counters.

The target antigen on platelet is a cryptic epitope that is normally hidden in platelet membrane glycoprotein; the glycoprotein being GP IIb/IIIa [24]. Although EDTA-PTCP have been reported in variety of diseases (autoimmune, neoplastic, liver, cardiovascular, viral etc.), a documented trigger for the production of antiplatelet antibodies is unknown [25]. Lelie *et al* [26] showed that the binding of antiplatelet antibodies detected in patients with septicemia and normal platelets is completely or partially EDTA-dependent. They suggested, the damaged platelets in patients with septicemia could expose cryptic antigens and induce the synthesis of antiplatelet antibodies.

The antibodies are autoantibodies of all the major classes. But, IgG antibodies are much more frequently involved than IgM antibodies, and IgA antibodies are rarely involved [14, 27]. These autoantibodies are naturally occurring antibodies with antiplatelet activity, devoid of pathologic significance and are capable of recognizing cryptic antigens expressed by aged or damaged platelets to remove these from circulation [25].

Role of EDTA: The chelating effect of EDTA is in some way responsible for agglutination of platelets. The GP IIb/IIIa glycoprotein complex in platelet membrane requires the presence of calcium ions to maintain its heterodimeric structure. EDTA because of its chelating effect can dissociate GP II b/IIIa complex, resulting in exposure of the target epitopes on GP IIb [15, 28]. This alteration in confirmation of GP IIb/IIIa is also associated with temperature [28].

However, EDTA is the most commonly used anticoagulant which prevents aggregation of cells and therefore used for blood cell counts. It does not cause platelet clumping in all the cases, but only in cases of EDTA-PTCP. This is probably related to the concentration of EDTA and represents the characteristic inhibitory effect of EDTA on platelet stickiness at higher concentrations of EDTA [1].

The pseudothrombocytopenia can also be because of technique related variables. Platelet clumping may be the result of poor mixing – too little and/or too late mixing, and/or a small, whole blood clot or small fibrin clots in an EDTA anticoagulated specimen. The improper collection of blood sample may cause thrombin release and a falsely low platelet count due to aggregation [29].

In the present study, the mean automated platelet counts in CPT anticoagulated blood at 0-30 minutes and at 3-4 hours as well as at 24 hours after blood collection were found to be comparable with the mean manual platelet counts (Table: 1, 2). Thus, the CPT anticoagulant was found to be a better anticoagulant for getting correct platelet counts in cases of EDTA- dependent pseudothrombocytopenia. These findings are consistent with that reported by Lippi *et al* [17].

Tri-sodium citrate do not alter cell counting and sizing after sampling in CPT mixture. Pyridoxal 5'- phosphate prevents platelet aggregation as it exhibits remarkable anti-aggregant and dis-aggregant effect *in vitro*. The pH is brought to neutrality by adding Tris to the CPT mixture.

Thus, inhibition of both platelet reaction and aggregation is prevented in CPT anticoagulant [17, 20]. Therefore, in routine hematological practice, CPT can be an alternative anticoagulant to K3.EDTA, most suitable for automated complete blood count and useful in avoiding EDTA-induced platelet clumping.

PTCP is time – dependent phenomenon, gradually developing in 0-2 hours of venepuncture [30-31]. Platelet agglutination is detectable within minutes and maximum after 60-90 min. The magnitude of agglutination and the rate at which the clumping proceeded were strongly affected by the platelet concentration in the mixture. In most, the agglutination persisted without disaggregation for more than 24 hours [30]. The size of the aggregates approximates to that of the lymphocytes; often giving rise to suspect flag “platelet clumping” and /or flagging of the platelet parameters [31].

In the present study, comparison of platelet count in EDTA anticoagulated blood at different time intervals showed significant difference between initial platelet count and that at 0-30 minutes and between initial platelet count and that at 3-4 hours. But, no statistical change was found in platelet count from 0-30 minutes to 3-4 hours in EDTA anticoagulated blood (Table 3).

Similarly, the comparison of initial platelet count in EDTA with platelet counts in CPT anticoagulated blood at different time intervals showed significant difference between initial platelet count in EDTA anticoagulated blood with platelet count in CPT anticoagulated blood at 0-30 minutes and that at 3-4 hours. But no statistical change was found in platelet count from 0-30 minutes to 3-4 hours in CPT anticoagulated blood (Table 4).

The lower mean platelet count in initial EDTA blood sample on which EDTA-PTCP was suspected is probably because these samples were different and collected by the clinical residents and at different time. The samples which we personally collected and used for cell counts at 0-30 minutes and 3-4 hours, did not show significant difference of cell counts with lapse of time over upto 24 hours. However, the counts in EDTA anticoagulated blood were still significantly lower than that in manual counts and with CPT anticoagulated blood.

Most of the studies have tried different other anticoagulants to get correct platelet count in cases of EDTA-PTCP and have found CPT anticoagulant as a better alternative for EDTA in cases of EDTA-PTCP [15, 17, 20] similar to the present findings.

Pseudothrombocytopenia can complicate an accurate determination of platelet count even with an underlying thrombocytopenic disorder. Therefore, the presence of apparently obvious cause of thrombocytopenia should not be considered to rule out the diagnosis of EDTA-PTCP, which is confirmed by identifying the platelet clumping in EDTA anti-coagulated blood [6]. It is thus important to be able to distinguish between reduced platelet counts due to technique related variables or due to patient's related medical condition [29].

5: Conclusions

Examination of well drawn peripheral blood smear for every case of thrombocytopenia is mandatory to rule out platelet clumping (PTCP). The new CPT mixture is an effective anticoagulant suitable for routine haematology and can be used as better alternative to EDTA in EDTA-PTCP cases. To get correct platelet count in these cases, the manual platelet count is the 'gold standard'. Unrecognized PTCP may result in unnecessary laboratory testing, bone marrow aspirations and unwarranted transfusions and will prevent needless evaluations of thrombocytopenia and related therapeutic decisions.

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Original Article

Coping strategies used by Mothers' of children with Leukemia in Pune, India

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Coping strategies,
 Mothers,
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 Children,
 Leukemia

Abstract

Background: The assessment of coping strategies used by the mothers of children with leukemia will provide a further basis of helping mothers' adaptation. This study was undertaken to assess the coping strategies used by mothers of children with leukemia in Bharati Hospital Pune, India.

Methods: This was an exploratory study of 60 mothers whose children diagnosed with leukemia within one year and taking treatment from Bharati Hospital, Pune, India. Data collection was conducted based upon coping strategy Scale including Problem solving (Acceptance, seeking support, and positive action) and emotional (avoidance, emotive and distancing) coping strategies. Correlation with selected demographic variables is also done. A total of 60 mothers whose children diagnosed with leukemia within one year of life participated in study.

Results: Results of this study showed 71.7 % of the mothers of children with leukemia are having poor coping strategies. The mothers have used both problem solving and emotional coping strategy equally as follows, seeking support (5.33 ± 0.75), then emotive coping strategy (4.8 ± 1.30), Acceptance (2.9 ± 0.51), Avoidance (2.5 ± 0.64) Distancing (1.9 ± 0.87) then positive action (1.6 ± 1.2). Duration of illness are the demographic variables which were found to have significant association with Coping strategies. It can be interpreted from the findings that the coping strategies are poor with in four months after diagnosis is made as p value is less than 0.05.

Conclusion: Familiarity with coping strategies and the method to use them could balance the emotional, psychological and social consequences of parents who have a child with leukemia. In this research mothers used a low level of coping strategies. Mothers of children with leukemia should be encouraged more to learn and use about various coping strategies. Necessary facilities should also be provided for implementation of these strategies.

1. Introduction

Children are the most precious blessings given to family. There is nothing in this world that can be more important than own baby. The lives of the parents completely adjust upon the arrival of their child. All parents have hopes, dreams and expectations for their children. When disease strikes these expectations are shattered the moment the doctor utters the diagnosis. Some parents describe it as a physical blow, like being slapped. As the numbness wears off, parents are forced to begin to cope to accept the diagnosis, mobilize their emotions and get on with their lives. But their lives are forever changed[1]. Taking care of a child with leukemia is one of the most draining and difficult task a parent can face.

A child's chronic illness affects the lives of all family members emotionally and physically. Roles and routine change and the demands of care giving must be negotiated. Financial recourses may be strained[2] Leukemia is the most common malignancies in children with a prevalence of 129 in one million and the second cause of death among children aged 5-14 years[3,4,5]. Parents who have a child suffering from cancer face distress in regard to multiple hospitalizations, chemotherapy side effects (hair loss, nausea, vomiting and infections). They try to provide support for their child as he or she undergoes a variety of tests and procedures[5]. Parents who have a child afflicted with cancer, would face distress and emotional problems, if they do not receive enough social and spiritual supports[6].

Childhood leukemia has remained a focal point of extensive etiologic, diagnostic and therapeutic research since its recognition as a clinical entity over a century ago[7]. It is one of the most common cancers in children, comprising more than a third of all childhood cancers. The quality of life of children with leukemia is reduced by fear and anxiety of parents after diagnosis, lack of information about the disease, treatment and care of the child[8].

Coping is a vital concept in nursing and its strategies can influence the nature of adaptation of a family. A nurse can support the

family by respecting them and serve as a support by making referrals, providing information about the illness or its management, allowing emotional expression by all family members, and by responding to the emotions when expressed. It is crucial for the nurse to take a long-term view of problems and not to expect all of them to be solved quickly [9]. Kazak and Barakat (1997) reported that children and families, who were well adapted to diagnosis and treatment, would cope better with the stressors [8,10].

Coping is part of transaction between the person and the environment where that transaction is appraised as stressful [11]. Coping means adjusting to or solving internal or external challenges. Coping is a person's attempt to control, manage or live with a stressful situation [12].

Coping strategies can be either problem focused or emotion focused. Problem focused coping involves an effort to solve the problem or meet the demand directly. Emotion focused coping occurs when nothing can be done and the people turns to cognitive process such as distancing, wishful thinking or self blame[12].

Patterson & McCubbin (2002) noted that mothers experiencing stressful events such as a child's chronic illness tended to use more coping behaviors than parents experiencing less stressful events [13]. Furthermore, Katz (2004) noted the severity of the child's illness appears to have a differential impact on coping, with parents of children who have life threatening conditions evidencing a larger repertoire of coping behaviors than parents whose children had not life threatening conditions [14].

The focus on the mother in the present study was due to the fact that they were generally easy to contact, and as the primary care giver they tended to be the ones who attended hospital appointments with their child. It has been acknowledged; today that men and women do differ in their grief reactions. For these reason there is an increasing urgency to investigate the needs, perception and coping style of mothers[15].

2. Materials and Methods

From February 2013 to August 2013, 60 mothers who had children suffering from leukemia taking treatment from Bharati Hospital, Pune, participated in present study. The study population was determined using available simple random sampling method. The inclusion criteria were duration of diagnosis for 1year, absence of any other diseases except leukemia.

Data were recorded in a questionnaire divided in to two parts. The first part covered demographic information including age of the child, Number of children, Duration of illness, gender and occupation of the mother. The second part consisted of the coping strategy scale, this had 24 items, of which 12 were problem solving coping strategy and 12 were emotion coping strategy. The subscale in the scale was for problem solving coping strategy ,acceptance,(1, 3,17,21) seeking support (2,4,13,12) positive action(8,10,18,19) For emotional coping avoidance (7,15,16,22), emotive (6,9,14,23) and distancing (5,11,20,24) . The scoring of this tool was based on the 3 point likert scale- 0 being never used the strategy, 1 meant some time used the strategy and 2 indicated that mothers often used the strategy. The scale was translated to the local language for better understanding by the mothers.

Data were statistically analyzed using Fishers Exact statistical tests to evaluate the coping strategies in relation to demographic information. A P value of less than 0.05 was considered significant.

3. Result

3.1 Section I: The frequency and percentage of demographic variables in experimental and control group are presented in table 1

Table 1: Description of samples (Mothers of children having leukemia) according to Demographic characteristics by frequency and percentage (N=60)

Demographic variable	Freq	%
Number of children		
One	13	21.7%
Two	30	50.0%
Three	14	23.3%
More than three	3	5.0%
Duration of illness		
0-4 months	24	40%
4-8 months	20	33.3%
8-12 months	16	26.7%
Age of the child		
0-3 years	18	30.0%
4-8 years	35	58.3%
8-12years	5	8.3%
12-15 years	2	3.3%
Gender		
Male	34	56.7%
Female	26	43.3%
Occupation of mother		
Non-working mother (House wife)	45	75.0%
Laborer	7	11.7%
Service	8	13.3%

The demographic information of mothers presented in Table 1 shows that most mothers are having two children (50%) and most of the children' (40%) duration after diagnosis is less than 4 months. The data revealed that 58.3% of the mothers have the children between 4-8 years of age and 56.7% are having male children. 75% of the mothers were house wife.

3.2 Section II

Table 02: Coping strategies of mothers of children with leukemia (N=60)

Coping	Freq	%
Poor (Score 0-16)	43	71.7%
Average (Score 17-32)	16	26.7%
Good (Score 33-48)	1	1.7%

The data from the table 2 indicates that 71.7 % of the mothers of children with leukemia are having poor coping strategies.

3.3 Coping strategies in subscale

Table 3: Mean of coping strategies ($\bar{X} \pm SD$)(N=60)

Coping strategies	$\bar{X} \pm SD$
Acceptance	2.9±0.51
Seeking support	5.33±0.75
Positive action	1.6±1.2
Avoidance	2.5±0.64
Emotive	4.8±1.30
Distancing	1.9±0.87

The results, as demonstrated in Table 3, showed that mothers have used the coping strategy, seeking support (5.33±0.75), then emotive coping strategy (4.8±1.30), Acceptance (2.9±0.51), Avoidance (2.5±0.64) Distancing (1.9±0.87) then positive action (1.6±1.2).

The association between coping strategies and demographic variables assessment was done using analysis of variance. The summary of the results of ANOVA are tabulated below:

Table 4. The association between coping strategies and demographic variables assessment

Demographic variable	F	p-value
No of children	0.3	0.846
Duration of illness	4.04	0.020
Age of the child	0.2	0.928
Gender	0.4	0.536
Occupation of mother	0.2	0.826

p-values corresponding to demographic variables, duration of illness was small. The null hypothesis is rejected. Duration of illness are the demographic variables which were found to have significant association with Coping strategies.It can be interpreted from the above findings that the coping strategies are poor with in four months after diagnosis is made as pvalue is less than 0.05.

4. Discussion

Results of this study showed 71.7 % of the mothers of children with leukemia are having poor coping strategies. The mothers have used both problem solving and emotional coping strategy equally as follows, seeking support (5.33±0.75), then emotive coping strategy (4.8±1.30), Acceptance (2.9±0.51), Avoidance (2.5±0.64) Distancing (1.9±0.87) then positive action (1.6±1.2). Duration of illness are the demographic variables which were found to have significant association with Coping strategies.It can be interpreted from the findings that the coping strategies are poor with in four months after diagnosis is made as p value is less than 0.05.

Barbarin (1985) showed that coping strategies are improved by seeking more information, concurrent with problem solving followed by efforts to restore emotional balance and religious beliefs [16]. In another study it was demonstrate that parents used both emotion and problem focused strategies for coping with their primary stressors [17]. Results of this study are showed that there was significant difference between coping strategies and duration of diagnosis of the cancer. Coping behavior is considered successful, if when reappraised, the stressor or threat is absent or more manageable. Common indications of effective coping are perceived helpfulness, reduction of anxiety and emotional distress, and reduction or elimination of the problem.

5. Conclusion

The findings have important implications for parents, researchers and health care professionals. The adequate use of all strategies would help mothers cope with their children's disease condition more efficiently. Mothers of children with leukemia should be encouraged more to learn and use about various coping strategies. Necessary facilities should also be provided for implementation of these strategies

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Case Report

Challenges in Rehabilitation of long standing ankylosis of temporo mandibular joint: A case report of a 65 years old lady

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Keywords:

Temporomandibular joint,
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Rehabilitation,
Mouthopening,
Surgical management.

Abstract

Temporomandibular joint ankylosis commonly occurs as a result of trauma to the face resulting in fusion of the temporal bone to condyle of the mandible. Immediate and appropriate care of facial fractures can minimise the risk of development of ankylosis. We report a case of TMJ ankylosis in a 65 year old lady with complaint of inability to open the mouth since 44 years. The lack of appropriate treatment at the time of trauma led to TMJ ankylosis and its sequele for 44 years. The ankylosis was surgically managed followed by aggressive physiotherapy. Surgeries in geriatric patient need to outweigh benefit over risk. The article describes challenges posed in rehabilitation of this patient.

1. Introduction

Temporomandibular (TMJ) ankylosis is an intracapsular union of the disc-condyle complex to the temporal articular surface that restricts mandibular movements, including the fibrous adhesions or bony fusion between condyle, disc, glenoid fossa, and eminence [1]. The most common causes for TMJ ankylosis are falls, road traffic accidents and sport injuries, including play accidents. TMJ ankylosis can also be caused by local or systemic infection such as otitis media and mastoiditis, tuberculosis, scarlet fever and gonorrhea, (10-49%), Paget's disease, pseudohypoparathyroidism and psoriasis, sickle cell anemia, fibrodysplasia ossificans progressiva. MJ ankylosis is commonly acquired developmental disorder of face in children. With most patients (70.0%) being in the 10-15 years' age group (mean age was 11.1 years $\pm$ 3.34) [2,3]. Here we report a case of 65 year old lady who sustained trauma at the age of 21 years of age, the outcome of such injury and challenges faced in rehabilitation of this patient.

2. Case report

We report a case of a 65 year old woman who presented with a history of at the age 21 years following which the mouth opening gradually reduced and became 0 within months. Patient didn't seek any treatment at that time because of her financial status and now she was bought to us by her son for providing treatment. Since then she has been unable to open her mouth for 44 years. She had difficulty in speech and was on restricted diet for long years. On examination there was no facial asymmetry or growth deficiency. Old scar was present on chin region. There was nil mouth opening and no condylar movements were palpable. (Figure 1).

Figure 1. Mouth opening and condylar movements

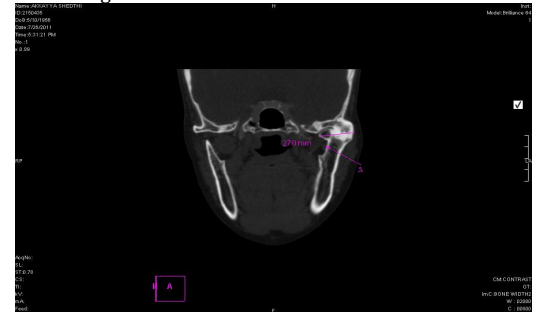


There was a bony hard mass palpable in left TMJ region. Intraorally upper and lower anterior teeth were missing with poor oral hygiene. The Missing upper anteriors were helpful in taking liquid and semisolid food. OPG, PA mandible and contrast enhanced CT scan with 3-D reconstruction was done which revealed pure bony ankylosis of left TMJ, fibrous ankylosis with deformed right condyle due to disuse, bilateral elongated coronoid processes (Figure 2&3).

Figure 2. CT scan with 3-D reconstruction



Figure 3. CT scan with 3-D reconstruction



Her systemic evaluation revealed she was fit for surgical intervention under general anaesthesia. She was taken up for bilateral gap arthroplasty with temporalis muscle interpositioning. Securing the airway was the biggest challenge in this case as there was no possibility of direct laryngoscopy because of nil mouth opening, therefore awake

fiberoptic nasotracheal intubation was carried out for securing the airway. The left TMJ ankylosis was approached first through Alkayat-Bramley approach. A preauricular incision with question mark shaped temporal extension was given and skin, subcutaneous tissue and temporoparietal fascia were incised sharply to reach the glistening white superficial layer of deep temporal fascia. Blunt dissection was done on this fascia to expose the TMJ and later temporalis muscle for interpositioning. An imaginary line drawn from upper point of tragus to a point 2cm above the fronto-zygomatic suture was the limit of anterior direction because anterior to this line the frontal and temporal branch of facial nerves crosses the Zygomatic arch in the same plane. An incision at 45 degree to the zygomatic arch and 2 cm above it was given on superficial layer of deep temporal fascia and dissection was carried inferiorly deep to this layer to reach the Zygomatic arch.

Periosteal incision was given on superior border of arch and entire width of arch along with ankylotic mass was exposed. Superior osteotomy was kept at the level of inferior border of arch and inferior osteotomy was marked at 1.5 cm below the superior cut. The entire ankylotic mass in its entire later-medial width and with elongated coronoid attached anteriorly was removed in toto. At this stage only 5 mm of mouth opening was achieved. The right side also was exposed in the same manner as left (Following Kaban, Parrot and Fissure protocol). The right condyle was found to be deformed, osteoporotic with fibrous adhesion obliterating the joint space. Right coronoid was also elongated with atrophic temporalis muscle. Right side condylectomy and coronoidectomy was performed and this time a mouth opening of 33 mm was achieved.

After achieving satisfactory mouth opening the native disc was secured with sutures in right joint space to act as interpositional material. On left side 5cm long and 2 cm wide temporalis muscle flap was elevated from posterior fibers interposed in the joint space and secured by suturing it to the remnants of lateral pterygoid on the medial aspect of remaining ramus. Vacuum drains were secured in bilateral surgical sites and layered closure of incision was done. Patient sustained the procedure well, an immediate postoperative mouth opening of 34 mm was achieved (Figure 4) and was kept hospitalized for 10 days to provide postoperative care, antibiotics, analgesics and nutrition. Daily physiotherapy in form of aggressive mouth opening exercise with use of acrylic mouth opening devices (Figure 5), guiding elastic therapy for mandibular closure and ultrasound therapy for muscle relaxation and pain relief were all started from third postoperative day.

Figure 4. Postoperative mouth opening



Figure 5. Acrylic mouth opening devices



3. Discussion

As a result of inability in opening the mouth the patient had poor oral hygiene and had not enjoyed a meal for a long time of 44years. This patient remained unoperated for many years, this could have been possible a result of a poor appreciation of the role of surgery in the management of TMJ ankylosis by the dentist who managed the initial trauma at 21 years of her age or lack of proper referral to centres delivering such surgical care. However this case demonstrates the evidence of fate of untreated cases of facial injuries resulting in Temporomandibular joint ankylosis. TMJ ankylosis results in trismus or inability to open the mouth. This can not only cause difficulty in intake of food and thus affects general well being but also cause difficulty in speech and maintenance of oral hygiene. This affects the personality of the individual and reflects greatly on one's social life. [4,5]

In today world the infectious reason for TMJ ankylosis has become nearly obsolete but one cannot rule out the probability of sustaining trauma to face. Particularly any trauma to the chin translates the impact to the condyles. [6,7] It is hypothesized that the formation of an intra-articular hematoma with subsequent scarring and new bone formation is the common precipitant. This new bone formed causes hypomobility and is termed as fibrous ankylosis if left untreated over time a fibrous ankylosis transforms into bony ankylosis resulting in total closure of mouth [8].

In this case the Kaban's protocol was followed in managing the bilateral TMJ ankylosis. The temporalis myofascial flap was interposed to prevent reankylosis. [9] Active physiotherapy and guarded watchful follow-up in initial stages is minimal invasive modality of management as long as any evidence of bony union is not seen. But immediate surgery can halt progression of a fibrous ankylosis to total joint ankylosis and its sequelae.

4. Conclusion

In Geriatric patient the systemic conditions like hypertension, diabetes and arthritis especially in women are commonly known factors that contraindicate a surgical option. While surgery is often considered as the last option in cases of TMJ ankylosis, surgery is the definitive treatment option. However risk should outweigh the benefits of surgical intervention. Surgical management in TMJ ankylosis results in adequate mouth opening but active and vigorous physiotherapy in both immediate and later post operative days can only prevent reankylosis.

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Case Report

Mucoepidermoid carcinoma of thyroid gland: A rare case report

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Keywords:

Mucoepidermoid Carcinoma,
Thyroid,
Rare tumor,
Primary

Abstract

Introduction: Mucoepidermoid carcinoma is a common neoplasm of the salivary gland but can also occur in other sites like oesophagus, breast, lungs, pancreas, etc. In thyroid gland it is very uncommon or rare and is said to be of low grade indolent neoplasm. In literature few cases have been reported.

Case report: 43 year old female presented with progressive midline swelling since 20 years with alteration in voice since two months. CT revealed heterogeneous enhancing lesion of 35x50x37 mm in left lobe of thyroid. FNAC revealed epithelial malignancy. Total thyroidectomy was done and specimen sent for histopathology.

Result: Microscopically the tumor showed cells arranged in follicular and trabecular pattern. These tumors cells were of columnar and mucin producing type arranged in glandular pattern. Some of the cells show squamous metaplastic changes. These glands or follicles lack colloid. Final diagnosis of mucoepidermoid carcinoma of thyroid was given.

Conclusion: Mucoepidermoid carcinoma of thyroid is low grade neoplasm which extends into adjacent tissue by local infiltration and unlikely to metastasize, hence prognosis is good. It can also have aggressive behaviour and hence a thorough search to be done histologically and also rule out other metastatic lesions.

1. Introduction

Mucoepidermoid carcinoma most commonly arises in the salivary gland but can also occur in other sites like esophagus, breast, lungs, pancreas, etc [1]. In thyroid gland it is very uncommon and is said to be low grade indolent neoplasm [4,5]. Here we present a case of unusual malignancy with review of available literature.

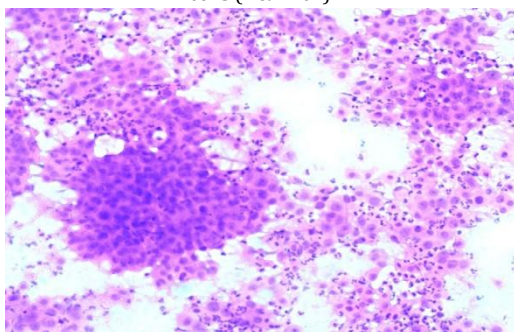
2. Case report

A 43 year old female presented with progressive midline swelling since 20 years with alteration in voice since two months. CT revealed heterogeneous enhancing lesion of 35x50x37 mm in left lobe of thyroid. FNAC was advised and revealed epithelial malignancy. Further the patient was posted for surgery and thyroidectomy with left radical neck dissection was done and sent for histopathology.

3. Result

FNAC revealed epithelial malignancy with pleomorphic epithelial cells with moderate cytoplasm, irregular ovoid nucleus, granular chromatin and distinct nucleoli which were arranged in dyscohesive clusters, syncytial aggregates, acinar pattern and scattered singly (Fig 1).

Figure1: FNAC of thyroid gland showing cluster of pleomorphic epithelial cells (H&E 10x)



Grossly, the thyroid lobe was enlarged with a nodular surface. Cut section showed greyish white solid appearance with multifocal central softened mucoid area (Fig 2). Five lymph nodes were retrieved from the fibrofatty tissue. Microscopically the tumor showed cells arranged in follicular and trabecular pattern. These tumors cells were of columnar and mucin producing type arranged in glandular type. Many of the cells show squamous differentiation (Fig 3). The mucin produced stained positive for PAS and Alcian Blue (Fig 4 and Fig 5). The lymph nodes showed hyperplasia only. Histologically diagnosed as Mucoepidermoid carcinoma of thyroid.

Figure 2: Thyroid lobe appears greyish white, solid with multifocal softened mucoid areas



Figure 3: Thyroid follicles with adjacent squamoid differentiation (H&E 10x)

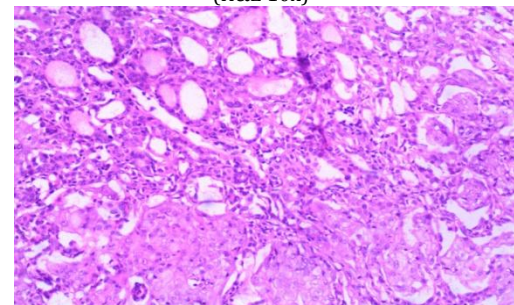


Figure 4: Shows tall clear cells with mucin in the centre and surrounding areas (PAS 10x)

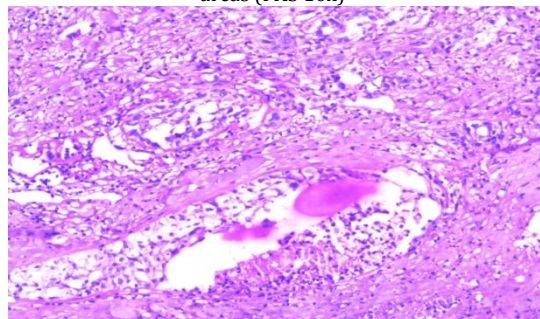
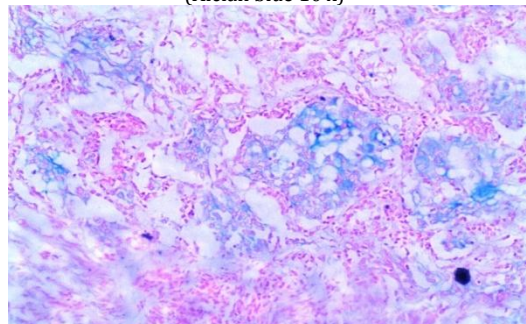


Figure 5: Positive blue staining of the mucinous material (Alcian blue 10 x)



4. Discussion

Primary mucoepidermoid carcinomas of thyroid gland are uncommon tumors and about 40 cases have been described since first report in 1977 by Rhatigan *et al*[1,6]. They originate from thyroid follicular epithelial cells and solid cell nests of the ultimobranchial body[1]. It is seen commonly in females (M:F::1:2) and can occur in any age group with the mean age of 37.9 years. The patients present with a thyroid mass. Lymph node metastasis is common (60%), but distant metastasis is rare (13%).

Histologically it is characterized by the presence of both squamous cells and mucin producing cuboidal cells². These tumors contain three cell types, i.e., mucin-secreting, epidermoid, and intermediate or basal cells[7].

Healy *et al* and Foote and Frazell developed this concept further and separated mucoepidermoid tumors into three grades of malignancy: low grade, high grade, and intermediate. Generally, the low grade carcinomas tend to have many cystic spaces lined by a single layer of mucous secreting epithelium. Epidermoid and intermediate cells are sparse and pleomorphism and mitoses are nearly absent. The intermediate types of tumors form solid nests of cells, are more cellular than low grade tumors, and have a greater preponderance of epidermoid and intermediate cell types with fewer cystic spaces. The cells have slight to moderate pleomorphism and occasional mitoses. High grade tumors tend to have only occasional mucous cells and the epidermoid and intermediate cells have considerable anaplasia and rather numerous mitoses[7].

Wenig *et al* reported six cases of thyroid mucoepidermoid carcinoma, four occurred in women and two in men with an age range of 29 to 57 (median, 46 years)[5]. Ryohei *et al* also described a case of primary mucoepidermoid carcinoma arising in the thyroid².

5. Conclusion

Mucoepidermoid carcinoma of thyroid is a low grade neoplasm which extends into adjacent tissue by local infiltration and unlikely to metastasize, hence prognosis is good [2]. A thorough clinical examination including detailed pathological and radiological information will help us in reaching a final conclusion⁶. Despite its low-grade appearance the morbidity and mortality associated with its ability to recur locally and metastasize justify the need for more aggressive surgical therapy [3].

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